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The Value of Lateral Spread Response Monitoring in Predicting the Clinical Outcome after Microvascular Decompression in Hemifacial Spasm: A Prospective Study on 100 patients.

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1. Introduction:

Hemifacial spasm (HFS) could be defined as a benign, chronic, involuntary movement of the facial muscles that typically begins in the orbicularis oculi and spreads to the other facial muscles over several years.[9, 19, 22, 24] It is an infrequent disorder with approximately 2:1 female to male ratio. The average annual incidence rate is 0.74 per 100 000 in men and 0.81 per 100 000 in women.[2] It is more common in the Asian population than in other populations.[7, 41, 48]

Usually, hemifacial spasm is caused by vascular compression of the facial nerve (VII) at the root exit zone (REZ). The best treatment option is Microvascular Decompression (MVD) representing an effective treatment for HFS.[3, 5] However, hemifacial spasm could occur secondary to rare causes, which include tumors, aneurysms, arteriovenous malformations, and dolichoectatic vertebrobasilar arteries in 0.4% to 2.2% of cases.[3, 21, 23, 33, 38, 42, 46]

Among all the abnormal findings that could be recorded in the electrophysiological investigations for patients with HFS such as F waves of the facial muscles,[11–13] blink reflexes,[6, 13, 24] Lateral Spread Response (LSR)[9, 11, 14, 29–31, 45, 49] remains a useful intraoperative tool to ensure the adequate decompression of the facial nerve. The question of whether intraoperative LSR monitoring was a reliable predictor of outcome was discussed with the conclusion that the prognostic value of LSR monitoring was indeed questionable, and the value of the LSR for predicting the long-term outcome of MVD remains to be investigated.

We tried in our study to correlate the intraoperative LSRs changes with the long term clinical outcome after surgery in order to assess the efficacy of the LSR monitoring in predicting the outcome of microvascular decompression in hemifacial spasm.

2. Patients and Methods:

2.1 Study design:

The local ethics committee approved this prospective study. The study was performed to determine the value of LSR intraoperative monitoring as an indicator of adequate decompression of the facial nerve root exit zone (VII REZ) and as a predictor of clinical outcome regarding improvement of the hemifacial spasm. The study was designed prospectively to include 100 patients who underwent endoscope-assisted microvascular decompression (EA-MVD) by the senior author (HWSS) between 2013 till April 2015 at our institution. All patients were examined clinically by the senior author to confirm diagnosis, and then scanned through 3-T Magnetic Resonance Imaging (MRI) scanners to obtain 3-D high-resolution T2-weighted gradient echo sequence imaging in the Steady State Free Precession (SSFP) technique which included constructive interference in steady state (CISS) and fast imaging employing steady state acquisition (FIESTA), and 3-D Time of Flight Magnetic Resonance Angiography (TOF-MRA). Images were acquired in axial plane covering the cerebellopontine angle with slice thickness no larger than 1 mm to diagnose the compression of VII REZ and predict the offending vessel. All patients were assessed after operation then on first day and on fifth day after operation before discharge, and then at 3, 6 and 12 months' interval after surgery. The follow-up period ranged from 6 to 32 months. The patients were asked to describe the degree of improvement according to their personal opinion and self-assessment on a scale of 0-100% where 100% represents no residual spasm and 0 represents no improvement of hemifacial spasm symptoms. A telephone call or an E-mail contact was established whenever the patient did not appear during the follow-up period with the same grading scale applied to assess the outcome. The patients were classified into 4 patterns of postoperative clinical course. Group A showed immediate improvement after surgery with a degree of improvement of 90-100% according to the previously mentioned scaling system used representing the best outcome. Group B showed gradual steady improvement of symptoms after surgery to reach a state of 50-90% of improvement during the first 3 months after surgery, when these patients showed improvement up to 90-100% of the symptoms during the one year follow-up, we still counted them in group B as they required more time to achieve full improvement compared to group A. Group C showed a relapse or recurrence of symptoms after a hemifacial spasm-free period. Group D showed minimal or no change in symptoms with a degree of improvement of 0-50% of the hemifacial spasm symptoms representing the worst outcome. Figure 1 shows a graph representing the average of patients of each group in terms of postoperative course of improvement. The difference between group C and D is whether the patient had a period after surgery free of hemifacial spasm and then the symptoms recurred (group C) or he/she reported no or slight improvement starting immediately after surgery

(group D). Also we classified the events of LSR intraoperative monitoring into 4 groups where group I showed complete relief of LSR after MVD, group II showed partial relief of LSR, group III showed no relief of LSR and group IV where no LSR could be detected from the start of operation. Examples of LSRs events are shown in Figure 2.

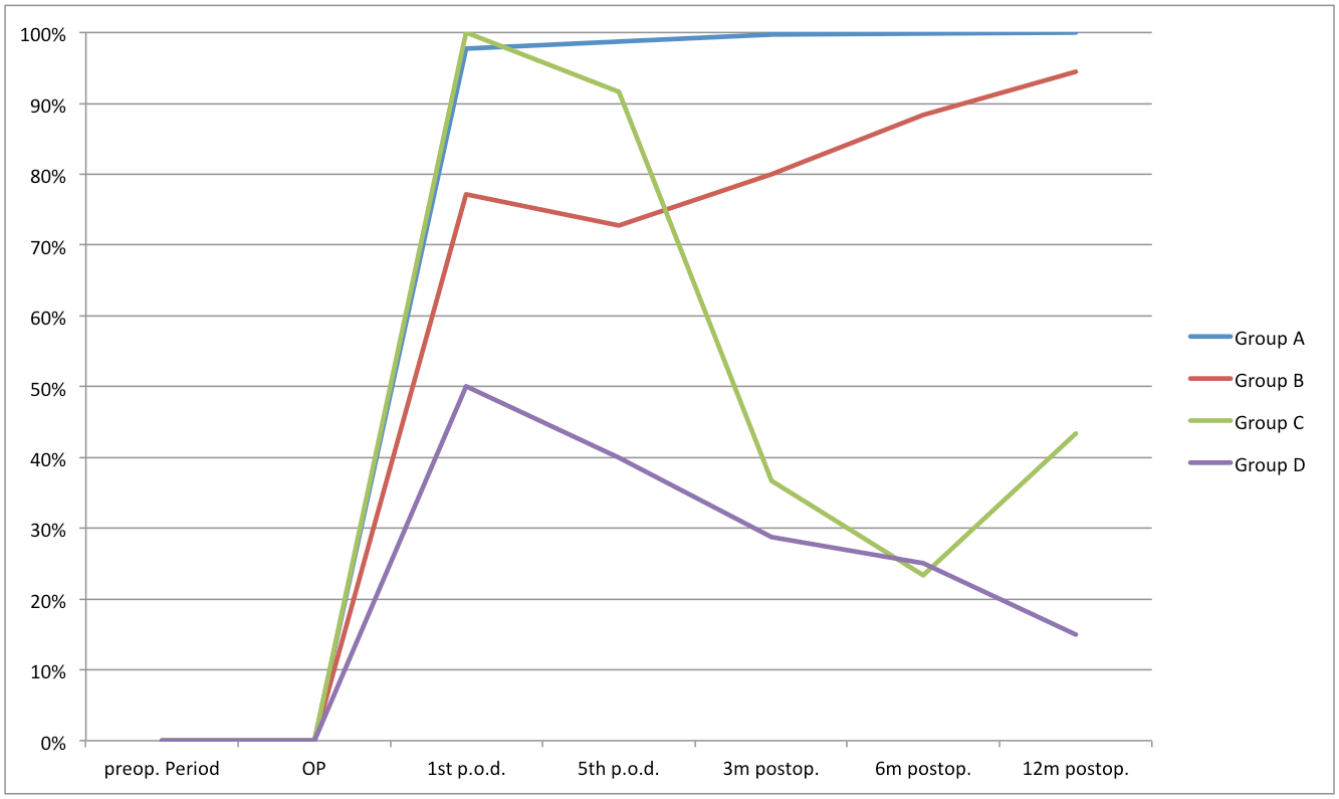

Fig. 1: Graph representing the average of patients of each group in terms of postoperative course of improvement.

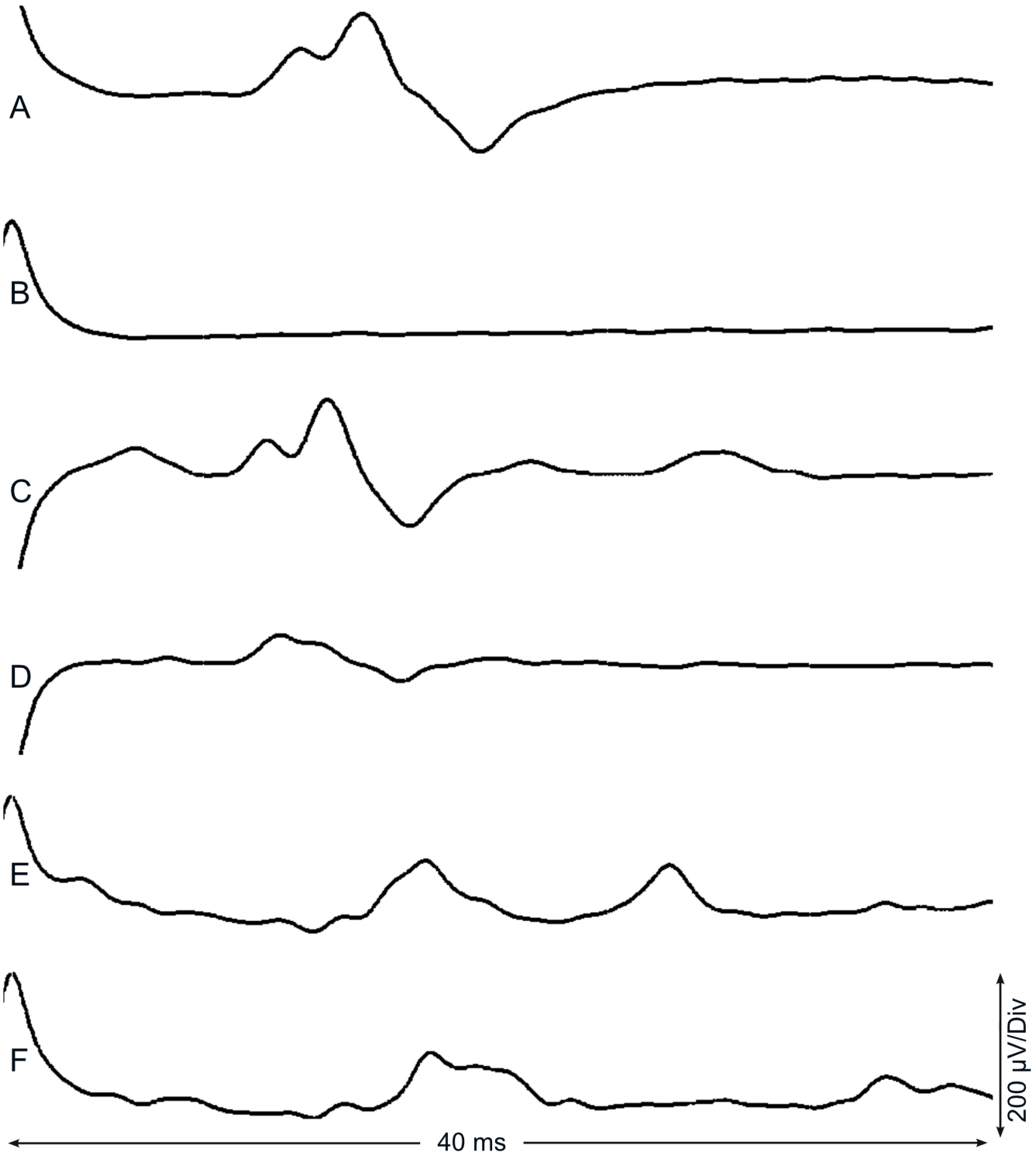

Fig. 2: Examples of LSRs events. They were recorded at amplitude 200 µV/Div and latency of 40mS. A: An example from group I before MVD. B: An example from group I after MVD where the LSRs are totally relieved. C: An example from group II before MVD. D: An example from group II after MVD where the LSRs are partially relieved. E: An example from group III before MVD. F: An example from group III after MVD where the LSRs do not change after MVD.

2.2 Endoscope-assisted microvascular decompression:

Patients were given short-acting muscle relaxants for intubation; no additional muscle relaxants were administered for the purpose of intraoperative electromyographic monitoring of the facial nerve in order to evaluate the disappearance of LSR as a sign of adequate decompression. MVD was performed in all patients through a lower retrosigmoid approach in the supine position with head tilt to the opposite side of complaint. This head position enabled us to minimize the cerebellar retraction if any required. The microscope was used for dissection and for decompression of the facial nerve. Rigid rod-lens endoscopes with a diameter of 2.7 mm and angles of view of 0º, 30º, and 45º (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) were used in all cases to explore the area around the facial nerve root exit zone before starting the decompression so that all offending vessels could be identified. The endoscopic inspection was valuable in most of our cases and added more information regarding the anatomy of the offending vessel as it allowed us to explore the ventral aspect of the facial root exit zone, specially the pontomedullary sulcus where most of the offending vessels are not easily identified using the microscope alone, without any retraction on the cerebellum. The added benefit from using the endoscope was mainly in cases of complex anatomy with multiple short perforators entering the brain stem in which the needed retraction exposes these vessels to higher risk of injury with subsequent complications. Using the endoscope before starting decompression enabled us to understand the anatomical situation better and accordingly plan an adequate decompression with least possible manipulation. Then, the VII REZ was made free using Teflon pledgets or sometimes a Teflon sling sutured to the petrous dura to ensure alleviation of the vascular compression. The dura was closed watertight with non-absorbable sutures with adjuvant usage of muscle graft or synthetic dura to ensure water tightness. Packing of the opened mastoid air cells with muscle graft and fibrin glue was done whenever needed. Then, the small bone flap was replaced and fixed with miniplates.

2.3 Intraoperative neurophysiological monitoring:

During surgery, brainstem auditory evoked potentials (BAEPs) and facial EMG monitoring were performed from the time of administration of general anesthesia until the time of dural closure. This means the whole operation time was recorded and the changes detected were observed and interpreted immediately through our neurophysiologist. The stimulating needle electrodes were inserted intradermally over the zygomatic and mandibular branches of the facial nerve, and a 0.2-msec pulse wave with an intensity of 5 to 20 mA was used. We tried to use the least possible amplitude capable of producing evident LSRs. In most of the patients the values were around 10 mA. The LSR were recorded all over the operation time during evoked facial EMG monitoring that appeared in the other

facial muscles, including the orbicularis oris, and the mentalis muscles, when the nerve that mainly innervates the frontalis muscle was stimulated. When the LSR was found to be persistent despite decompression, we explored further endoscopically all around the facial nerve and especially at the REZ for any suspicious underlying structure that could represent residual compression. In addition, all patients who received MVD underwent preoperative baseline and continuous intraoperative BAEP monitoring. The right and left ears were stimulated independently; using alternating rarefaction and condensation clicks with at least a 95-dB hearing level. A stimulus rate of 11.1 Hz was used. White noise was applied to the contralateral ear at the 65-dB hearing level. The observation interval was 12 msec. At least 1000 responses were averaged to an epoch. The recording electrodes for BAEP monitoring were positioned as follows: Ch1, vertex to left ear mastoid Cz/A1; and Ch2, vertex to right ear mastoid Cz/A2. The amplifier bandpass was 100–1000 Hz for all channels. Baseline responses were obtained after anesthesia induction and patient positioning.

2.4 Statistical analysis:

Results from clinical evaluation after surgery in the form of four groups; A, B, C and D for clinical outcome and the intraoperative LSRs events in the form of four groups; I, II, III and IV were collected and compared. We tried to find a significant correlation between the relief of the LSRs and the clinical outcome. We also studied the correlation between botulinum toxin injections and the presence or absence of the LSRs and its relief and whether it affects the clinical outcome after surgery or not. Additionally, we categorized the patients into five groups according to the duration of complaint; less than 3 years, 3 to 6 years, 6 to 9 years, 9 to 12 years and more than 12 years, to study the correlation between the duration of complaint and its effect on the LSRs findings and changes as well as the clinical outcome. Finally, we studied the correlation between grooving of the nerve seen during decompression and the LSRs changes monitored during surgery as well as the clinical outcome. All our results were written in the form of contingency tables. We implemented statistical tests using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina) through Fischer's exact test to analyze the contingency tables and calculate the p-value for each correlation to find whether it is significant or not. A p-value of 0.05 or less was considered to be significant.

3. Results:

3.1 Demographics:

The patient population included 35 males and 65 females with age ranging from 22 to 81 years and a mean age of 53.7 years. Symptoms were right-sided in 44 and left-sided in 56 patients. The duration of complaints ranged from 1 year to 23 years with mean duration of 7.9 years. Four patients were recurrent cases; three were operated at least one year before second surgery in our center and the other was operated 15 months before at another institution. Botulinum toxin injections were tried by 67 patients before surgery as a modality of treatment for HFS but aborted either because of side effects or the unsatisfying outcome. These patients who received botulinum toxin injections previously have stopped that treatment at least 3 months prior to surgery. The demographic data are provided in (Table 1).

No	Gender	Age	Duration Of Complaint (y)	Side	Botox	LSR before MVD	LSR after MVD	LSR group	Offending Vessel	Clinical outcome group	VII grooving
1	Female	71	5	L	No	Present	Absent	I	PICA	B	No
2	Female	70	7	R	No	Present	Present	II	AICA	B	No
3	Male	55	2	R	No	Present	Present	II	AICA	A	No
4	Female	50	10	L	No	Present	Present	II	Teflon	A	No
5	Male	54	17	L	No	Present	Absent	I	AICA, VA	A	Yes
6	Female	61	7	L	Yes	Present	Present	III	PICA	B	No
7	Male	69	14	L	Yes	Absent	Absent	IV	PICA, VA	A	Yes
8	Female	40	10	L	Yes	Present	Absent	I	PICA, VA	D	Yes
9	Female	56	2	L	No	Present	Absent	I	AICA, VA	A	Yes
10	Male	25	7	R	No	Present	Absent	I	AICA	A	No
11	Female	44	11	L	No	Present	Absent	I	AICA	A	No
12	Male	53	12	R	No	Present	Absent	I	PICA	B	Yes
13	Male	23	5	R	Yes	Present	Present	III	AICA	B	No
14	Female	37	2	R	No	Present	Absent	I	AICA	B	No
15	Female	51	18	L	No	Present	Present	III	Teflon	B	No
16	Female	73	10	L	No	Present	Present	II	AICA	B	Yes
17	Female	66	8	L	No	Present	Present	III	VA	D	No
18	Male	41	5	R	No	Present	Present	III	AICA	A	No
19	Female	65	17	R	No	Present	Present	III	PICA	B	No
20	Female	53	11	R	Yes	Present	Absent	I	AICA	C	No
21	Male	59	8	L	Yes	Present	Absent	I	PICA	B	Yes
22	Male	77	7	R	Yes	Absent	Absent	IV	AICA	A	No
23	Female	34	2.5	L	Yes	Present	Absent	I	AICA	B	Yes
24	Female	56	4	L	Yes	Present	Absent	I	PICA	B	Yes
25	Female	51	2	R	No	Present	Absent	I	PICA	A	No
26	Female	45	3	L	No	Present	Absent	I	AICA	A	No
27	Female	71	9	L	Yes	Present	Partially relieved	II	PICA	B	No
28	Female	81	7	L	Yes	Present	Absent	I	VA, PICA	A	No
29	Male	58	11	R	Yes	Present	Absent	I	PICA	A	No
30	Female	77	5	L	Yes	Present	Partially relieved	II	AICA, PICA	B	No
31	Female	74	2	L	No	Present	Present	III	AICA	A	Yes
32	Female	47	8	R	Yes	Present	Present	III	PICA	B	No
33	Male	51	8	L	No	Present	Absent	I	PICA	A	No
34	Male	51	4	L	Yes	Present	Partially relieved	II	VA, AICA	A	No
35	Female	58	11	R	No	Present	Partially relieved	II	AICA	A	No
36	Female	43	1	L	No	Absent	Absent	IV	AICA	A	No
37	Female	59	4	R	No	Present	Absent	I	AICA	C	No
38	Male	54	13	R	Yes	Present	Absent	I	PICA	A	No
39	Female	56	4	L	Yes	Present	Partially relieved	II	AICA	A	Yes
40	Female	55	20	R	Yes	Present	Absent	I	AICA	B	No
41	Female	68	3	L	Yes	Absent	Absent	IV	AICA	A	Yes
42	Female	74	15	R	Yes	Present	Absent	I	AICA, PICA	A	No
43	Male	46	4	L	Yes	Present	Absent	I	PICA	A	Yes
44	Male	38	3	L	Yes	Present	Absent	I	PICA	D	Yes
45	Male	51	7	L	No	Present	Absent	I	VA, AICA, PICA	B	No

46	Female	76	8	R	Yes	Absent	Absent	IV	PICA, AICA	B	No
47	Male	36	3	L	No	Present	Absent	I	AICA	A	Yes
48	Male	48	10	R	Yes	Present	Partially relieved	II	AICA	A	No
49	Female	54	9	R	Yes	Present	Absent	I	PICA, AICA	A	No
50	Female	61	10	R	Yes	Present	Absent	I	PICA	A	Yes
51	Female	39	2	L	Yes	Present	Present	I	PICA	A	No
52	Male	47	10	R	Yes	Present	Absent	I	PICA	B	Yes
53	Female	59	5	R	Yes	Absent	Absent	IV	AICA	A	No
54	Female	41	4	R	Yes	Present	Partially relieved	II	VA	B	Yes
55	Female	44	10	R	Yes	Absent	Absent	IV	PICA	A	No
56	Female	41	11	L	Yes	Present	Absent	I	Teflon	B	No
57	Male	46	3	L	Yes	Present	Absent	I	VA, AICA	D	Yes
58	Male	58	12	L	Yes	Present	Absent	I	AICA, Arachnoid	A	No
59	Female	58	6	L	Yes	Present	Absent	I	PICA	A	Yes
60	Female	66	10	R	Yes	Absent	Absent	IV	PICA	B	Yes
61	Female	53	7	R	Yes	Present	Absent	I	AICA, PICA	A	No
62	Female	61	7	L	Yes	Present	Present	III	VA, PICA	A	Yes
63	Female	62	8	L	Yes	Present	Absent	I	PICA	A	No
64	Female	53	21	R	Yes	Absent	Absent	IV	AICA	A	No
65	Male	65	2	L	No	Absent	Absent	IV	PICA	A	Yes
66	Male	48	5	L	Yes	Present	Absent	I	VA, AICA	A	No
67	Female	46	5	L	No	Present	Absent	I	PICA	A	No
68	Female	59	13	R	Yes	Present	Absent	I	AICA	A	No
69	Female	32	6	R	Yes	Present	Absent	I	PICA, AICA	A	No
70	Male	58	17	L	Yes	Present	Absent	I	AICA	A	No
71	Male	54	5	R	Yes	Present	Absent	I	AICA	B	Yes
72	Male	43	8	L	No	Absent	Absent	IV	PICA	A	Yes
73	Male	33	8	R	Yes	Present	Absent	I	AICA	B	No
74	Female	47	10	R	Yes	Absent	Absent	IV	PICA	A	Yes
75	Female	64	4	L	No	Absent	Absent	IV	PICA	A	No
76	Male	46	18	R	Yes	Present	Absent	I	PICA	A	No
77	Female	67	1	L	No	Absent	Absent	IV	PICA	A	No
78	Female	72	12	R	Yes	Present	Absent	I	PICA, VA	A	Yes
79	Female	56	2	L	Yes	Absent	Absent	IV	PICA	B	No
80	Female	53	8	L	Yes	Present	Absent	I	AICA, PICA, VA	A	No
81	Female	52	4	R	Yes	Present	Absent	I	AICA, PICA	B	No
82	Female	22	4	R	Yes	Present	Absent	I	PICA	A	No
83	Female	47	7	L	No	Absent	Absent	IV	AICA, PICA	A	No
84	Male	43	10	L	Yes	Present	Partially relieved	II	PICA, VA	A	No
85	Female	54	12	R	No	Present	Absent	I	Teflon	A	No
86	Female	63	23	L	Yes	Absent	Absent	IV	AICA	A	No
87	Female	53	2	L	Yes	Present	Partially relieved	II	PICA, VA	A	No
88	Female	46	5	L	Yes	Absent	Absent	IV	PICA	B	Yes
89	Female	65	3	L	Yes	Present	Absent	I	PICA	A	No
90	Male	52	10	L	Yes	Present	Absent	I	AICA	C	No
91	Female	57	3	R	No	Present	Absent	I	AICA	B	No

92	Male	54	15	R	Yes	Present	Absent	I	AICA, VA	A	No
93	Female	63	20	R	Yes	Present	Absent	I	VA	B	No
94	Male	43	6	L	Yes	Present	Present	IV	AICA	A	No
95	Female	42	12	L	Yes	Present	Absent	I	PICA	A	No
96	Male	52	6	L	No	Present	Absent	I	AICA, VA	A	No
97	Male	47	10	L	Yes	Absent	Absent	IV	AICA, VA	B	Yes
98	Male	55	5	R	Yes	Present	Present	II	PICA	B	No
99	Female	50	2	R	Yes	Present	Present	III	PICA	A	No
100	Female	76	9	L	Yes	Present	Absent	I	AICA, VA	A	No

3.2 Intraoperative LSR monitoring:

According to the fore mentioned classification, LSR was totally relieved in 56 patients (group I), partially relieved in 14 patients (group II), no change in LSR was detected in 10 patients (group III) and was not detected from the start of surgery in 20 patients (group IV).

We found that the 14 patients of group II that represents partial relief of the LSRs after MVD and 9 patients out of 10 of group III that represents no change in LSR after MVD showed satisfactory clinical outcome (All were in group A or B, see table 1 for details). Also we found that the 3 patients of group C representing recurrence of symptoms after a HFS free period and the 3 patients out of 4 of group D representing the worst treatment outcome showed an intraoperative complete relief of LSR after MVD (group I).

We could not find a significant correlation between the use of botulinum toxin injections and the presence or absence of the LSRs and its relief (p-value was 0.6). Neither the duration of symptoms nor the facial nerve grooving showed a significant correlation with the intraoperative LSRs findings and changes monitored (p-values were 0.6 and 0.6 respectively).

3.3 Offending vessel(s) detected intraoperatively:

El Refaee et al.[7] categorized type of compression into simple where only one blood vessel is offending the VII REZ or complex where the REZ is compressed by multiple vessels. Tandem compression is found when REZ is compressed at one point but through 2 blood vessels one pushing the other against VII REZ. Accordingly, we faced 69 cases of simple compression; 31 cases caused by Anterior Inferior Cerebellar Artery (AICA), 35 cases caused by Posterior Inferior Cerebellar Artery (PICA) and 3 cases caused by Vertebral Artery (VA). 26 cases of complex compression; 24 cases were caused by 2-vessels compression from which two cases were Tandem compression (Fig. 3A, 3B). Two cases were caused by 3-vessels compression (Fig. 3C, 3D). All of the patients had typical proximal compression at the VII REZ except for one patient; in whom beside the typical proximal compression,

dense arachnoid membranes were found to be strangulating the facial nerve. We found a visible groove in the facial nerve at the site of compression in 29 patients while this finding could not be detected in the remaining 71 patients included in our study. The vessels causing compression in each case as well as the presence of facial nerve grooving are summarized in Table 1.

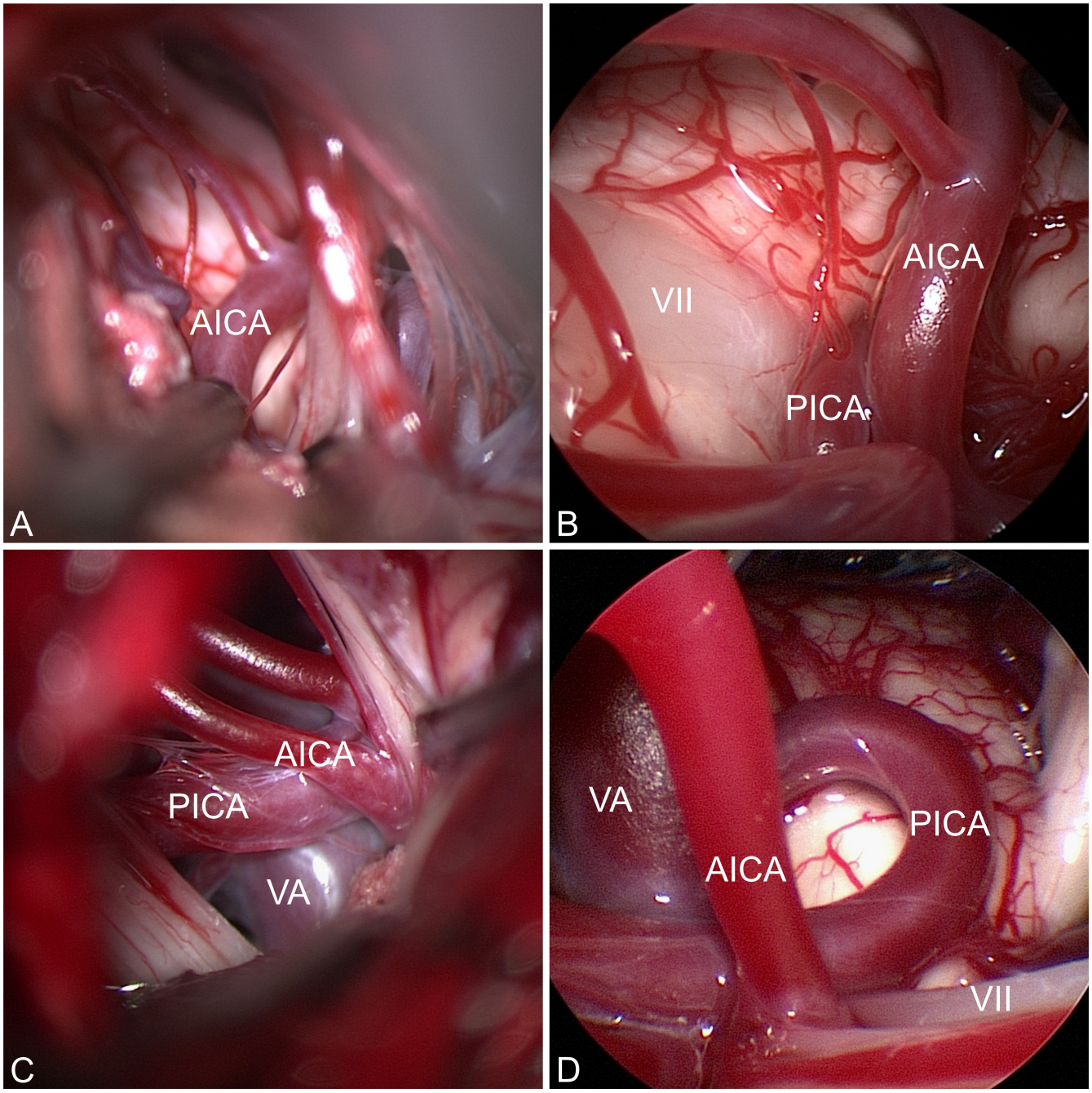

Fig. 3: Comparison of microscopic and endoscopic views of the vascular compression site shows the obvious benefit of the endoscopic visualization in detecting the vascular conflict.

A: Microscopic picture showing tandem compression by PICA and AICA. B: Endoscopic picture of the

same compression site. C: Microscopic picture showing a complex 3-vessels compression (VA, PICA and AICA). D: Endoscopic picture showing the same compression site.

3.4 Operative outcomes:

According to the fore mentioned classification and the graph representing each patient's clinical outcome, we had 62 patients where HFS was relieved directly after operation with described clinical improvement of 90-100% (group A). Thirty-one patients described a steady and gradual improvement over the next 3 months after surgery with clinical improvement of 50-90% of the preoperative state (group B), twenty-eight out of these thirty-one patients showed improvement up to 90-100% during the long-term one year follow-up. These 28 patients were still considered belonging to group B as they required longer time to achieve full improvement compared to group A. Three patients suffered from a relapse after a HFS-free period describing recurrence of symptoms, two described 50% improvement while the other described only 10% improvement (group C). Four patients reported minimal change in symptoms where the improvement was described by one of them to be about 40% while another described 80% improvement for a few days after surgery, one month later the symptoms recurred with only 20% improvement (group D). All these patients of group D showed at least a limited reduction in the hemifacial spasm for few days after surgery then the symptoms recurred. We considered the patients who were satisfied with the outcomes are those who reported improvement reaching 90-100% after one year follow-up and those who were not satisfied are of groups C and D. The overall percentage of the satisfied patients with the clinical outcome was 90%, these patients represent the 62 patients of group A describing improvement of 90-100% immediately after surgery and the 28 patients -out of 31- of group B who showed gradual improvement during the first postoperative year to reach a final improvement of 90-100%. Statistical analysis did not reveal a significant correlation between the relief of the intraoperative LSRs and the clinical outcome, (p-value was 0.9). For those who did not reach a satisfying improvement they are still in follow up to detect a late improvement, otherwise, will be investigated to decide whether a second operation is recommended or not.

We expected that the best clinical outcome represented in groups A and B should be matching with the groups in which the LSRs were totally or partially relieved represented in groups I and II. While, the patients who were not satisfied with the outcome of surgery represented in groups C and D should be matching with the groups in which the LSRs were not relieved or were not able to be monitored from the start represented in groups III and IV. This correlation could not be proven statistically (p-value was 0.5).

We could not find a significant correlation between the use of botulinum toxin injections and the

clinical outcome (p-value was 0.9). Also there was no correlation between the duration of symptoms prior to surgery and the clinical outcome (p-value was 0.7). Finally, we could not correlate the presence of grooving in facial nerve documented during surgery with a worse outcome represented in groups C and D (p-value was 0.09).

3.5 Postoperative complications:

Forty-two patients suffered from conductive hearing loss (CHL) after surgery which can be explained due to soiling of the opened mastoid air cells during the craniotomy with saline solution causing middle ear effusion. The saline irrigation was used during the surgery and to fill the operative field before dural closure to minimize pneumocephalus. These patients showed remarkable improvement over the next few postoperative days and were controlled by a second audiometry before discharge which proved that the hearing affection was relieved.

We had 7 patients who suffered postoperatively from cerebrospinal fluid (CSF) rhinorrhea. Six of them were managed with a continuous lumbar drainage for 5 days. One patient presented 1.5 months after surgery with CSF rhinorrhea which was surgically repaired and simultaneously a lumbar drainage was placed for 5 days. We had 5 patients who suffered from cranial nerve affection after surgery. Six patients suffered from delayed facial palsy which started 9-11 days after surgery and then totally resolved within 3 months after surgery. One of the theories to explain the delayed facial palsy after MVD is an activation of a dormant herpes infection through the surgery. We tried to investigate all the patients for a possible Herpes infection so we sent a CSF sample taken by the time of surgery for laboratory examination but we have always received negative results. The cause of this facial affection is to be further investigated. One patient suffered from transient abducens palsy which resolved before discharge. Unexpectedly, one patient died after the surgery. She was discharged on day 5 after surgery without complaints. The spasm had resolved completely. At home 10 days after surgery, the patient suffered from fever, generalized malaise, vomiting and disturbed conscious level. Clinical and radiological investigations as well as a CSF analysis at another institution suspected herpes simplex encephalitis which may have resulted from an activation of a dormant viral infection. Although treatment with Acyclovir was started immediately, the patient deteriorated rapidly till she was deeply comatose and died within few days.

4. Discussion:

Since the first accurate description of hemifacial spasm by Gowers[8] in 1884, a remarkable growth in the medical literature that described the pathophysiology and the management of this syndrome has occurred. Although many authors had theorized about the condition's origin, Campbell and Keedy[4] in 1947 proposed that the cause and triggering factor for hemifacial spasm were vascular abnormalities in the posterior fossa. Jannetta[15, 17] and Rand[39] developed the current surgical paradigm of neurovascular conflict as the cause of cranial nerve related neurological conditions such as hemifacial spasm, with microvascular decompression to be the most effective surgical option for treatment.[40]

There are two postulated hypotheses for the underlying mechanism that could explain this disease. One theory is the central cause theory: HFS originates from the hyperexcitability of the facial motor neuron itself. The other theory is the peripheral cause theory: HFS is the result of an ephaptic transmission of the facial nerve fibers that is facilitated by injury to the myelin.[11] Therefore, some abnormal findings in the electrophysiological investigations for patients of HFS have been detected such as F waves of the facial muscles,[11–13] blink reflexes,[6, 13] and LSR.[9, 11, 14, 29–31, 45, 49]

The history of LSR monitoring dates back to the 1980s where the hypothesis that favors damage to axons of the facial nerve as the sole cause of HFS assumes that injuring the facial nerve results in hyperexcitability of a portion of the nerve and ephaptic transmission between fibers.[28] Nielsen[35] found support for this hypothesis from studies of patients with HFS in whom he electrically stimulated one branch of the facial nerve and recorded a response from muscles innervated by a different branch of the facial nerve. In a related study of 62 patients with HFS, Nielsen[34] found that electrical stimulation of the supraorbital nerve that elicits the blink reflex in these patients, in addition gave rise to a response from a muscle innervated by a different branch of the facial nerve. This lateral spread of excitation was explained by ephaptic transmission at the location of injury (REZ of the facial nerve). This ephaptic transmission is assumed to be responsible for the synkinesis observed in HFS. Nielsen and Jannetta[36] found support for this hypothesis in their electrophysiological study of 59 patients with HFS before and after microvascular decompression surgery. The results of several studies involving other nerves, as well as of studies of the facial nerve, seem to support this hypothesis.

The hypothesis that the phenomena directly associated with the lesion of the facial nerve cause the spasm as well as the synkinesis is supported by many studies of the effects of damaging peripheral nerves. Kugelberg[26] using compression of the arm (by a blood pressure cuff) to study the effect of mild injury (ischemia) on a peripheral nerve found that local irritation of a nerve can result in the development of local "trigger zones" and a high sensitivity to mechanical stimulation, as well as in the generation of spontaneous discharges. In these studies, local damage to a nerve caused spontaneous

activity in the motor fibers.

The LSR can be recorded using electromyography (EMG) monitoring of the muscles that are innervated by the other branches of the facial nerve,[11, 25, 32] when one branch of the facial nerve is electrically stimulated. It was noticed that the LSR observed in other muscles disappears immediately after the offending vessel is moved away from the facial nerve.[25, 29, 30] Accordingly, the LSR is supposed to be a useful indicator in identifying the offending vessels and in confirming adequate decompression of the facial nerve intraoperatively. There has been much debate, however, about the clinical usefulness of this abnormal phenomenon as a reliable indicator. Some authors have advocated performing routine EMG monitoring of the facial musculature for detecting this abnormal finding to ensure that adequate decompression was achieved,[14, 31] whereas others have questioned whether intraoperative LSR monitoring is a reliable indicator of the surgical outcome.[10, 22] The role of the LSR for predicting the long-term effectiveness of MVD remains to be investigated. In our study, we found the LSRs events statistically insignificant in predicting the clinical outcome. We believe the best-case scenario is to have the LSRs totally relieved after decompression which gives us a sense of assurance for an adequate decompression. On the contrary, the persistence of the LSRs urged us to explore the VII REZ endoscopically again to make sure that there was not any missed offending vessel. After confirming adequate decompression, we found that the persistence of LSRs was not related to a worse clinical outcome.

Moller and Jannetta[31] reported that spasms are likely to persist if LSR is still observed at the end of the microvascular decompression. Some authors[12, 16, 18, 20, 43] have suggested that the disappearance of LSR with intraoperative EMG monitoring is a good indicator of favorable outcomes in patients with HFS; while others[10, 12, 13, 20] have reported that persistence of LSR after decompression does not always mean a poor prognosis. This could be explained, as the hyperexcitability of the VII nerve caused by the vascular compression, especially with long duration of complaint, is sometimes not immediately reversible after adequate decompression. It may take some time till the nerve reaches its normal state again. Therefore, they reported that approximately one-third of their patients were spasm free only after delays as long as 4 months to 1 year, despite an apparently effective decompression.[19, 27] However, others[44] reported that persistence or suppression of LSR at the end of the procedure was not always correlated with the long-term effects of microvascular decompression.

Recently, it has been agreed upon that a postoperative follow-up interval of 3 months is the minimum for predicting outcomes and that 1 year is the minimum for judging postoperative results.[37] We agree with this statement when looking on our series of over 200 patients. In one patient, it took 10 months

until the spasm completely disappeared. In this study, we had a follow-up period of one year and for those who did not reach a satisfying improvement are still to be followed up to detect a late improvement or to be investigated to decide whether a second operation is recommended or not.

Wang et al.[47] studied the effect of botulinum toxin injections on the clinical outcome after microvascular decompression in hemifacial spasm. He categorized the patients into two groups whether received botulinum toxin injections prior to surgery or not. There was no significant difference in outcomes and complications between the two groups. The lateral spread response disappeared in 60% of the patients who received prior botulinum toxin injections as compared with 74% in patients who did not use it before. This difference was statistically insignificant. In our study, we also could not find a significant correlation between the use of botulinum toxin injections and the clinical outcome or the LSR findings and changes monitored during surgery (p-values were 0.9 and 0.6 respectively).

We assumed that the long duration of complaint exposes the facial nerve to more physical damage as well as more severe neurophysiological changes. Accordingly, we expected to find the worse outcomes and the persistent LSRs after decompression in these cases. But we found that the duration of symptoms has no significant correlation with the intraoperative LSRs findings and changes monitored as well as the clinical outcome.

Kim et al.[20] suggested in their study that the severity of indentation predicted the clinical outcome. They hypothesized that severe indentation would be associated with poor outcomes after MVD. However, the results demonstrated that patients with no or mild indentation of the REZ of the facial nerve had rather poor outcomes which suggests that the surgeon could find the optimal site for decompression on the REZ more easily. Another possibility is that patients with no or mild indentation on the REZ of the facial nerve might have secondary HFS rather than primary HFS by neurovascular compression. In our study, we considered nerve grooving seen by the surgeon during surgery at the compression site is a sign of physical damage to the nerve structure. Accordingly, we expected worse outcome in such patients. We tried to correlate the presence of this nerve grooving with the clinical outcome and the LSRs but both of them were not significant (p-values were 0.09 and 0.6 respectively).

It is to be noted that facial synkinesis or post-herpetic facial spasm can induce symptoms similar to those of primary HFS. These disorders should be differentiated from the start, as they are generally associated with disappointing surgical results. Additionally, vascular compression may not be the only cause of spasm in all cases. Aoki and Nagao[1] reported a case of HFS in which no vascular abnormality was observed during surgery and mere manipulation and surrounding dissection of the nerve resulted in symptom resolution. We found a similar situation in our operated recurrent cases, where no actual compression could be detected. In these patients, dissection of the Teflon from the

facial nerve as well as mere manipulation and massage of the facial nerve resulted in resolution of the symptoms in these recurrent cases.

5. Conclusion:

We conclude that the lateral spread responses intraoperative monitoring may only represent an intraoperative tool to guide for an adequate decompression of the facial nerve. However, it failed to represent a reliable indicator in predicting the clinical outcome after adequate microvascular decompression.

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7. List of abbreviations:

HFS, hemifacial spasm; TN, trigeminal neuralgia; EA-MVD, endoscope-assisted microvascular decompression; LSR, lateral spread response; BAEPs, brainstem auditory evoked potentials; V, Trigeminal nerve; VI, Abducens nerve; VII, Facial nerve; REZ, root exit zone; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery; VA, vertebral artery;

Keywords: endoscope-assisted, hemifacial spasm, intraoperative monitoring, LSR, lateral spread, microvascular decompression.

8. Zusammenfassung:

Background: Microvascular Decompression represents an effective treatment for hemifacial spasm. The use of lateral spread responses (LSRs) monitoring remains a useful intraoperative tool to ensure adequate decompression of the facial nerve.

Objective: To assess the value of LSRs intraoperative monitoring as a prognostic indicator for the outcome of microvascular decompression in hemifacial spasm.

Methods: Our study included 100 patients prospectively. The patients were classified into 4 groups whether LSRs were totally, partially, not relieved or not detected from the start. According to clinical outcome, the patients were classified into 4 groups depending on the clinical course after surgery and the residual symptoms if any. Then, correlations were made between LSRs events and treatment outcome to detect its reliability as a prognostic indicator.

Results: LSRs were relieved totally in 56% of the patients, partially relieved in 14%, not relieved in 10% and were not detected in 20% of the patients from the start. HFS was relieved directly after operation in 62% with clinical improvement of 90-100%. 31% described 50-90% improvement over the next 3 months after surgery. Almost all of these 31% (28 out of 31 patients) reported further clinical improvement of 90-100% within one year after surgery. 3% suffered from a relapse after a HFS-free period and 4% reported minimal or no improvement describing 0-50% of the preoperative state. The percentage of the satisfied patients with the clinical outcome who reported after one year a clinical improvement of 90-100% was 90%. Statistical analysis did not find a significant correlation between the relief of LSRs and clinical outcome.

Conclusion: LSRs may only represent an intraoperative tool to guide for an adequate decompression but failed to represent a reliable prognostic indicator for treatment outcome.

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An dieser Stelle möchte ich mich von Herzen bei all denjenigen bedanken, die dazu beigetragen haben, dass ich die Promotion in Angriff genommen, durchgeführt und nun auch zu Ende gebracht habe.

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10. Eidesstattliche Erklärung

Eidesstattliche Erklärung

Hiermit erkläre ich, dass ich die vorliegende Dissertation selbständig verfasst und keine anderen als die angegebenen Hilfsmittel benutzt habe.

Die Dissertation ist bisher keiner anderen Fakultät, keiner anderen wissenschaftlichen Einrichtung vorgelegt worden.

Ich erkläre, dass ich bisher kein Promotionsverfahren erfolglos beendet habe und dass eine Aberkennung eines bereits erworbenen Doktorgrades nicht vorliegt.

Datum Unterschrift

11. Publikationen:

- El Damaty A, El Refaee E, Aly K, Zohdi AM (2013) Success rate of endoscopic third ventriculostomy in infants below six months of age with congenital obstructive hydrocephalus (a preliminary study of eight cases). Asian J Neurosurg 8(3):147
- El Damaty A, Manwaring JC, Schroeder HWS (2014) The guillotine knife: a novel tool for safe endoscopic cutting of intracranial membranes: Technical note. J Neurosurg 1–4
- Manwaring JC, El Damaty A, Baldauf J, Schroeder HWS (2014) The small-chamber irrigation technique (SCIT): a simple maneuver for managing intraoperative hemorrhage during endoscopic intraventricular surgery. Neurosurgery 10 Suppl 3:375–379; discussion 379

Acceptance letter:

25-Jan-2016

Dear Dr. El Damaty:

It is a pleasure to accept your manuscript entitled "The Value of Lateral Spread Response Monitoring in Predicting the Clinical Outcome after Microvascular Decompression in Hemifacial Spasm: A Prospective Study on 100 patients." in its current form for publication in the Neurosurgical Review.

Thank you for your fine contribution. On behalf of the Editors of the Neurosurgical Review, we look forward to your continued contributions to the Journal.

Sincerely,
Prof. Helmut Bertalanffy
Editor-in-Chief, Neurosurgical Review
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ORIGINAL ARTICLE

The value of lateral spread response monitoring in predicting the clinical outcome after microvascular decompression in hemifacial spasm: a prospective study on 100 patients

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Abstract Microvascular decompression represents an effective treatment for hemifacial spasm. The use of lateral spread response (LSR) monitoring remains a useful intraoperative tool to ensure adequate decompression of the facial nerve. The aim of this study was to assess the value of LSRs intraoperative monitoring as a prognostic indicator for the outcome of microvascular decompression in hemifacial spasm. Our study included 100 patients prospectively. The patients were classified into four groups whether LSRs were totally, partially, not relieved, or not detected from the start. According to clinical outcome, the patients were classified into four groups depending on the clinical course after surgery and the residual symptoms if any. Then, correlations were made between LSR events and treatment outcome to detect its reliability as a prognostic indicator. LSRs were relieved totally in 56 % of the patients, partially relieved in 14 %, not relieved in 10 %, and were not detected in 20 % of the patients from the start. HFS was relieved directly after operation in 62 % with clinical improvement of 90–100 %. Thirty-one percent described 50–90 % improvement over the next 3 months after surgery. Almost all of these 31 % (28 out of 31 patients) reported further clinical improvement of 90–100 % within 1 year after surgery. Three percent suffered from a relapse after a HFS-free period, and 4 % reported minimal or no improvement describing 0–50 % of the preoperative state. The percentage of the satisfied patients with the clinical outcome who reported after 1 year a clinical improvement of 90–100 % was 90 %. Statistical analysis did not find a significant correlation between the relief of LSRs and clinical outcome. LSRs may only represent an intraoperative tool to guide for an adequate decompression but failed to represent a reliable prognostic indicator for treatment outcome.

Keywords Endoscope-assisted · Hemifacial spasm · Intraoperative monitoring · LSR · Lateral spread · Microvascular decompression

Introduction

Hemifacial spasm (HFS) could be defined as a benign, chronic, involuntary movement of the facial muscles that typically begins in the orbicularis oculi and spreads to the other facial muscles over several years [9, 19, 22, 24]. It is an infrequent disorder with approximately 2:1 female to male ratio. The average annual incidence rate is 0.74 per 100,000 in men and 0.81 per 100,000 in women [2]. It is more common in the Asian population than in other populations [7, 41, 48].

Usually, hemifacial spasm is caused by vascular compression of the facial nerve (VII) at the root exit zone (REZ). The best treatment option is microvascular decompression (MVD) representing an effective treatment for HFS [3, 5]. However, hemifacial spasm could occur secondary to rare causes, which include tumors, aneurysms, arteriovenous malformations, and dolichoectatic vertebrobasilar arteries in 0.4 to 2.2 % of cases [3, 21, 23, 33, 38, 42, 46].

Among all the abnormal findings that could be recorded in the electrophysiological investigations for patients with HFS such as F waves of the facial muscles [11–13] and blink reflexes [6, 13, 24], lateral spread response (LSR) [9, 11, 14,

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29–31, 45, 49] remains a useful intraoperative tool to ensure the adequate decompression of the facial nerve. The question of whether intraoperative LSR monitoring was a reliable predictor of outcome was discussed with the conclusion that the prognostic value of LSR monitoring was indeed questionable, and the value of the LSR for predicting the long-term outcome of MVD remains to be investigated.

Objective

We tried in our study to correlate the intraoperative LSR changes with the long-term clinical outcome after surgery in order to assess the efficacy of the LSR monitoring in predicting the outcome of microvascular decompression in hemifacial spasm.

Methods

Study design

The local ethics committee approved this prospective study. The study was performed to determine the value of LSR intraoperative monitoring as an indicator of adequate decompression of the facial nerve root exit zone (VII REZ) and as a predictor of clinical outcome regarding improvement of the hemifacial spasm. The study was designed prospectively to include 100 patients who underwent endoscope-assisted microvascular decompression (EA-MVD) by the senior author (HWSS) between 2013 and April 2015 at our institution. All patients were examined clinically by the senior author to confirm diagnosis, and then scanned through 3-T magnetic resonance imaging (MRI) scanners to obtain 3-D high-resolution T2-weighted gradient echo sequence imaging in the steady-state free precession (SSFP) technique which included constructive interference in steady state (CISS) and fast imaging employing steady-state acquisition (FIESTA), and 3-D Time of flight magnetic resonance angiography (TOF-MRA). Images were acquired in axial plane covering the cerebellopontine angle with slice thickness no larger than 1 mm to diagnose the compression of VII REZ and predict the offending vessel. All patients were assessed after operation then on first day and on fifth day after operation before discharge, and then at 3-, 6-, and 12-month intervals after surgery. The follow-up period ranged from 6 to 32 months. The patients were asked to describe the degree of improvement according to their personal opinion and self-assessment on a scale of 0–100 % where 100 % represents no residual spasm and 0 represents no improvement of hemifacial spasm symptoms. A telephone call or an E-mail contact was established whenever the patient did not appear during the follow-up period with the same grading scale applied to assess the outcome. The patients were classified into four patterns of postoperative clinical course. Group A showed immediate improvement after surgery with a degree of improvement of 90–100 % according to the previously mentioned scaling system used representing the best outcome. Group B showed gradual steady improvement of symptoms after surgery to reach a state of 50–90 % of improvement during the first 3 months after surgery; when these patients showed improvement up to 90–100 % of the symptoms during the 1-year follow-up, we still counted them in group B as they required more time to achieve full improvement compared to group A. Group C showed a relapse or recurrence of symptoms after a hemifacial spasm-free period. Group D showed minimal or no change in symptoms with a degree of improvement of 0–50 % of the hemifacial spasm symptoms representing the worst outcome. Figure 1 shows a graph representing the average of patients of each group in terms of postoperative course of improvement. The difference between groups C and D is whether the patient had a period after surgery free of hemifacial spasm and then the symptoms recurred (group C) or he/she reported no or slight improvement starting immediately after surgery (group D). Also, we classified the events of LSR intraoperative monitoring into four groups where group I showed complete relief of LSR after MVD, group II showed partial relief of LSR, group III showed no relief of LSR, and group IV where no LSR could be detected from the start of operation. Examples of LSRs events are shown in Fig. 2.

Endoscope-assisted microvascular decompression

Patients were given short-acting muscle relaxants for intubation; no additional muscle relaxants were administered for the purpose of intraoperative electromyographic monitoring of the facial nerve in order to evaluate the disappearance of LSR as a sign of adequate decompression. MVD was performed in all patients through a lower retrosigmoid approach in the supine position with head tilt to the opposite side of complaint. This head position enabled us to minimize the cerebellar retraction if any required. The microscope was used for dissection and for decompression of the facial nerve. Rigid rod-lens endoscopes with a diameter of 2.7 mm and angles of view of 0°, 30°, and 45° (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) were used in all cases to explore the area around the facial nerve root exit zone before starting the decompression so that all offending vessels could be identified. The endoscopic inspection was valuable in most of our cases and added more information regarding the anatomy of the offending vessel as it allowed us to explore the ventral aspect of the facial root exit zone, specially the pontomedullary sulcus where most of the offending vessels are not easily identified using the microscope alone, without any retraction on the cerebellum. The added benefit from using the endoscope was mainly in cases of complex anatomy

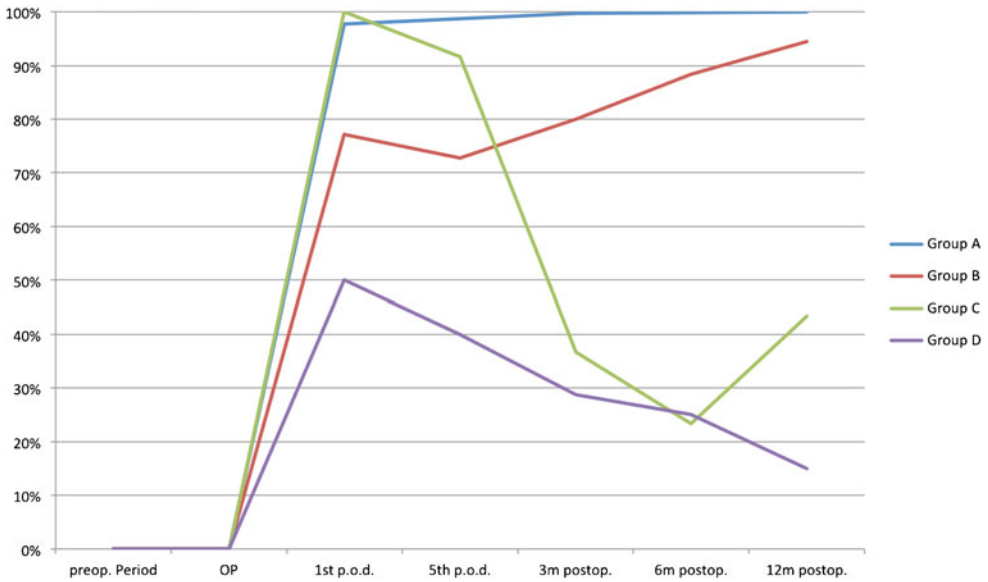

Fig. 1 Graph representing the average of patients of each group in terms of postoperative course of improvement

with multiple short perforators entering the brain stem in which the needed retraction exposes these vessels to higher risk of injury with subsequent complications. Using the endoscope before starting decompression enabled us to understand the anatomical situation better and accordingly plan an adequate decompression with least possible manipulation. Then, the VII REZ was made free using Teflon pledgets or sometimes a Teflon sling sutured to the petrous dura to ensure alleviation of the vascular compression. The dura was closed watertight with non-absorbable sutures with adjuvant usage of

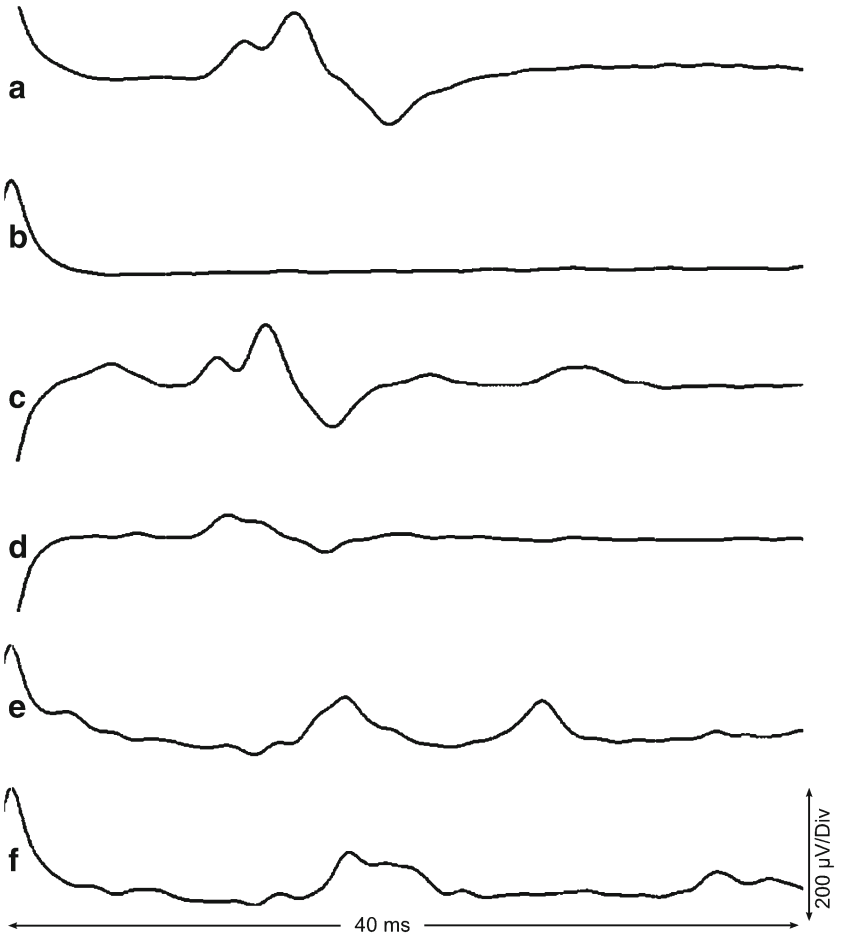

Fig. 2 Examples of LSRs events. They were recorded at amplitude 200 μV/Div and latency of 40mS. **a** An example from group I before MVD. **b** An example from group I after MVD where the LSRs are totally relieved. **c** An example from group II before MVD. **d** An example from group II after MVD where the LSRs are partially relieved. **e** An example from group III before MVD. **f** An example from group III after MVD where the LSRs do not change after MVD

muscle graft or synthetic dura to ensure water tightness. Packing of the opened mastoid air cells with muscle graft and fibrin glue was done whenever needed. Then, the small bone flap was replaced and fixed with miniplates.

Intraoperative neurophysiological monitoring

During surgery, brainstem auditory-evoked potentials (BAEPs), and facial EMG monitoring were performed from the time of administration of general anesthesia until the time of dural closure. This means the whole operation time was recorded and the changes detected were observed and interpreted immediately through our neurophysiologist. The stimulating needle electrodes were inserted intradermally over the zygomatic and mandibular branches of the facial nerve, and a 0.2-msec pulse wave with an intensity of 5 to 20 mA was used. We tried to use the least possible amplitude capable of producing evident LSRs. In most of the patients, the values were around 10 mA. The LSR were recorded all over the operation time during evoked facial EMG monitoring that appeared in the other facial muscles, including the orbicularis oris and the mentalis muscles, when the nerve that mainly innervates the frontalis muscle was stimulated. When the LSR was found to be persistent despite decompression, we explored further endoscopically all around the facial nerve and especially at the REZ for any suspicious underlying structure that could represent residual compression. In addition, all patients who received MVD underwent preoperative baseline and continuous intraoperative BAEP monitoring. The right and left ears were stimulated independently, using alternating rarefaction and condensation clicks with at least a 95-dB hearing level. A stimulus rate of 11.1 Hz was used. White noise was applied to the contralateral ear at the 65-dB hearing level. The observation interval was 12 msec. At least 1000 responses were averaged to an epoch. The recording electrodes for BAEP monitoring were positioned as follows: Ch1, vertex to left ear mastoid Cz/A1; and Ch2, vertex to right ear mastoid Cz/A2. The amplifier bandpass was 100–1000 Hz for all channels. Baseline responses were obtained after anesthesia induction and patient positioning.

Statistical analysis

Results from clinical evaluation after surgery in the form of four groups; A, B, C, and D for clinical outcome and the intraoperative LSRs events in the form of four groups; I, II, III, and IV were collected and compared. We tried to find a significant correlation between the relief of the LSRs and the clinical outcome. We also studied the correlation between botulinum toxin injections and the presence or absence of the LSRs and its relief and whether it affects the clinical outcome after surgery or not. Additionally, we categorized the patients into five groups according to the duration of complaint, less than 3 years, 3 to 6 years, 6 to 9 years, 9 to 12 years, and more than 12 years, to study the correlation between the duration of complaint and its effect on the LSRs findings and changes as well as the clinical outcome. Finally, we studied the correlation between grooving of the nerve seen during decompression and the LSRs changes monitored during surgery as well as the clinical outcome. All our results were written in the form of contingency tables. We implemented statistical tests using SAS version 9.1 (SAS Institute Inc, Cary, NC) through Fischer's exact test to analyze the contingency tables and calculate the p value for each correlation to find whether it is significant or not. A p value of 0.05 or less was considered to be significant.

Results

Demographics

The patient population included 35 males and 65 females with age ranging from 22 to 81 years and a mean age of 53.7 years. Symptoms were right-sided in 44 and left-sided in 56 patients. The duration of complaints ranged from 1 to 23 years with mean duration of 7.9 years. Four patients were recurrent cases, three were operated at least 1 year before second surgery in our center, and the other was operated 15 months before at another institution. Botulinum toxin injections were tried by 67 patients before surgery as a modality of treatment for HFS but aborted either because of side effects or the unsatisfying outcome. These patients who received botulinum toxin injections previously have stopped that treatment at least 3 months prior to surgery. The demographic data are provided in (Table 1).

Intraoperative LSR monitoring

According to the fore mentioned classification, LSR was totally relieved in 56 patients (group I) and partially relieved in 14 patients (group II); no change in LSR was detected in 10 patients (group III) and was not detected from the start of surgery in 20 patients (group IV).

We found that the 14 patients of group II that represents partial relief of the LSRs after MVD and 9 patients out of 10 of group III that represents no change in LSR after MVD showed satisfactory clinical outcome (All were in group A or B, see Table 1 for details). Also, we found that the three patients of group C representing recurrence of symptoms after a HFS-free period and the three patients out of four of group D representing the worst treatment outcome showed an intraoperative complete relief of LSR after MVD (group I).

We could not find a significant correlation between the use of botulinum toxin injections and the presence or absence of the LSRs and its relief (p value was 0.6). Neither the duration

Table 1 List of patients

No.	Gender	Age	Duration of complaint (year)	Side	Botox	LSR before MVD	LSR after MVD	LSR group	Offending vessel	Clinical outcome group	VII grooving
1	Female	71	5	L	No	Present	Absent	I	PICA	B	No
2	Female	70	7	R	No	Present	Present	II	AICA	B	No
3	Male	55	2	R	No	Present	Present	II	AICA	A	No
4	Female	50	10	L	No	Present	Present	II	Teflon	A	No
5	Male	54	17	L	No	Present	Absent	I	AICA, VA	A	Yes
6	Female	61	7	L	Yes	Present	Present	III	PICA	B	No
7	Male	69	14	L	Yes	Absent	Absent	IV	PICA, VA	A	Yes
8	Female	40	10	L	Yes	Present	Absent	I	PICA, VA	D	Yes
9	Female	56	2	L	No	Present	Absent	I	AICA, VA	A	Yes
10	Male	25	7	R	No	Present	Absent	I	AICA	A	No
11	Female	44	11	L	No	Present	Absent	I	AICA	A	No
12	Male	53	12	R	No	Present	Absent	I	PICA	B	Yes
13	Male	23	5	R	Yes	Present	Present	III	AICA	B	No
14	Female	37	2	R	No	Present	Absent	I	AICA	B	No
15	Female	51	18	L	No	Present	Present	III	Teflon	B	No
16	Female	73	10	L	No	Present	Present	II	AICA	B	Yes
17	Female	66	8	L	No	Present	Present	III	VA	D	No
18	Male	41	5	R	No	Present	Present	III	AICA	A	No
19	Female	65	17	R	No	Present	Present	III	PICA	B	No
20	Female	53	11	R	Yes	Present	Absent	I	AICA	C	No
21	Male	59	8	L	Yes	Present	Absent	I	PICA	B	Yes
22	Male	77	7	R	Yes	Absent	Absent	IV	AICA	A	No
23	Female	34	2.5	L	Yes	Present	Absent	I	AICA	B	Yes
24	Female	56	4	L	Yes	Present	Absent	I	PICA	B	Yes
25	Female	51	2	R	No	Present	Absent	I	PICA	A	No
26	Female	45	3	L	No	Present	Absent	I	AICA	A	No
27	Female	71	9	L	Yes	Present	Partially relieved	II	PICA	B	No
28	Female	81	7	L	Yes	Present	Absent	I	VA, PICA	A	No
29	Male	58	11	R	Yes	Present	Absent	I	PICA	A	No
30	Female	77	5	L	Yes	Present	Partially relieved	II	AICA, PICA	B	No
31	Female	74	2	L	No	Present	Present	III	AICA	A	Yes
32	Female	47	8	R	Yes	Present	Present	III	PICA	B	No
33	Male	51	8	L	No	Present	Absent	I	PICA	A	No
34	Male	51	4	L	Yes	Present	Partially relieved	II	VA, AICA	A	No
35	Female	58	11	R	No	Present	Partially relieved	II	AICA	A	No
36	Female	43	1	L	No	Absent	Absent	IV	AICA	A	No
37	Female	59	4	R	No	Present	Absent	I	AICA	C	No
38	Male	54	13	R	Yes	Present	Absent	I	PICA	A	No
39	Female	56	4	L	Yes	Present	Partially relieved	II	AICA	A	Yes
40	Female	55	20	R	Yes	Present	Absent	I	AICA	B	No
41	Female	68	3	L	Yes	Absent	Absent	IV	AICA	A	Yes
42	Female	74	15	R	Yes	Present	Absent	I	AICA, PICA	A	No
43	Male	46	4	L	Yes	Present	Absent	I	PICA	A	Yes
44	Male	38	3	L	Yes	Present	Absent	I	PICA	D	Yes
45	Male	51	7	L	No	Present	Absent	I	VA, AICA, PICA	B	No
46	Female	76	8	R	Yes	Absent	Absent	IV	PICA, AICA	B	No
47	Male	36	3	L	No	Present	Absent	I	AICA	A	Yes
48	Male	48	10	R	Yes	Present	Partially relieved	II	AICA	A	No

Table 1 (continued)

No.	Gender	Age	Duration of complaint (year)	Side	Botox	LSR before MVD	LSR after MVD	LSR group	Offending vessel	Clinical outcome group	VII grooving
49	Female	54	9	R	Yes	Present	Absent	I	PICA, AICA	A	No
50	Female	61	10	R	Yes	Present	Absent	I	PICA	A	Yes
51	Female	39	2	L	Yes	Present	Present	I	PICA	A	No
52	Male	47	10	R	Yes	Present	Absent	I	PICA	B	Yes
53	Female	59	5	R	Yes	Absent	Absent	IV	AICA	A	No
54	Female	41	4	R	Yes	Present	Partially relieved	II	VA	B	Yes
55	Female	44	10	R	Yes	Absent	Absent	IV	PICA	A	No
56	Female	41	11	L	Yes	Present	Absent	I	Teflon	B	No
57	Male	46	3	L	Yes	Present	Absent	I	VA, AICA	D	Yes
58	Male	58	12	L	Yes	Present	Absent	I	AICA, Arachnoid	A	No
59	Female	58	6	L	Yes	Present	Absent	I	PICA	A	Yes
60	Female	66	10	R	Yes	Absent	Absent	IV	PICA	B	Yes
61	Female	53	7	R	Yes	Present	Absent	I	AICA, PICA	A	No
62	Female	61	7	L	Yes	Present	Present	III	VA, PICA	A	Yes
63	Female	62	8	L	Yes	Present	Absent	I	PICA	A	No
64	Female	53	21	R	Yes	Absent	Absent	IV	AICA	A	No
65	Male	65	2	L	No	Absent	Absent	IV	PICA	A	Yes
66	Male	48	5	L	Yes	Present	Absent	I	VA, AICA	A	No
67	Female	46	5	L	No	Present	Absent	I	PICA	A	No
68	Female	59	13	R	Yes	Present	Absent	I	AICA	A	No
69	Female	32	6	R	Yes	Present	Absent	I	PICA, AICA	A	No
70	Male	58	17	L	Yes	Present	Absent	I	AICA	A	No
71	Male	54	5	R	Yes	Present	Absent	I	AICA	B	Yes
72	Male	43	8	L	No	Absent	Absent	IV	PICA	A	Yes
73	Male	33	8	R	Yes	Present	Absent	I	AICA	B	No
74	Female	47	10	R	Yes	Absent	Absent	IV	PICA	A	Yes
75	Female	64	4	L	No	Absent	Absent	IV	PICA	A	No
76	Male	46	18	R	Yes	Present	Absent	I	PICA	A	No
77	Female	67	1	L	No	Absent	Absent	IV	PICA	A	No
78	Female	72	12	R	Yes	Present	Absent	I	PICA, VA	A	Yes
79	Female	56	2	L	Yes	Absent	Absent	IV	PICA	B	No
80	Female	53	8	L	Yes	Present	Absent	I	AICA, PICA, VA	A	No
81	Female	52	4	R	Yes	Present	Absent	I	AICA, PICA	B	No
82	Female	22	4	R	Yes	Present	Absent	I	PICA	A	No
83	Female	47	7	L	No	Absent	Absent	IV	AICA, PICA	A	No
84	Male	43	10	L	Yes	Present	Partially relieved	II	PICA, VA	A	No
85	Female	54	12	R	No	Present	Absent	I	Teflon	A	No
86	Female	63	23	L	Yes	Absent	Absent	IV	AICA	A	No
87	Female	53	2	L	Yes	Present	Partially relieved	II	PICA, VA	A	No
88	Female	46	5	L	Yes	Absent	Absent	IV	PICA	B	Yes
89	Female	65	3	L	Yes	Present	Absent	I	PICA	A	No
90	Male	52	10	L	Yes	Present	Absent	I	AICA	C	No
91	Female	57	3	R	No	Present	Absent	I	AICA	B	No
92	Male	54	15	R	Yes	Present	Absent	I	AICA, VA	A	No
93	Female	63	20	R	Yes	Present	Absent	I	VA	B	No
94	Male	43	6	L	Yes	Present	Present	IV	AICA	A	No
95	Female	42	12	L	Yes	Present	Absent	I	PICA	A	No
96	Male	52	6	L	No	Present	Absent	I	AICA, VA	A	No

Table 1 (continued)

No.	Gender	Age	Duration of complaint (year)	Side	Botox	LSR before MVD	LSR after MVD	LSR group	Offending vessel	Clinical outcome group	VII grooving
97	Male	47	10	L	Yes	Absent	Absent	IV	AICA, VA	B	Yes
98	Male	55	5	R	Yes	Present	Present	II	PICA	B	No
99	Female	50	2	R	Yes	Present	Present	III	PICA	A	No
100	Female	76	9	L	Yes	Present	Absent	I	AICA, VA	A	No

HFS hemifacial spasm, *TN* trigeminal neuralgia, *EA-MVD* endoscope-assisted microvascular decompression, *LSR* lateral spread response, *BAEPs* brainstem auditory evoked potentials, *V* trigeminal nerve, *VI* abducent nerve, *VII* facial nerve, *REZ* root exit zone, *SCA* superior cerebellar artery, *AICA* anterior inferior cerebellar artery, *PICA* posterior inferior cerebellar artery, *VA* vertebral artery

of symptoms nor the facial nerve grooving showed a significant correlation with the intraoperative LSR findings and changes monitored (p values were 0.6 and 0.6, respectively).

Offending vessel(s) detected intraoperatively

El Refaee et al. [7] categorized the type of compression into simple where only one blood vessel is offending the VII REZ or complex where the REZ is compressed by multiple vessels. Tandem compression is found when REZ is compressed at one point but through two blood vessels one pushing the other against VII REZ. Accordingly, we faced 69 cases of simple compression; 31 cases caused by anterior inferior cerebellar artery (AICA), 35 cases caused by posterior inferior cerebellar artery (PICA), and 3 cases caused by vertebral artery (VA). Twenty-six cases of complex compression, 24 cases were caused by two-vessel compression from which two cases were tandem compression (Fig. 3a, b). Two cases were caused by three-vessel compression (Fig. 3c, d). All of the patients had typical proximal compression at the VII REZ except for one patient; in whom beside the typical proximal compression, dense arachnoid membranes were found to be strangulating the facial nerve. We found a visible groove in the facial nerve at the site of compression in 29 patients while this finding could not be detected in the remaining 71 patients included in our study. The vessels causing compression in each case as well as the presence of facial nerve grooving are summarized in Table 1.

Operative outcomes

According to the fore mentioned classification and the graph representing each patient's clinical outcome, we had 62 patients where HFS was relieved directly after operation with described clinical improvement of 90–100 % (group A). Thirty-one patients described a steady and gradual improvement over the next 3 months after surgery with clinical improvement of 50–90 % of the preoperative state (group B); 28 out of these 31 patients showed improvement up to 90–100 % during the long-term 1-year follow-up. These 28 patients were still considered belonging to group B as they required longer time to achieve full improvement compared to group A. Three patients suffered from a relapse after a HFS-free period describing recurrence of symptoms, two described 50 % improvement while the other described only 10 % improvement (group C). Four patients reported minimal change in symptoms where the improvement was described by one of them to be about 40 % while another described 80 % improvement for a few days after surgery, 1 month later the symptoms recurred with only 20 % improvement (group D). All these patients of group D showed at least a limited reduction in the hemifacial spasm for few days after surgery then the symptoms recurred. We considered the patients who were satisfied with the outcomes are those who reported improvement reaching 90–100 % after 1-year follow-up, and those who were not satisfied are of groups C and D. The overall percentage of the satisfied patients with the clinical outcome was 90 %; these patients represent the 62 patients of group A describing improvement of 90–100 % immediately after surgery and the 28 patients—out of 31—of group B who showed gradual improvement during the first postoperative year to reach a final improvement of 90–100 %. Statistical analysis did not reveal a significant correlation between the relief of the intraoperative LSRs and the clinical outcome (p value was 0.9). For those who did not reach a satisfying improvement, they are still in follow-up to detect a late improvement, otherwise, will be investigated to decide whether a second operation is recommended or not.

We expected that the best clinical outcome represented in groups A and B should be matching with the groups in which the LSRs were totally or partially relieved represented in groups I and II, while the patients who were not satisfied with the outcome of surgery represented in groups C and D should be matching with the groups in which the LSRs were not relieved or were not able to be monitored from the start represented in groups III and IV. This correlation could not be proven statistically (p value was 0.5).

We could not find a significant correlation between the use of botulinum toxin injections and the clinical outcome (p value was 0.9). Also, there was no correlation between the duration of symptoms prior to surgery and the clinical outcome (p value was 0.7). Finally, we could not correlate

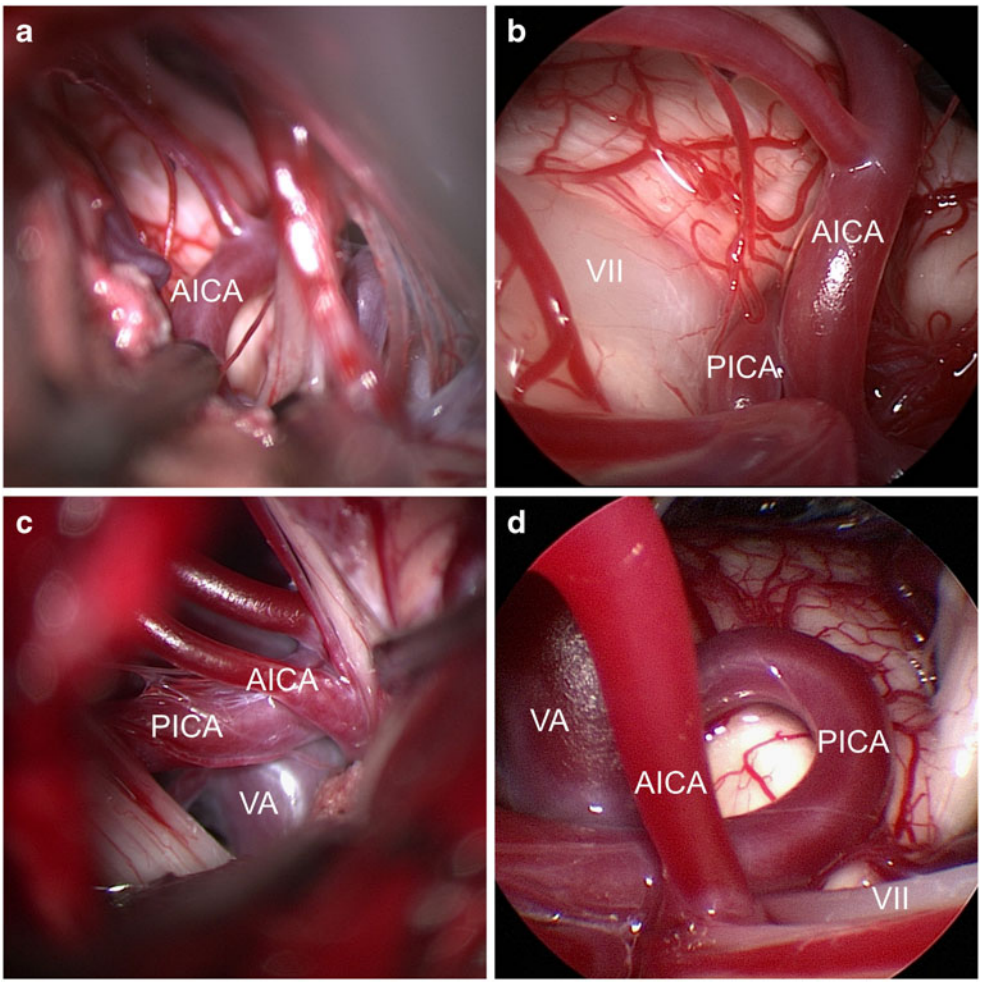

Fig. 3 Comparison of microscopic and endoscopic views of the vascular compression site shows the obvious benefit of the endoscopic visualization in detecting the vascular conflict. **a** Microscopic picture showing tandem compression by PICA and AICA. **b** Endoscopic picture of the same compression site. **c** Microscopic picture showing a complex three-vessel compression (VA, PICA, and AICA). **d** Endoscopic picture showing the same compression site

the presence of grooving in facial nerve documented during surgery with a worse outcome represented in groups C and D (p value was 0.09).

Postoperative complications

Forty-two patients suffered from conductive hearing loss (CHL) after surgery which can be explained due to soiling of the opened mastoid air cells during the craniotomy with saline solution causing middle ear effusion. The saline irrigation was used during the surgery and to fill the operative field before dural closure to minimize pneumocephalus. These patients showed remarkable improvement over the next few postoperative days and were controlled by a second audiometry before discharge which proved that the hearing affection was relieved.

We had seven patients who suffered postoperatively from cerebrospinal fluid (CSF) rhinorrhea. Six of them were managed with a continuous lumbar drainage for 5 days. One patient presented 1.5 months after surgery with CSF rhinorrhea which was surgically repaired, and simultaneously, a lumbar drainage was placed for 5 days. We had five patients who suffered from cranial nerve affection after surgery. Six patients suffered from delayed facial palsy which started 9–11 days after surgery and then totally resolved within 3 months after surgery. One of the theories to explain the delayed facial palsy after MVD is an activation of a dormant herpes infection through the surgery. We tried to investigate all the patients for a possible herpes infection so we sent a CSF sample taken by the time of surgery for laboratory examination, but we have always received negative results. The cause of this facial affection is to be further investigated. One patient suffered from transient abducens palsy which resolved before discharge. Unexpectedly, one patient died after the surgery. She was discharged on day 5 after surgery without complaints. The spasm had resolved completely. At home, 10 days after surgery, the patient suffered from fever, generalized malaise, vomiting, and disturbed conscious level. Clinical and radiological investigations as well as a CSF analysis at another institution suspected herpes simplex encephalitis which may have resulted from an activation of a dormant viral infection. Although treatment with Acyclovir was started immediately, the patient deteriorated rapidly till she was deeply comatose and died within few days.

Discussion

Since the first accurate description of hemifacial spasm by Gowers [8] in 1884, a remarkable growth in the medical literature that described the pathophysiology and the management of this syndrome has occurred. Although many authors had theorized about the condition's origin, Campbell and Keedy [4] in 1947 proposed that the cause and triggering factor for hemifacial spasm were vascular abnormalities in the posterior fossa. Jannetta [15, 17] and Rand [39] developed the current surgical paradigm of neurovascular conflict as the cause of cranial nerve-related neurological conditions such as hemifacial spasm, with microvascular decompression to be the most effective surgical option for treatment [40].

There are two postulated hypotheses for the underlying mechanism that could explain this disease. One theory is the central cause theory: HFS originates from the hyperexcitability of the facial motor neuron itself. The other theory is the peripheral cause theory: HFS is the result of an ephaptic transmission of the facial nerve fibers that is facilitated by injury to the myelin [11]. Therefore, some abnormal findings in the electrophysiological investigations for patients of HFS have been detected such as F waves of the facial muscles [11–13], blink reflexes [6, 13] and LSR [9, 11, 14, 29–31, 45, 49].

The history of LSR monitoring dates back to the 1980s where the hypothesis that favors damage to axons of the facial nerve as the sole cause of HFS assumes that injuring the facial nerve results in hyperexcitability of a portion of the nerve and ephaptic transmission between fibers [28]. Nielsen [35] found support for this hypothesis from studies of patients with HFS in whom he electrically stimulated one branch of the facial nerve and recorded a response from muscles innervated by a different branch of the facial nerve. In a related study of 62 patients with HFS, Nielsen [34] found that electrical stimulation of the supraorbital nerve that elicits the blink reflex in these patients, in addition, gave rise to a response from a muscle innervated by a different branch of the facial nerve. This lateral spread of excitation was explained by ephaptic transmission at the location of injury (REZ of the facial nerve). This ephaptic transmission is assumed to be responsible for the synkinesis observed in HFS. Nielsen and Jannetta [36] found support for this hypothesis in their electrophysiological study of 59 patients with HFS before and after microvascular decompression surgery. The results of several studies involving other nerves, as well as of studies of the facial nerve, seem to support this hypothesis.

The hypothesis that the phenomena directly associated with the lesion of the facial nerve cause the spasm as well as the synkinesis is supported by many studies of the effects of damaging peripheral nerves. Kugelberg [26] using compression of the arm (by a blood pressure cuff) to study the effect of mild injury (ischemia) on a peripheral nerve found that local irritation of a nerve can result in the development of local "trigger zones" and a high sensitivity to mechanical stimulation, as well as in the generation of spontaneous discharges. In these studies, local damage to a nerve caused spontaneous activity in the motor fibers.

The LSR can be recorded using electromyography (EMG) monitoring of the muscles that are innervated by the other branches of the facial nerve [11, 25, 32], when one branch of the facial nerve is electrically stimulated. It was noticed that the LSR observed in other muscles disappears immediately after the offending vessel is moved away from the facial nerve [25, 29, 30]. Accordingly, the LSR is supposed to be a useful indicator in identifying the offending vessels and in confirming adequate decompression of the facial nerve intraoperatively. There has been much debate, however, about the clinical usefulness of this abnormal phenomenon as a reliable indicator. Some authors have advocated performing routine EMG monitoring of the facial musculature for detecting this abnormal finding to ensure that adequate decompression was achieved [14, 31], whereas others have questioned whether intraoperative LSR monitoring is a reliable indicator of the surgical outcome [10, 22]. The role of the LSR for predicting the long-term effectiveness of MVD remains to be investigated. In our study, we found the LSR events statistically insignificant in predicting the clinical outcome. We believe the best case scenario is to have the LSRs totally relieved after decompression which gives us a sense of assurance for an adequate decompression. On the contrary, the persistence of the LSRs urged us to explore the VII REZ endoscopically again to make sure that there was not any missed offending vessel. After confirming adequate decompression, we found that the persistence of LSRs was not related to a worse clinical outcome.

Moller and Jannetta [31] reported that spasms are likely to persist if LSR is still observed at the end of the microvascular decompression. Some authors [12, 16, 18, 20, 43] have suggested that the disappearance of LSR with intraoperative EMG monitoring is a good indicator of favorable outcomes in patients with HFS, while others [10, 12, 13, 20] have reported that persistence of LSR after decompression does not always mean a poor prognosis. This could be explained, as the hyperexcitability of the VII nerve caused by the vascular compression, especially with long duration of complaint, is sometimes not immediately reversible after adequate decompression. It may take some time till the nerve reaches its normal state again. Therefore, they reported that approximately one third of their patients were spasm free only after delays as long as 4 months to 1 year, despite an apparently effective decompression [19, 27]. However, others [44] reported that persistence or suppression of LSR at the end of the procedure was not always correlated with the long-term effects of microvascular decompression.

Recently, it has been agreed upon that a postoperative follow-up interval of 3 months is the minimum for predicting outcomes and that 1 year is the minimum for judging postoperative results [37]. We agree with this statement when looking on our series of over 200 patients. In one patient, it took 10 months until the spasm completely disappeared. In this study, we had a follow-up period of 1 year and for those who did not reach a satisfying improvement are still to be followed up to detect a late improvement or to be investigated to decide whether a second operation is recommended or not.

Wang et al. [47] studied the effect of botulinum toxin injections on the clinical outcome after microvascular decompression in hemifacial spasm. He categorized the patients into two groups whether received botulinum toxin injections prior to surgery or not. There was no significant difference in outcomes and complications between the two groups. The lateral spread response disappeared in 60 % of the patients who received prior botulinum toxin injections as compared with 74 % in patients who did not use it before. This difference was statistically insignificant. In our study, we also could not find a significant correlation between the use of botulinum toxin injections and the clinical outcome or the LSR findings and changes monitored during surgery (p values were 0.9 and 0.6, respectively).

We assumed that the long duration of complaint exposes the facial nerve to more physical damage as well as more severe neurophysiological changes. Accordingly, we expected to find the worse outcomes and the persistent LSRs after decompression in these cases. But we found that the duration of symptoms has no significant correlation with the intraoperative LSRs findings and changes monitored as well as the clinical outcome.

Kim et al. [20] suggested in their study that the severity of indentation predicted the clinical outcome. They hypothesized that severe indentation would be associated with poor outcomes after MVD. However, the results demonstrated that patients with no or mild indentation of the REZ of the facial nerve had rather poor outcomes which suggests that the surgeon could find the optimal site for decompression on the REZ more easily. Another possibility is that patients with no or mild indentation on the REZ of the facial nerve might have secondary HFS rather than primary HFS by neurovascular compression. In our study, we considered nerve grooving seen by the surgeon during surgery at the compression site is a sign of physical damage to the nerve structure. Accordingly, we expected worse outcome in such patients. We tried to correlate the presence of this nerve grooving with the clinical outcome and the LSRs but both of them were not significant (p values were 0.09 and 0.6 respectively).

It is to be noted that facial synkinesis or post-herpetic facial spasm can induce symptoms similar to those of primary HFS. These disorders should be differentiated from the start, as they are generally associated with disappointing surgical results. Additionally, vascular compression may not be the only cause of spasm in all cases. Aoki and Nagao [1] reported a case of HFS in which no vascular abnormality was observed during surgery and mere manipulation and surrounding dissection of the nerve resulted in symptom resolution. We found a similar situation in our operated recurrent cases, where no actual compression could be detected. In these patients, dissection of the teflon from the facial nerve as well as mere manipulation and massage of the facial nerve resulted in resolution of the symptoms in these recurrent cases.

Conclusion

We conclude that the lateral spread response intraoperative monitoring may only represent an intraoperative tool to guide for an adequate decompression of the facial nerve. However, it failed to represent a reliable indicator in predicting the clinical outcome after adequate microvascular decompression.

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Compliance with ethical standards The local ethics committee approved this prospective study.

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Comments

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This prospective study is regarding the efficacy of lateral spread response (LSR) monitoring during microvascular decompression (MVD) surgery for hemifacial spasm. In this study, the efficacy of LSR during MVD is a very interesting issue, but still under debate. When monitoring during MVD, we sometimes experience the phenomenon of disappearance of LSR only after opening the dura and drainage of cerebrospinal fluid (CSF). This finding must be a very confusing event for a surgeon. Accordingly, it is very important to compare LSR response between before and after the insertion of Teflon. Also, we need highly sophisticated and dedicated monitoring team and systems to confirm adequate decompression during MVD.

The authors performed endoscope-assisted MVD in this study. It is well-known that endoscope-assisted surgery can provide a panoramic surgical view and helpful confirmation of adequate decompression. However, to draw a conclusion of substantial benefit from the endoscope-assisted MVD, additional validation and research would be necessary.

This study reinforces the reader's knowledge about the various complications of MVD. We should keep in mind that herpes infection-associated meningitis can be a possible cause of death after MVD, because reactivation of Herpes labialis has a very common incidence after cranial nerve surgery including MVD.