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Advancements in surgical strategies and technologies for cranial nerve disorders

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Advancements in surgical strategies and technologies for cranial nerve disorders

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Editorial: Advancements in surgical strategies and technologies for cranial nerve disorders

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KEYWORDS

trigeminal neuralgia, cranial nerve disorders, hyperexcitability, hemifacial spasm, microvascular decompression (MVD), percutaneous ballon compression, surgical strategy, minimal invasive operation

Editorial on the Research Topic
Advancements in surgical strategies and technologies for cranial nerve disorders

Category

Cranial nerve disorders can generally be categorized into two principal classifications: hypofunctional states, which are defined by diminished or compromised neural activity, and hyperfunctional conditions, distinguished by exaggerated or inordinately intensified nerve reactions. The former group includes clinical presentations such as anosmia, visual impairment, external ophthalmoplegia, facial palsy, and facial anesthesia, *etc*. In contrast, the latter comprises well-known conditions such as hemifacial spasm, trigeminal neuralgia, glossopharyngeal neuralgia, and post-herpetic neuralgia following herpes zoster infection, *etc*. Hypofunctional states generally arise due to structural nerve damage, often induced by a variety of factors including schwannomas, traumatic injuries, or external compression from neighboring neoplasms, as well as inadvertent iatrogenic interventions.

Mechanism

In hyperexcitability disorders of the cranial nerves, the key factor is that ectopic action potentials originate within the nerves themselves, rather than from the brainstem nuclei or ganglia (1). Under normal conditions, movements related to facial expressions are initiated by impulses generated in the cerebral cortex, whereas facial sensations are perceived through stimulation of sensory receptors located in the facial region. The most prevalent cause of hemifacial spasm (HFS) or trigeminal neuralgia (TN) is neurovascular conflict (2, 3). In patients with a constricted cerebellopontine angle (CPA), the proximity between cranial nerve roots and adjacent blood vessels gradually increases with age, ultimately exerting considerable pressure on the nerve (4). Due to the interfacial friction caused by the pulse, the nerve undergoes demyelination. When this pathological process advances to a certain stage, a cascade of signaling pathways mediated by inflammatory cytokines is triggered, ultimately leading to the expression of specific transmembrane proteins on the nerve surface (5, 6). These transmembrane proteins include mechanosensitive ion and voltage-gated channels. With pulsatile compressions, it drives the resting potential toward depolarization forming a state of subthreshold membrane potential oscillation. Under such precarious conditions, a precise mechanical stimulus may significantly lower the threshold required for membrane depolarization, thereby facilitating the activation of sodium channels and ultimately triggering propagatable action potentials. When these ectopic action potentials propagate to the nerve-muscle junctions, an attack of irregular muscle constriction occurs while to the central cortex, an illusion of sharp pain is perceived (1, 7–9, 21).

This etiological explanation clarifies why elderly individuals of Asian descent exhibit a heightened predisposition to conditions such as trigeminal neuralgia and hemifacial spasm. Due to distinct anatomical characteristics, the cerebellopontine angle in East Asians tends to be more compact compared to that of other racial groups. As aging progresses, the brain undergoes atrophy while blood vessels experience sclerosis, gradually drawing these structures into closer proximity within the confined CPA space (4).

This hypothesis effectively explains how emotional stimuli can trigger paroxysmal attacks. When individuals experience emotions such as nervousness or excitement, their heart rate and blood pressure undergo physiological changes. These changes generate a "precisely calibrated compression"—defined by specific frequency and amplitude that correspond to the individual's heartbeat and blood pressure—which acts upon the targeted nerve and triggers an impulse. In the absence of such pressure, the pulsative stimulus is effectively removed, thereby accounting for the prompt alleviation of symptoms frequently witnessed following a successful microvascular decompression (MVD) procedure (1). Postoperative recurrence may be attributed to improper placement of Teflon, which can induce granuloma formation, as the nerve root in TN patients remains highly vulnerable to neoplastic involvement as well as vascular compression (10). Besides, it may illustrate the clinical phenomenon that secondary TN or HFS cases are often caused by local epidermoid cysts or meningiomas rather than schwannomas perse (11, 12). In fact, due to their expansive growth pattern along the nerve sheath, schwannomas may act as an insulating barrier, protecting the nerve root from direct compression.

Strategy

A clear and logically consistent understanding of the pathogenesis is essential for guiding effective treatment strategies. The principle of MVD is to carefully detach the offending vessel from the nerve root, rather than inserting Teflon material between them for insulation. A successful operation depends on adequate exposure of the affected cranial nerve root segment (3). In addition, the use of oversized or excessive Teflon felt should be avoided, as it may impair visualization and hinder accurate identification of the offending artery. Regardless of the vessel, neoplasm, or Teflon, any pulsatile contact may potentially trigger an ectopic impulse (10). A recommended approach involves initiating the dissection at the level of the caudal cranial nerves, followed by careful mobilization of the parent artery in a proximal and lateral direction, with small pieces of Geofoam strategically placed between the artery and the brainstem. By the time the facial nerve is reached, the offending vessel is often already displaced (13). Furthermore, safety considerations hold paramount importance in this functional neurosurgical procedure (14). The use of a sling technique within such a confined operative space is generally not suggested (1). Once an ideal leverage point for arterial displacement is identified, the decompression process becomes more efficient. It is essential to align the positioning of the artery with the natural direction of blood flow, ensuring long-term stability as the Geofoam is gradually resorbed, without causing recoil (15). In summary, the procedure should be performed using the most straightforward and time-efficient method available.

Simplification

In addition to these classical techniques, simplified and minimally invasive approaches must not be overlooked. Our foremost priority lies in maximizing patient satisfaction rather than executing complex surgical interventions; thus, the procedure should be carried out expeditiously with minimal disruption to cerebral function. In recent years, percutaneous balloon compression (PBC) has gained increasing acceptance within the medical community (16). During inflation of the balloon with contrast agent in Meckel's cave, a pear-shaped opacity is typically observed on lateral fluoroscopy. This image consists of a rounded base oriented toward the semilunar ganglion, a central portion encompassing the rootlets, a head corresponding to the trigeminal root as it crosses the porus (neck), and a stalk directed toward the catheter tip. It is remarkable that the vast expanse of Meckel's cave is predominantly occupied by rootlets, with merely a small anterior portion housing the trigeminal ganglion (17). When a balloon is inflated within the cave, both the rootlets and the ganglion are subjected to compression, with the highest pressure concentrated at the narrowest zone through which the nerve fibers pass via the porus. A large-headed "pear" may indicate an increased risk of postoperative diplopia, facial hypoesthesia, and masticatory weakness due to possible damage to the abducent nerve or the trigeminal nerve fibers, including the motor branch. Considering that the rootlets consist of regenerative axons linked to peripheral nerves, while the ganglion houses neurons related to the non-renewable elements of the central nervous system, it becomes justifiable to apply targeted pressure on the ganglion as a preventive measure against recurrence (18, 19). Due to the structural distinctions between the slender, unmyelinated nociceptive neurons responsible for pain perception and the thicker, myelinated tactile neurons involved in touch sensation, precise control over the placement and timing of the PBC enables selective ablation of pain-transmitting nerves while largely sparing other sensory neural pathways (20).

Summary

In conclusion, the future management of cranial nerve disorders should prioritize a deeper understanding of the underlying pathogenesis and embrace less invasive therapeutic strategies. Surgical techniques must be further refined to achieve greater simplicity and precision, with the ultimate vision being the successful treatment of these conditions through non-invasive or minimally invasive means.

Author contributions

JZ: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. SL: Data curation, Project administration, Supervision, Visualization, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Efficacy and safety of ultrasound-guided pulsed radiofrequency in the treatment of the ophthalmic branch of postherpetic trigeminal neuralgia

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Objective: To investigate the efficacy and safety of ultrasound-guided pulsed radiofrequency (PRF) targeting the supraorbital nerve for treating the ophthalmic branch of postherpetic trigeminal neuralgia.

Methods: A retrospective cohort study was conducted involving patients who presented at the Department of Pain, Affiliated Hospital of Southwest Medical University from January 2015 to January 2022. The patients were diagnosed with the first branch of postherpetic trigeminal neuralgia. In total, 63 patients were included based on the inclusion and exclusion criteria. The patients were divided into the following two groups based on the treatment method used: the nerve block (NB) group ($n = 32$) and the PRF + NB group (radiofrequency group, $n = 31$). The visual analog scale (VAS) score, Pittsburgh Sleep Quality Index (PSQI) score, and pregabalin dose were compared between the two groups before treatment, 1 week after the procedure, and 1, 3, and 6 months post-procedure, and the complications, such as local infection, local hematoma, and decreased visual acuity, were monitored post-treatment.

Results: No significant difference was found in terms of pretreatment age, sex, course of disease, preoperative VAS score, preoperative PSQI score, and preoperative pregabalin dose between the two groups ($P > 0.05$). The postoperative VAS score, PSQI score, and pregabalin dose were significantly decreased in both groups. Furthermore, significant differences were found between the two groups at each preoperative and postoperative time point ($P < 0.05$). The VAS score was lower in the radiofrequency group than in the NB group at 1, 3, and 6 months, and the difference was statistically significant ($P < 0.05$). The PSQI score was lower in the radiofrequency group than in the NB group at 1 week, 1, 3, and 6 months post-procedure, and the difference was statistically significant ($P < 0.05$). The dose of pregabalin was lower in the radiofrequency group than in the NB group at 1 week, 1, 3, and 6 months post-procedure, and the difference was statistically significant at 3 and 6 months ($P < 0.05$). After 6 months of treatment, the excellent rate of VAS score in the radiofrequency group was 70.96%, and the overall effective rate was 90.32%, which was higher than that in the NB group. The difference in the efficacy was statistically significant ($P < 0.05$).

Conclusion: PRF targeting the supraorbital nerve can effectively control the pain in the first branch of the trigeminal nerve after herpes, enhance sleep quality, and reduce the dose of pregabalin. Thus, this study shows that PRF is safe under ultrasound guidance and is worthy of clinical application.

KEYWORDS

herpes zoster, pulsed radiofrequency, trigeminal neuralgia, ultrasound guidance, nerve block

1 Introduction

Postherpetic trigeminal neuralgia is a condition in which facial skin herpes arises due to varicella-zoster virus (VZV) infection of the trigeminal ganglion or branches. Facial pain stops or reappears after herpes scab. This type of facial pain belongs to one of the special types of postherpetic neuralgia (PHN) and often presents with burning, shock-like, and needle-like pain. Severe pain can often last for many months or even years (1). Pregabalin, oxcarbazepine, and other first-line antineuralgia drug treatments are commonly used; however, increasing the drug dose may lead to dizziness, drowsiness, and other drug-related side effects, which limit the usage of drugs. The nerve block (NB) is effective in treating PHN; however, it requires repeated multiple injections of analgesic solutions and is, therefore, often not ideal. Because analgesic solution contains steroid hormones, repeated injections can increase the risk of infection in patients with diabetes and individuals with low immunity, limiting the use of NBs to some extent (2).

Recently, pulsed radiofrequency (PRF) has been used to generate high voltage around nerve tissue via pulsed current, regulate pain afferent pathway nerves, reduce inflammatory mediators around damaged nerves, and activate descending inhibitory pathways of pain to produce analgesic effects (3). PRF exhibits no destructive effect on nerve fibers, can reduce pain, and also exhibits less hypoesthesia, soreness, burning pain, and motor nerve injury post-treatment. It should be gradually applied to patients with neuralgia (3). Present studies on postherpetic trigeminal neuralgia have reported that semilunar ganglion nerve block of the trigeminal nerve, ozone injection, PRF, and puncture therapy can be performed under the guidance of computed tomography (CT) and digital subtraction angiography (DSA) (4). However, these methods involve deeper regions of the brain and have the disadvantages of oculocardiac reflex, intracranial infection, ophthalmic nerve injury, and large radiation during puncture and treatment, making them difficult to perform widely (1, 5). Furthermore, very few relevant studies on the use of PRF for targeting peripheral nerves in postherpetic trigeminal neuralgia have been reported. Whether the radiofrequency of trigeminal nerve branches can compensate for this defect and maintain efficacy is not known. Recently, with the development of musculoskeletal ultrasound, accurate PRF targeting peripheral nerves is not possible (6). Therefore, in this retrospective study, we analyzed the efficacy and safety of ultrasound-guided PRF targeting the supraorbital nerve for treating the ophthalmic branch of postherpetic trigeminal neuralgia.

2 Materials and methods

2.1 Clinical data

This study was retrospective in nature, and the Clinical Trial Ethics Committee of the Affiliated Hospital of Southwest Medical University agreed to the study protocol and approved the application form for waiving the signed consent form(registration number: KY2023245). The study meets the relevant requirements of the Declaration of Helsinki of the World Medical Association. The data included in the analysis were de-identified. In total, 86 patients with the ophthalmic branch of postherpetic trigeminal neuralgia who were diagnosed and treated at the Department of Pain, Affiliated Hospital of Southwest Medical University from January 2015 to January 2023, were selected, and 63 patients (Figure 1) were included based on the inclusion criteria and exclusion criteria. There was no sex limitation, the patients' age ranged from 42 to 86 years (63.58 ± 11.87), and the duration of the treatment was 30–7,200 days (206.04 ± 917.89). The patients were divided into the following two groups based on the treatment method: the nerve block group (NB group) and the PRF-combined NB group, hereinafter referred to as the radiofrequency combined NB group (PRF group). In total, 32 patients were present in the NB group, and 31 patients were present in the PRF group.

The inclusion criteria were as follows: (1) the area involving the nerve was the first branch of the trigeminal nerve; (2) the diagnosis of the patient was PHN (2); (3) no significant pain relief was achieved after nonsurgical treatment (including drugs and traditional therapy); and (4) the visual analog scale (VAS) score was $\geq$ 4.

The exclusion criteria were as follows: (1) patients with local ulcerated infection; (2) those with severe cardiopulmonary failure; (3) those with mental disorders; (4) those with coagulopathy; (5) those in which other treatments, such as spinal cord stimulation, trigeminal semilunar ganglion balloon compression, and traditional Chinese medicine, were used during treatment; (6) those who received other treatment options after discharge; and (7) those lost to follow-up or with incomplete data.

2.2 Treatment methods

The experimental set-up included radiofrequency equipment and drug ultrasound model Terason t3000TM ultrasound system (manufactured by Teratech, Burllington, MA01803, USA). A high-frequency linear array probe was used for probe selection. The radiofrequency thermostat (model R-2000BA1, Beijing Beiqi Medical Technology Co., Ltd.) and radiofrequency electrode

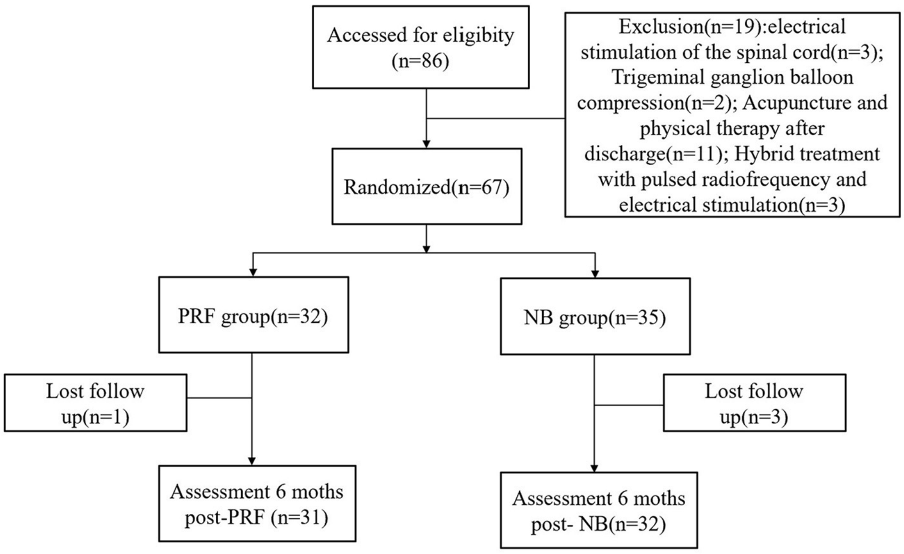

FIGURE 1
Study population and follow-up flowchart.

trocar (model 20G, Innoman Medical Technology Co., Ltd.) were used. As a part of the experimental protocol, lidocaine hydrochloride injection (Double-Crane Pharmaceutical Co Ltd), dexamethasone sodium phosphate injection (Dexamethasone, Zhengzhou, Zhuofeng Pharmaceutical Co. Ltd), and mecobalamin injection (Mecobalamin, Mecobalamin) were also used. Both groups were treated with ultrasound-guided supraorbital nerve therapy.

In the NB group, the patients were placed in the supine position with a padded pillow below the head. The neck was slightly flexed, and the frontofacial eyebrow arch was located via ultrasound. Continuous hyperechoic cortical acoustic shadows, i.e., the eyebrow arch, were observed. The ultrasound was moved caudally, and the hyperechogenicity showed interrupted notches, i.e., the supraorbital foramen or supraorbital notch (Figure 2). After routine disinfection and draping, local intradermal injection of 1% lidocaine anesthesia was administered. To perform the ultrasound-guided in-plane technique, a needle was subcutaneously punctured through the skin, avoiding the supraorbital artery, to the supraorbital foramen (or supraorbital notch). Then, 1 mL of the analgesic complex solution was injected (containing 40 mg of 2% lidocaine injection + 0.5 mg of mecobalamin injection + 5 mg of dexamethasone sodium phosphate injection + 10 mL of 0.9% sodium chloride in). After injecting, the patient was observed for 15 min and returned to the ward after confirming that there was no abnormality.

In the radiofrequency group, the localization was the same as that in the NB group. After routine disinfection and draping, 1% lidocaine was injected as the local anesthesia. The supraorbital artery was avoided under ultrasound guidance. After radiofrequency electrode trocar puncture into the supraorbital foramen (or supraorbital notch), frontoparietal tingling sensation was induced via electrical stimulation at 0.2–0.3 V and 50 Hz. A tingling sensation was induced in all patients. PRF selection parameters were as follows: 70 V, 2 Hz, 20 mS, 40°C, and 6 min and 70 V, 2 Hz, 20 mS, 42.0°C, and 6 min. Then, 1 mL of analgesic complex solution was injected at the end of surgery. After the surgery was complete, the patient was observed for 15 min and returned to the ward after confirming that there was no abnormality.

2.3 Efficacy evaluation methods

2.3.1 Pain evaluation

Pain was evaluated using the VAS score, which was expressed as the intensity of pain from 0 to 10. A score of 0 indicated no pain, whereas a score of 10 indicated severe pain. The patients expressed the degree of pain based on their personal pain perception. Patients were assessed preoperatively and 1 week, 1 month, 3 months, and 6 months postoperatively.

2.3.2 Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) was used for sleep quality scoring, which consisted of 24 questions divided into seven categories (7). Each category had a score of 0–3 points; 0 points indicated no problem in sleeping whereas 3 points indicated difficulty in sleeping. The total score of each category accumulated, with a total score range of 0–2l. The higher the score, the worse the sleep quality.

2.3.3 Pregabalin dose

Pregabalin dose was recorded at 6 months after surgery.

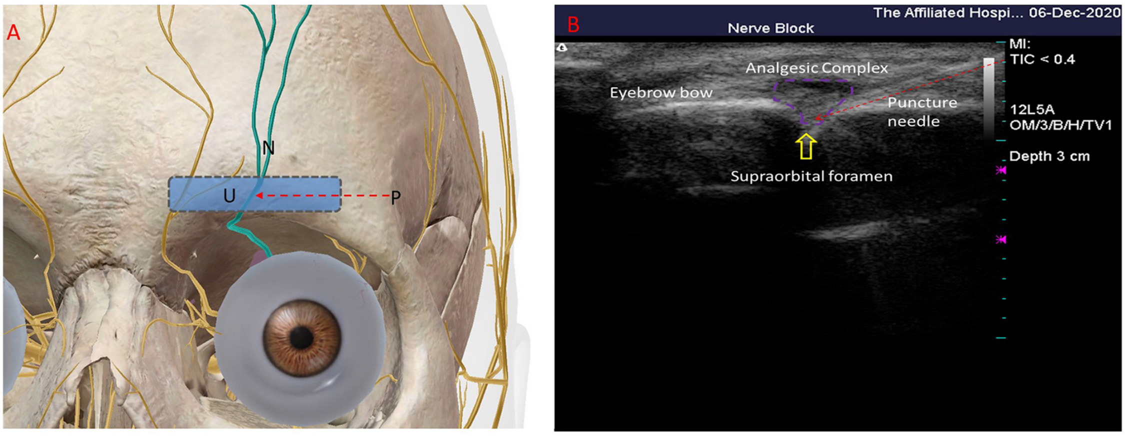

FIGURE 2
Ultrasound-guided supraorbital nerve treatment. **(A)** Schematic of ultrasound probe placement; P, puncture needle; U, ultrasound line array probes; N, supraorbital nerve. **(B)** The signal interrupted on the arch of the eyebrow is the supraorbital notch (indicated by the yellow arrow in the figure); the puncture needle is a strongly echogenic acoustic shadow above the red arrow, oriented as indicated by the red arrow in the figure; the hypoechoic surrounding the supraorbital notch is the analgesic complex fluid—the area surrounded by the purple line.

2.3.4 Efficacy evaluation

The VAS weighted calculation method was used to evaluate the pain relief of patients at 6 months after surgery. Combined with the modified MacNab evaluation criteria, (8) the efficacy was divided into the following four levels: excellent, good, fair, and poor. The excellent effect was that the pain disappeared and the VAS score decreased by > 75%. The good effect was that the VAS score decreased by 51%–75%. The fair effect was that the VAS score decreased by 26%–50%, and the poor effect was that the VAS score decreased by ≤ 25%.

The response rate was calculated as follows: (excellent + good + fair)/total number of cases × 100%.

2.3.5 Complications during surgical treatment

The patients were followed up for 6 months after surgery. Incidence of local infection, local hematoma, scalp numbness, abnormal vision, and other complications during and after PRF was recorded.

2.4 Statistical methods

Data was processed using the IBM SPSS 26.0 software, and GraphPad Prism9 was used for mapping the results. The data conforming to normal distribution are expressed as mean ± standard deviation (± *s*), and the differences between the two groups were compared using an independent sample *t*-test. The intragroup comparisons were performed using one-way ANOVA, and repeated comparisons were performed using Bonferroni. Enumeration data are presented as frequency and rate, and differences were compared using the χ^2 test. Rank data were compared using the nonparametric rank-sum test. A $P < 0.05$ was considered statistically significant.

3 Results

3.1 Comparison of preoperative general conditions between the NB and PRF group

There was no significant difference in age, sex, course of disease, VAS and PSQI scores, and pregabalin dose between the two groups before surgery ($P > 0.05$) (Table 1).

3.2 Observations regarding the VAS score

The postoperative VAS scores of both PRF and NB groups were lower than the preoperative VAS scores at 1 week, 1 month, 3 months, and 6 months after surgery. The VAS scores of the PRF group gradually decreased from 1 to 6 months after surgery. The difference between the two groups at postoperative 1, 3, and 6 months was statistically significant ($P < 0.01$) (Figure 3), i.e., the VAS scores at a postoperative interval of 1 month indicated that the PRF group had better pain control (Figure 3).

3.3 Observations regarding the PSQI score

Compared with the preoperative conditions, significant differences were found in the general conditions in the NB group at postoperative intervals of 1 week, 1 month, 3 months, and 6 months ($P < 0.05$), indicating that the sleep quality was improved after the surgery. When compared within the groups at postoperative 1 week, 1 month, 3 months, and 6 months, the general conditions showed no statistically significant differences ($P > 0.05$). Compared with preoperative conditions, there were significant differences in the general conditions in the PRF group at postoperative intervals of 1 week, 1 month, 3 months, and 6 months (*P*

TABLE 1 Comparison of preoperative general conditions between the two groups.

Group	Number of cases	Age	Sex (male/female case)	Disease duration (Day, $\bar{x} \pm s$)	Preoperative VAS score (min, $\bar{x} \pm s$)	Preoperative PSQI score (min, $\bar{x} \pm s$)	Pregabalin (mg, $\bar{x} \pm s$)
NB group	32	63.5 ± 12.1	21/11	107.1 ± 255.5	6.7 ± 0.7	16.4 ± 2.7	192.1 ± 68.5
PRF group	31	63.6 ± 11.7	18/13	308.0 ± 1,285.5	6.4 ± 0.8	16.3 ± 1.9	179.0 ± 76.6
t (χ^2) value	-	−0.059	0.610	−0.867	1.676	0.189	0.719
P-value	-	0.953	0.544	0.389	0.099	0.851	0.475

VAS, visual analog scale; PSQI, Pittsburgh Sleep Quality Index; NB, nerve block; and PRF, pulsed radiofrequency.

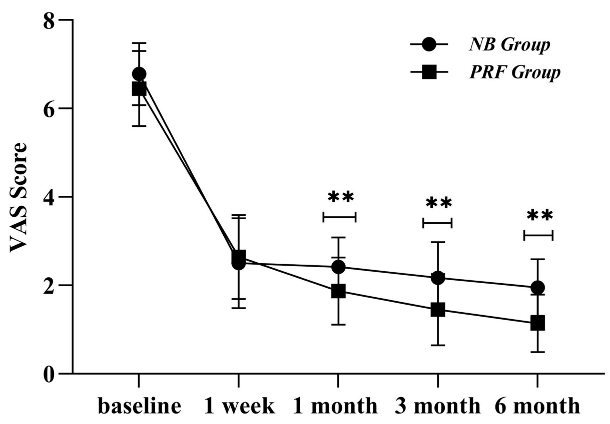

FIGURE 3
Postoperative VAS scores of the two groups of cases; **indicates $P < 0.01$.

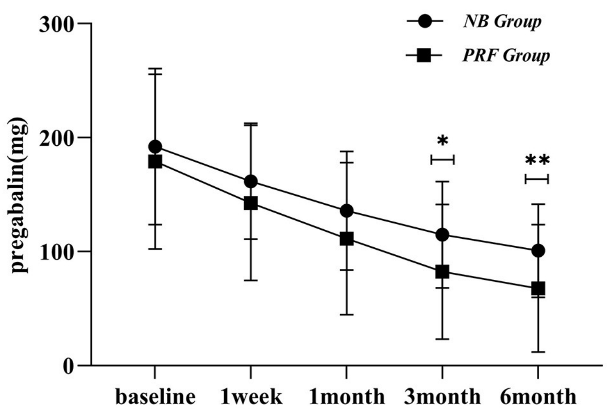

FIGURE 5
Comparison of postoperative oral pregabalin in the two groups, *indicates $P < 0.05$, **indicates $P < 0.01$.

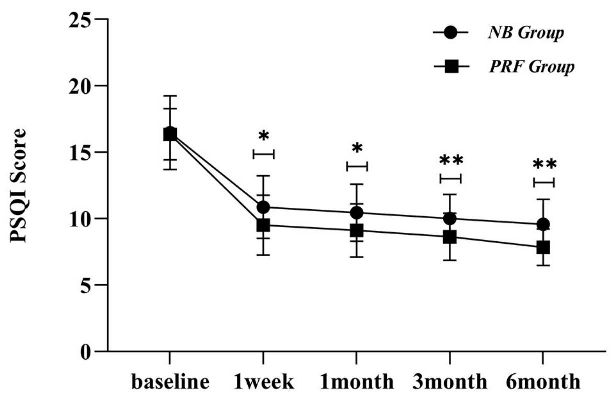

FIGURE 4
Postoperative PSQI scores in both groups; *indicates $P < 0.05$, **indicates $P < 0.01$.

< 0.05), indicating that the sleep quality was improved after the surgery.

The comparative PSQI scores between the PRF group and the NB group at postoperative intervals of 1 week, 1 month, 3 months, and 6 months are presented in Figure 4, and the differences were statistically significant ($P < 0.05$). The PSQI scores of the PRF group were lower than those of the NB group after the surgery, indicating that the sleep quality in the PRF group was better than that of the NB group.

3.4 Pregabalin dose

Compared with the preoperative conditions, there were significant differences in the general conditions in the NB group at postoperative intervals of 1 week, 1 month, 3 months, and 6 months ($P < 0.05$), indicating that the dose of oral pregabalin was reduced after the surgery. When compared within the groups at postoperative intervals of 1 week, 1 month, and 3 months, the general conditions showed no statistically significant differences ($P > 0.05$). However, there were statistically significant differences between general conditions at postoperative 6 months and postoperative intervals of 1 week, 1 month, and 3 months ($P < 0.05$). Compared with the preoperative conditions, there were significant differences in the general conditions in the PRF group at postoperative intervals of 1 week, 1 month, 3 months, and 6 months ($P < 0.05$), indicating that the dose of oral pregabalin decreased after the surgery (Figure 5).

There were significant differences in pregabalin dose between the PRF and NB groups at postoperative intervals of 3 and 6 months ($P < 0.05$). The PRF group was administered fewer pregabalin doses after surgery than those administered in the NB group.

3.5 Efficacy evaluation of treatments in the two groups at a postoperative interval of 6 months

After a follow-up of 6 months, the effect in the PRF group was excellent compared with that in the NB group, with an overall response rate of 90.32%, whereas the overall response rate in the NB group was 81.25%. The nonparametric rank-sum test analysis of the response rate in the two groups showed a Z value of −2.055 and *P*-values of >0.040 and <0.05, indicating that the differences were statistically significant (Table 2). Both the PRF and NB groups showed alleviation of the pain of patients with PHN, with patients in the PRF group presenting long-term pain relief owing to the higher excellent, good, and overall response rates.

3.6 Complications

No treatment-related complications, including local infection, local hematoma, and decreased visual acuity, were observed during treatment in both groups. Among the patients in the PRF group, one patient developed frontofacial scalp numbness, which was relieved after 1 week of intramuscular cobalamin, and three patients developed periocular ecchymosis, which was relieved after 1 week.

4 Discussion

O'Neill et al. (9) reported that approximately 10%−15% of herpes zoster cases involve the trigeminal nerve. Bouhassira et al. stated that PHN is a severe condition accompanied by local skin itching, hyperalgesia, and paresthesia, with pain lasting from months to decades, which considerably affects daily life and work (10). Traditional drugs and NBs are often unsatisfactory in treating PHN, which mainly manifested as intolerance to the side effects of the drug treatment or shorter maintenance time (2). Herein, PRF of the supraorbital nerve was used to treat the ophthalmic branch of PHN. PRF treatment could effectively relieve pain, improve sleep quality, and reduce the dose of pregabalin administered. All treatments in patients of the PRF group were ultrasound-guided, and the supraorbital nerve could innervate the frontofacial region through the supraorbital foramen or supraorbital notch out of the eyebrow arch, which is the anatomical basis for treating frontofacial PHN (Figure 2). Javier et al. used ultrasound-guided PRF of the infraorbital nerve to treat the second branch of PHN and reported that the structures around the nerve and blood vessels were observable under ultrasound, which facilitated avoiding of blood vessels (6); however, only one case was enrolled in this study, whereas studies on ultrasound-guided PRF of the supraorbital nerve are lacking. Using high-frequency ultrasound scanning, we found that the hyperechoic bone was interrupted by the supraorbital foramen or notch and observed the supraorbital artery, which provided a theoretical basis for our study.

Herein, we found differences between the VAS scores of the two groups at postoperative intervals of 1, 3, and 6 months and between the PSQI scores at a postoperative interval of 1 week. Furthermore, the PSQI and VAS scores in the PRF group were lower than those in the NB group, and the PRF group presented better pain control and sleep quality improvement than those in the NB group. The reason for this observation was that PRF regulation of the peripheral nerves has a good effect on neuralgia; Erdine et al. found that PRF can affect adenosine triphosphate metabolism and ion channel function in the sensory nerves, continuously and reversibly inhibit the occurrence of C-fiber-evoked potentials, and stimulate the central process to activate the brainstem descending inhibitory system to achieve endogenous analgesia (11); thus, it blocks pain conduction through related nerves. Liu et al. enrolled 32 patients with the first branch of PHN and used DSA-guided PRF of the trigeminal ganglion (5), and the results showed that the pain was considerably reduced in 30 patients after the PRF treatment. Compared with our study, the difference lay in the guidance mode and therapeutic target, which was operated under DSA, and the therapeutic position was the semilunar ganglion of the trigeminal nerve. Herein, we set the radiofrequency parameters for high voltage and long duration, with voltage being 70 V and time being 6 min at 40°C and 6 min at 42°C (12). The therapeutic parameters were 42°C, 2 Hz, 20 ms, and 8 min. Wan et al. used CT-guided puncture of the semilunar ganglion of the trigeminal nerve to treat the first branch of the postherpetic trigeminal nerve, with 60 patients in the long-term high-voltage group (40 V → 60 V to 100 V, 2 Hz, 20 mS, 900 S) and 60 patients in the standard group (40 V, 2 Hz, 20 mS, 120 S) for three cycles (13), and the results showed that the long-term high-voltage group had higher VAS score, 36-item short-form survey score, and pregabalin dose than those of the standard radiofrequency group; the adverse reactions were observed mainly in seven patients of the standard group and 11 patients of the long-term high-voltage group presenting with facial swelling. Herein, the supraorbital nerve was selected as the treatment target, and ultrasound guidance was employed for a long duration of 12 min at 70 V, which was one of the reasons for the high, excellent, and good rates (70.96%). Combined with clinical practice, our observation regarding CT-guided transforamen ovale puncture of the semilunar ganglion of the trigeminal nerve was as follows: The difficulties in regulating the semilunar ganglion of the trigeminal nerve were because of the need for guidance by a large-scale medical equipment, high technical requirements, long puncture path, swellings in easy-to-puncture blood vessels, decrease in the heart rate induced by the easy-to-occur vagal reflex when entering the foramen ovale, increased blood pressure, severe cardiac arrest, finding of the ophthalmic branch of the semilunar ganglion of the trigeminal nerve after entering the foramen ovale, increased radiation exposure due to repeated puncture scan, cerebrospinal fluid leakage, and the risk of a cerebral hemorrhage.

Liu et al. conducted a retrospective analysis of 32 patients with PHN (5); DSA was used to guide the percutaneous puncture of the semilunar ganglion of the trigeminal nerve, and 93.75% of patients achieved considerable pain relief, with only two patients returning to the hospital for treating recurrence; however, a control group was lacking in the study. Herein, six cases in the NB group and three cases in the PRF group had poor effects, which was higher than those in the aforementioned studies. The reasons for this observation were as follows: ① NB was

TABLE 2 Efficacy evaluation at postoperative 6 months in both groups.

Group	Number of cases	Superior (case, %)	Good effect (case, %)	Fair effect (case, %)	Poor effect (case, %)	Overall response rate
NB group	32	7,21.87%	10,31.25%	9,28.12%	6,18.75%	26,81.25%
PRF group	31	15,48.38%	7,22.58%	6,19.35%	3,3.22%	28,90.32%
Z-value		-2.055				
P-value		0.040				

NB, nerve block; PRF, pulsed radiofrequency.

effective but the duration was short and easy to repeat; ② the supraorbital nerve was one of the many branches of the ophthalmic branch, and other branches may not be regulated; and ③ the regulation of semilunar ganglion of the trigeminal nerve may be superior compared to the peripheral nerve regulation. Regarding other treatment methods, Liu et al. (14) performed subcutaneous short-course peripheral nerve stimulation in 26 patients with the first branch of PHN in the subacute phase (30–90 days). The postoperative VAS score was considerably reduced, with a VAS score of >3 being reduced to <4%, with an effective rate higher than that in the present study, and medication was also reduced; the reason was believed to be the long-term regulation of the diseased nerve (15), which was consistent with the results of long-term nerve regulation in the sciatic nerve injury rat model (5). Zhao et al. (16) reported a case study where cervical spinal cord stimulation combined with supraorbital subcutaneous electrical stimulation and transforamen ovale electrode placement achieved good clinical efficacy. Even though this was at the forefront of clinical practice, it was rarely carried out, and the study lacked large-sample data to confirm the efficacy and safety.

Gabrhelík et al. and Eghtesadi et al. reported that PRF is currently the more commonly used treatment for neuropathic pain (15, 17), especially for PHN (18, 19). PRF plays an important role in pain diagnosis and treatment and is an effective and convenient neuromodulation technique, that can efficiently alleviate pain and improve sleep quality when used in combination with NB. Simultaneously, ultrasound can be utilized to observe the real-time and dynamic adhesion and edema of the tissue around the supraorbital nerve to avoid important tissues such as the eyeball, supraorbital artery, and other structures, and allows treatment to be focused on the target tissues with lesions, optimization of the treatment plan, improvement of the efficacy, and providing of a new treatment plan and method for the ophthalmic branch of PHN. This study was a retrospective analysis; the patients lacked preintervention balance but were screened according to the inclusion criteria and followed up for 6 months, which is a relatively short follow-up time; thus, further study is needed for validating the long-term efficacy of the PHN treatment.

In conclusion, supraorbital nerve PRF can effectively control the pain of the first branch of the trigeminal nerve after herpes zoster, improve the quality of sleep, and reduce the dose of pregabalin; it is safe to be operated under ultrasound guidance, and it has little damage to the ocular tissues, vascular nerves, and so on. This method provides a new treatment option and treatment modality for the ocular branch of postherpetic trigeminal neuralgia. However, the first branch of postherpetic trigeminal neuralgia includes branches of the supraorbital nerve, the supratrochlear nerve, and the nasociliary nerve. This method treats most of the area innervated by the first branch of the trigeminal nerve, and the other innervated areas of the nerve still need to be further researched and explored for effective treatment modalities and methods. The parameters of PRF treatment of the first branch of trigeminal neuralgia after herpes zoster, such as the length of time of the pulse treatment and the amplitude of the voltage, need to be further explored and studied.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving humans were approved by the Affiliated Hospital of Southwest Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the local legislation and institutional requirements.

Author contributions

FL: Writing—original draft, Writing—review & editing. GG: Formal analysis, Writing—review & editing. YZ: Data curation, Writing—review & editing. CO: Supervision, Writing—review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Correlation between bony structures of the posterior cranial fossa and the occurrence of hemifacial spasm

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Objective: To quantitatively study the measurement data related to the bony posterior cranial fossa and explore the correlation between bony posterior cranial fossa morphology and the occurrence of hemifacial spasm.

Methods: A total of 50 patients with hemifacial spasm who attended the Department of Neurosurgery of China-Japan Friendship Hospital from October 2021 to February 2022 were included, and 60 patients with minor head trauma excluding skull fracture and intracranial abnormalities were included as controls. Cranial multilayer spiral CTs (MSCTs) were performed in both groups, and multiplanar reconstruction (MPR) was used as a postprocessing method to measure data related to the posterior cranial fossa in both groups.

Results: Compared with the control group, the anteroposterior diameter (labeled AB) and the height (labeled BE) of the bony posterior cranial fossa, the anteroposterior diameter of the foramen magnum (labeled BC), the length of the clivus (labeled AB), and the length of the posterior occipital (labeled CD) in the HFS group were all reduced, and the differences were statistically significant. BE is positively correlated with AB and CD, with a stronger correlation observed between BE and AB ($r = 0.487$, $p < 0.01$). AB is negatively correlated with AD ($r = -0.473$, $p < 0.01$). The remaining correlations between the data were not statistically significant. There was no overlap in the 95% confidence interval for any of the measurements between the hemifacial spasm group and the control group.

Conclusion: There is a correlation between the posterior cranial fossa and hemifacial spasm.

KEYWORDS

hemifacial spasm, multiplanar reconstruction, posterior cranial fossa, skull, length

Introduction

Hemifacial spasm (HFS) is a common clinical cranial nerve disease that clinically manifests as episodic, recurrent, involuntary tics of facial expression muscles in the area of facial nerve innervation. The disease progresses slowly, the duration of the disease is long, and severe symptoms have a huge impact on the patient's life and work (1, 2). The vast majority of HFS cases are caused by vascular compression in the root exit zone (REZ) of the facial nerve,

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and microvascular decompression (MVD) is the only effective way to cure the disease by relieving the compression of the REZ blood vessels of the facial nerve (3–6). However, why HFS occurs in some people, how vascular compression nerves are produced, and whether there are anatomical specificities associated with the disease are unclear. In studies on the pathogenesis of HFS, no studies have been reported on the correlation between posterior fossa-related bone data and the pathogenesis of HFS in HFS patients. Therefore, we designed this case-control study to perform multislice hyperlux CT (MSCT) examination of the brain in HFS and control patients using multiple plane reconstruction (MPR) as a postprocessing method, quantitatively studying the relevant measurement data of the bony posterior fossa, and exploring the correlation between posterior fossa bony abnormalities and the incidence of HFS to further deepen the understanding of the etiology of HFS.

Materials and methods

Patient population

Fifty patients with HFS diagnosed in the neurosurgery department of China-Japan Friendship Hospital from October 2021 to February 2022 were selected by the random number table method, and patients with intracranial space-occupying lesions, vascular malformations, hydrocephalus and other secondary conditions were excluded. Because MSCT examination is radioactive, based on ethical considerations, the control group included 60 patients with mild head trauma who were admitted to China-Japan Friendship Hospital at the same time, excluding patients with skull fracture and intracranial abnormalities and excluding patients with HFS and brain surgery history. There were 30 males and 20 females in the HFS group, with an average age of 49.04 years. There were 36 males and 24 females in the control group, with an average age of 48.51 years. There was no significant difference in age or sex between the two groups. The study was designed with the approval of the Ethics Committee, and all subjects were informed of the nature of the study and signed an informed consent form.

Imaging examination and measurement methods

Philips Health care 256-slice spiral CT examinations were performed, and the standard optimized skull scanning plan was applied. The current was 250 mA, the voltage was 120 kV, the spiral scanning layer thickness was 2 mm, the interval was 2 mm, and the pitch was 10 mm. Reconstruction parameters: the layer thickness of the standard algorithm was 1.0 mm, and the reconstruction interval was 0.6 mm. The scanning range included the entire skull from the lower edge of the first cervical vertebra. The scanned data were reconstructed by the bone algorithm to obtain the original axial images, which were then transmitted to the image postprocessing workstation for the reconstruction of the sagittal image by MPR, with a window width/window position of 1,500 HU/400 HU. As shown in Figure 1, items measured on sagittal images with posterior fossa osseous data included: (1) the length of the clivus (marked AB), which was the distance from the vertex of the dorsum sellae to the bony front of the anterior lip of the foramen magnum; (2) the anterior-posterior diameter (marked as BC), which was the distance between the anterior and posterior bony edges of the lip of the foramen magnum; and (3) the length of the posterior occipital (marked as CD), which was the distance between the bony posterior edge of the foramen magnum and the intraoccipital tuberosity. (4) The anterior-posterior diameter (labeled AD) was the distance from the dorsum sellae to the intraoccipital tuberosity. (5) The height (labeled BE) was the minimum distance between the line from

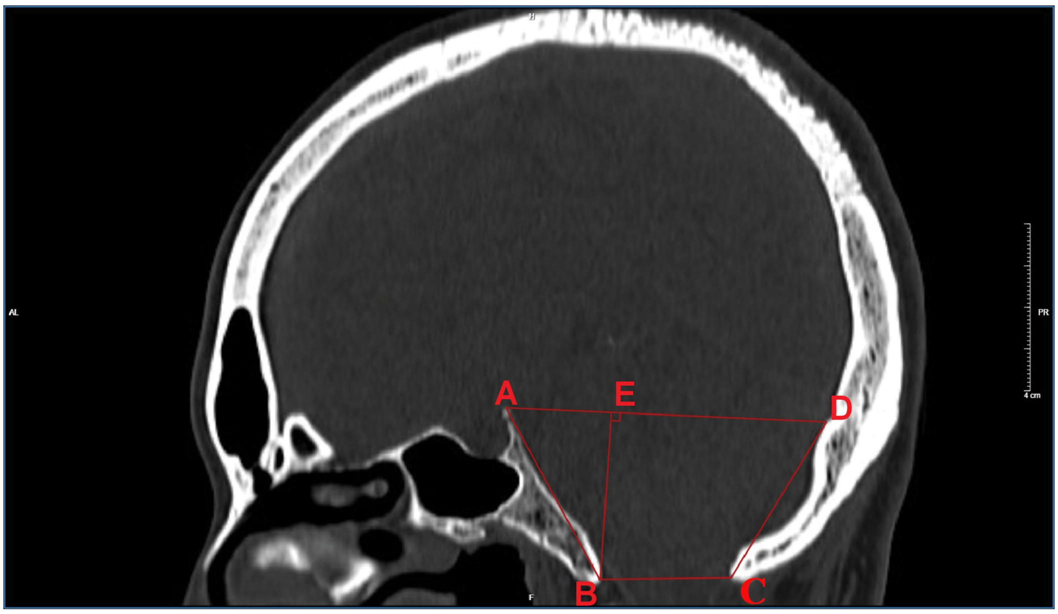

FIGURE 1
Schematic diagram of measuring method.

TABLE 1 Comparison of MSCT three-dimensional reconstruction measurement results between the control group and the hemifacial spasm group ($\bar{x} \pm s$).

Variable (mm)	Control (*n* = 60)	HFS (*n* = 50)	*T* value	*p*-value
AB	47.49 ± 2.71	44.29 ± 5.48	3.977	<0.001
BC	35.43 ± 2.57	32.99 ± 3.20	4.425	<0.001
CD	46.15 ± 5.09	42.62 ± 5.15	3.597	<0.001
AD	83.81 ± 5.17	77.69 ± 9.49	4.292	<0.001
BE	40.39 ± 2.73	36.94 ± 3.15	6.172	<0.001

TABLE 2 The calculation results of Pearson correlation coefficient (*r*) among the hemifacial spasm group.

Variable (mm)	AB	BC	CD	AD	BE
AB	1				
BC	−0.069	1			
CD	−0.029	−0.150	1		
AD	−0.473**	0.185	0.189	1	
BE	0.487**	0.015	0.318*	−0.118	1

*$p < 0.05$; **$p < 0.01$.

TABLE 3 95% CIs for measurements of bony posterior fossa in the control and hemifacial spasm groups.

Variable (mm)	Control (*n* = 60)	HFS (*n* = 50)
AB	46.79–49.19	42.74–45.85
BC	34.77–36.10	32.09–33.91
CD	44.83–47.46	41.16–44.09
AD	82.47–85.15	74.99–80.39
BE	39.69–41.10	36.04–37.83

the sellar tubercle to the intraoccipital tuberosity and the line from the anterior to the posterior lip of the foramen magnum.

Statistical analyses

SPSS23.0 statistical software was used for statistical analysis. All measurement data were first subjected to the Shapiro–Wilk test for normality, and the results indicated that the data met the assumption of normal distribution at the significance level of $\alpha = 0.05$ ($p > 0.05$). The enumeration data were subjected to $\chi 2$ tests, and the measurement results of measurement data were all expressed as $\bar{x} \pm s$. Independent sample *t* tests were used for intergroup comparisons to calculate the Pearson correlation coefficient (*r*). The 95% confidence intervals were calculated for both sets of measurements. $p < 0.05$ was considered statistically significant.

Results

The comparison of the measurement results of the bony posterior fossa between the HFS group and the control group is shown in Table 1. The results showed that, compared with the control group, the measured values of AB, BC, CD, AD and BE in the posterior fossa of patients in the HFS group were decreased, and the differences were statistically significant. The calculation results of Pearson correlation coefficient (*r*) among the data (Table 2) indicate that BE is positively correlated with AB and CD, with a stronger correlation observed between BE and AB ($r = 0.487$, $p < 0.01$). AB is negatively correlated with AD ($r = -0.473$, $p < 0.01$). The remaining correlations between the data were not statistically significant. The 95% confidence intervals showed no overlap between the two groups (Table 3). Our results suggest that the size reduction and morphological abnormalities of the posterior fossa are associated with the development of HFS. Figure 2 shows two typical cases in the HFS group.

Discussion

The incidence of HFS is related to a variety of factors. Jannetta et al. have shown that with age, tortuous sclerosis of the intracranial artery, coupled with brain tissue atrophy, increases the probability of contact between the facial nerve REZ and adjacent blood vessels (6, 7). Other studies have shown that posterior fossa developmental malformations and volume reduction lead to congestion of the posterior fossa contents, increase the chance of vascular compression of the facial nerve REZ, and thickening of arachnoid adhesions to fix blood vessels to facial nerves or limit the elasticity and mobility of blood vessels, all of which contribute to the continuous compression of nerves by blood vessels (7–9). There have been case reports that patients with cerebellar tonsillar hernia and HFS who undergo simple posterior cranial decompression with the suboccipital median approach without facial nerve MVD not only alleviate the symptoms of cerebellar tonsillar hernia but also improve the symptoms of HFS (10). Concomitant HFS can be observed in some cases, such as in cases of cerebellar hematoma, posterior fossa tumor, hydrocephalus, and cerebellar tonsillar herniation, suggesting that a relatively small posterior fossa volume may be a risk factor for the development of HFS (11–13). Pontine cerebellar angle area tumors accounted for 0.8% of the cases of secondary HFS. In addition to the tumor directly compressing the facial nerve, there are also some tumors far away from the facial nerve REZ. The cause of the pathogenesis is simple vascular compression, and the mechanism may be due to the presence of tumors resulting in a relatively narrow posterior cranial space, increasing the probability of blood vessels contacting the facial nerve REZ (14).

The narrow space of the posterior cranial socket leads to crowding of the contents of the pontine cerebellar corner pool, which increases the chance of contact between blood vessels and the facial nerve REZ, and the facial nerve REZ is subjected to long-term compression of blood vessels and demyelinating changes, thereby transmitting signal impulses between nerve fibers and short circuiting, resulting in facial muscle

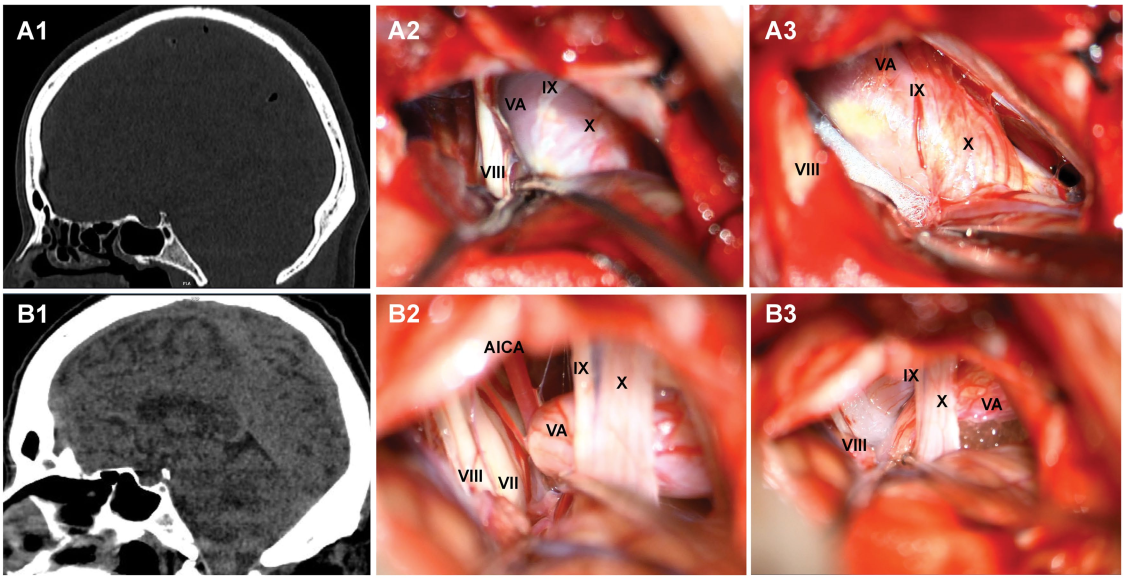

FIGURE 2
Two typical cases of hemifacial spasm. **A1, B1**: MPR post-processing after multi-slice spiral CT examination of the brain indicates that the posterior cranial fossa is narrow; **A2, B2**: exploration of the root of facial nerve in the cerebellopontine angle region revealed the compression of responsible vessels; **A3, B3**: placing padding cotton to separate the responsible blood vessels.

twitching, so theoretically, people with a small posterior fossa space are more likely to develop HFS (8, 15). Literature reports show that women have a more crowded posterior fossa than men, and the probability of HFS in women is higher than that in men. There are also differences in the morphology and structure of the posterior fossa between different ethnic groups, and the incidence of HFS also varies (1).

Based on the above reasons, studying the relationship between posterior fossa volume and bony abnormalities and the pathogenesis of HFS is of great value for further understanding the etiology of HFS. In previous studies, there were some indicators to evaluate the morphology of the posterior fossa. On the one hand, due to the limitations of imaging technology at that time, the accuracy of the data was not satisfactory. On the other hand, some indicators require external measurement software, which lacks operability and simplicity. In this study, MSCT 3D reconstruction technology was used to measure the relevant data of the bony posterior fossa in the HFS group and control group, including the anteroposterior diameter of the bony posterior fossa, height of the bony posterior fossa, anteroposterior diameter of the foramen magnum, slope length, and posterior occipital length, which could basically reflect the bony structure morphology of the posterior fossa. Our results show that the measurement results of MSCT reconstruction of the bony posterior fossa are an important reference for the study of the etiology of HFS. Measuring the relevant data of the posterior fossa can provide a certain basis for clinical interpretation of the onset of hemifacial spasm. Posterior fossa size reduction and morphological abnormalities are associated with the onset of HFS.

Improvement of the accuracy of the results of this study requires analysis of larger samples at a later stage. In this study, MSCT scans were followed by only bone algorithm reconstruction, and soft tissue reconstruction was ignored, which could be supplemented in later studies. Prior to surgery, no vascular-related examinations were conducted on the patients. In subsequent research, we intend to emphasize the study of the relationship between vascular tortuosity morphology and hemifacial spasm, while also exploring whether morphological parameters are associated with the incidence of postoperative complications and the postoperative efficacy. Our results show that developmental abnormalities of the slope in HFS patients are more pronounced than other parts of the posterior fossa. However, no further and more comprehensive analysis of such abnormalities has been carried out, and further research on developmental abnormalities of the slope and sphenoid bone in HFS patients needs to be further improved.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/supplementary material.

Ethics statement

The studies involving humans were approved by China-Japan Friendship Hospital. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article. The animal studies were approved by China-Japan Friendship Hospital. Written informed consent was obtained from the owners for the participation of their animals in this study. Both studies were conducted in accordance with the local legislation and institutional requirements.

Author contributions

TT: Writing – original draft, Writing – review & editing. WY: Data curation, Writing – review & editing. QW: Data curation, Formal analysis, Writing – review & editing. YY: Supervision, Writing – review & editing. LZ: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Management of Meige syndrome with bilateral trigeminal and facial nerves combing

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Objective: Meige syndrome (MS) is an adult-onset segmental dystonia for which no satisfactory remedy currently exists. Our team developed a novel surgical approach called bilateral trigeminal/facial nerve combing (BTFC). This study aimed to evaluate the outcomes of patients who underwent BFTC (Clinical Trial Registry Number: ChiCTR2000033481).

Method: We assigned 22 patients with MS to undergo BTFC. The primary outcome was assessed using the movement subscale of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS-M) at 12 months postoperatively. The second outcome was evaluated using the Medical Outcome Study (MOS) 36-item Short Form Health Survey (SF-36), the dysfunction subscale of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS-D), and the sub-item scores of the BFMDRS-M. Safety outcomes included the House-Brackmann (HB) functional grading score and the visual analog scale (VAS) for facial numbness.

Results: At the final follow-up at 12 months, the BFMDRS-M showed a mean improvement of 70.7% from baseline. Mean scores of the BFMDRS-M sub-motor (including the eyes, mouth, and speech/swallowing) improved by 65.6, 81.00, and 60%, respectively. The median score of the total BFMDRS-D score was 0.70 ± 1.17 compared with 1.86 ± 2.21 at baseline. There were no serious operative complications in this population. The quality of life of the patients significantly improved ($P < 0.05$).

Conclusion: BFTC has proven to be effective in relieving the symptoms of Meige syndrome. This novel surgical approach offers a new alternative treatment for patients who have failed to respond to medications, botulinum toxin injections, and deep brain stimulation (DBS).

Clinical Trial Registration: https://www.chictr.org.cn/bin/project/edit?pid=54567, ChiCTR2000033481.

KEYWORDS

Meige syndrome, combing, trigeminal nerves, facial nerve, BFMDRS-M

Introduction

There are currently no curative solutions for Meige syndrome (MS). According to current guidelines, botulinum toxin injection into the facial musculature is the recommended first-line treatment. However, its efficacy diminishes over time, and some patients may develop antibodies that render the therapy ineffective. In addition, botulinum toxin injections can cause weakness in adjacent muscles and may even aggravate pre-existing dysphagia or dysarthria (1). Deep brain stimulation (DBS) is an alternative, but the effective rate is only 45–53% (2). More effective treatments are urgently needed to improve patients' long-term quality of life.

Current theories suggest that the symptoms of MS are closely related to an imbalance of neurotransmitters in the brain and abnormal functional connections between different brain regions, leading to abnormal cranial nerve function in the head and the face. Neurophysiological findings indicate that the blink reflex circuit is hyperexcitable in patients with MS.

We have discovered from thousands of previous microvascular decompressions (MVDs) that a selective comb. of the trigeminal (V) or facial (VII) nerves is feasible (3, 4) as long as intraoperative monitoring ensures that neither the amplitude of the blink reflex R2 nor the amplitude of the facial EMG decreases by more than 30%.

Therefore, we hypothesized that reducing the hyperexcitability of the blink reflex circuit by combing. the cisternal segments of the trigeminal and facial nerves may alleviate the symptoms of patients with MS.

Based on the above hypothesis, our team conducted a pilot study between 2019 and 2020 involving six patients with MS. Three patients underwent unilateral trigeminal/facial nerve combing on the side with prominent symptoms, followed by a second-stage procedure on the other side 3 months later. The other three patients underwent a one-stage BTFC.

After 1 year, the Burke-Fahn-Marsden Dystonia Rating Scale-Movement (BFMDRS-M) scores in the two-stage group decreased significantly compared to the one-stage group, with a mean reduction of 67.4 and 40.0%, respectively.

However, the efficacy and safety of bilateral combing of the facial and trigeminal nerves need to be further investigated. Therefore, we conducted this single-center prospective clinical trial.

Methods

Trial design and population

We conducted a single-arm trial involving patients with MS at Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine from July 2020 to February 2022. Adult patients (40–75 years of age) with primary MS were eligible for inclusion. The key inclusion criteria included: (1) a confirmed diagnosis of MS; (2) the ability to tolerate general anesthesia; and (3) the normal structure of facial and trigeminal nerves as confirmed by an MRI scan. A detailed list of the inclusion and exclusion criteria is available in Supplementary Appendix 1.

The trial protocol was approved by the Institutional Review Board of Xinhua Hospital. The trial was conducted in accordance with the principles of the Declaration of Helsinki and was registered at the Chinese Clinical Trials Registry (ChiCTR2000033481; 2 June 2020). Written informed consent was obtained from all participants prior to enrollment. All listed authors made significant contributions and vouched for the completeness and accuracy of this report and its adherence to the protocol. The trial complied with the CONSORT guideline.

All patients were evaluated by a movement disorders specialist at our center using a video documentation of the preoperative and postoperative neurological assessments. The examiner was not involved in the initial treatment and was blinded to patient information. The BFMDRS-M and disability subscales were used to evaluate the severity of dystonia (5).

Interventions

Standard surgical procedures

All surgical procedures were performed at Xinhua Hospital Affiliated to Shanghai JiaoTong University School of Medicine. The specific procedure for bilateral trigeminal and facial nerve combing techniques is shown schematically in Figure 1. In brief, short-acting muscle relaxants were used only for tracheal intubation and were not maintained during the operation. Neurophysiological monitoring was employed intraoperatively to measure the amplitudes of the blink reflex (BR) and stimulation-electromyography (stim-EMG) in real time.

The operation was first performed on one side with the patients in a lateral decubitus position using a standard suboccipital retrosigmoid approach. The entire intracranial portion of the trigeminal and facial nerves was exposed. The neurovascular relationship was carefully evaluated to identify any vessels in contact with the nerves. Gelatine sponges were inserted to separate the involved vessels from the nerves. Then, the dorsal third cisternal segment of the trigeminal nerve was combed longitudinally using a custom-made micro-knife (Suzhou, Qimai Inc.). The combing procedure stopped when the amplitude of the blink reflex dropped by 30%. Subsequently, the micro-knife was inserted vertically into the cisternal segment of the facial nerve and combed longitudinally until the amplitude of the stim-EMG dropped by 30%. Afterward, the same procedures were performed contralaterally.

The specific details of intraoperative neurophysiological monitoring are described in Supplementary Appendix 2 and presented schematically in Supplementary Figure 1. All patients received oral drug therapy for 12 months postoperatively, including mecobalamin (0.5 mg tid) and vitamin B12 (20 mg tid), to promote nerve function recovery.

Outcomes

The primary efficacy endpoint was the movement subscale of the BFMDRS-M at 12 months postoperatively, evaluated by two independent investigators using a video recording of the assessments.

The secondary outcomes were (1) changes from baseline to month 12 in the Medical Outcome Study (MOS) 36-item Short Form Health Survey (SF-36), (2) changes from baseline to month

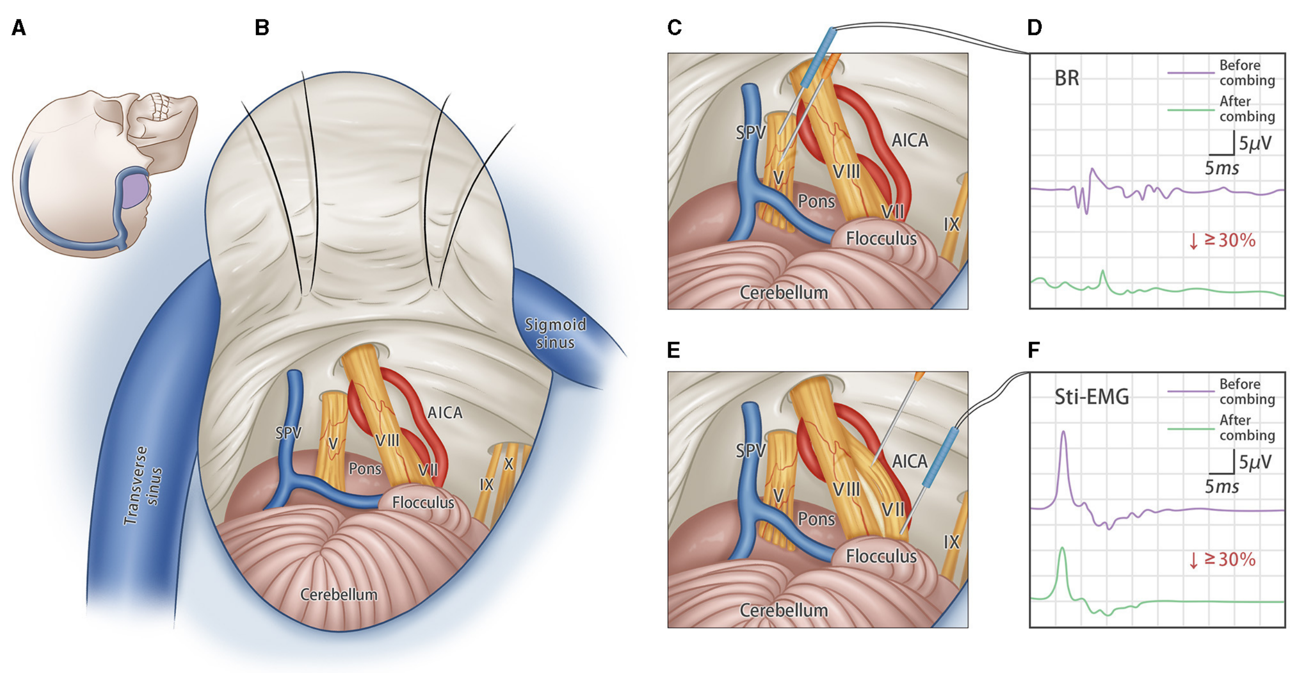

FIGURE 1
Bilateral trigeminal-facial nerves combing surgery. **(A)** Schematic incision of standard retrosigmoid approach; **(B)** Schematic diagram of intraoperative exposure of important structures, showing the CN-V and CN-VII; **(C)** The sensory fibers of the trigeminal root are combed several times longitudinally by using the custom-made micro-knife. **(D)** A concentration probe was used to stimulate the CN-V nerve directly, and the degree of combing was assessed by changes in the amplitude of the blink reflex (BR) before and after combing. Combing stops when the R2 amplitude of BR decreases by more than 30%. **(E)** The facial nerve is combed several times along the nerve fibers. **(F)** Concentric probe is used to directly stimulate the CN-VII nerve, and the degree of combing is assessed by changes in the amplitude of the stimulate-electromyography (stim-EMG). Combing stops when the amplitude of stim-EMG decreases by more than 30%.

12 in the disability subscale of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS-D), and (3) changes from baseline to month 12 in sub-item scores of BFMDRS-M, which includes the assessments of the eyes, mouth, speech/swallowing, and neck.

The primary safety endpoint were as follows:

1. The House-Brackmann (HB) functional grading score at 12 months and
2. The visual analog scale (VAS) for facial numbness at 12 months.

Additionally, intraoperative neurophysiological monitoring and its relationship with BFMDRS-M score and safety outcomes were also analyzed.

Statistical analysis

The trial sample size ($n = 20$) was calculated to ensure 80% power to detect a 10-point (SD = 5) increase in the BFMDRS-M score and to identify any adverse events or other safety outcomes with an expected incidence of at least 8% (6, 7).

An analysis of the primary outcomes was performed using the full analysis set (FAS). For continuous outcomes, the median (95% CI) of the paired difference between baseline and 1 year after surgery was estimated and tested using the Wilcoxon matched-pairs signed rank test. Categorical outcomes were analyzed using McNemar's test. No multiplicity adjustment was applied for secondary endpoints. A sensitivity analysis for the primary outcome was conducted using the per protocol set (PP). Adverse events (AEs) were assessed in the safety set (SS). Multiple imputations were used to address the missing data. All statistical analyses were conducted using R (version 4.2). A p-value of <0.05 (two-sided) was considered statistically significant.

Results

Patients

From 1 July 2020 and 20 February 2022, 26 patients were screened, of whom 22 were enrolled. Four patients were not enrolled because they either declined to provide consent (two patients) or were unwilling to undergo surgery (two patients). Two of the 22 patients were lost to at postoperative follow-up, resulting in 20 patients being included in the outcome analysis. A flow diagram of the enrollment of patients and follow-up is shown in Figure 2.

The clinical characteristics of the patients are summarized in Table 1. The ages of the patients ranged from 41 to 71 years (median age 58.27 years, IQR 49.00–65.50). The median duration

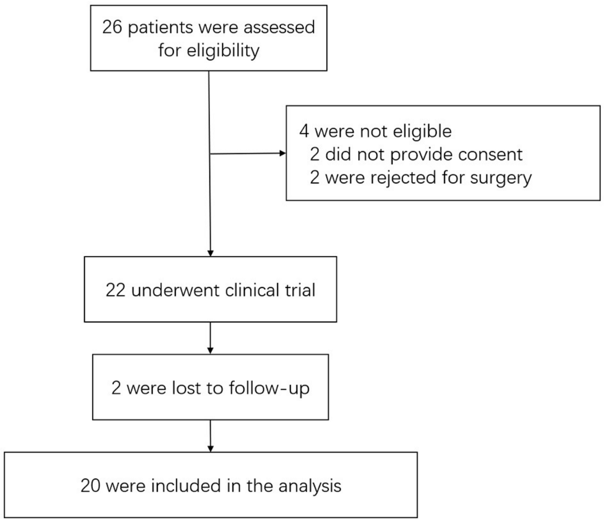

FIGURE 2
Flow diagram.

TABLE 1 Demographic and baseline characteristics of the patients.

Characteristic	Overall ($N = 22$)
Female sex—no. (%)	16 (72.7)
Median age (IQR)—year	58.27 [49.00, 65.50]
Duration of illness (IQR)—months	27.00 [12.00, 48.00]
Botulinum toxin (BTX) treatment history—no. (%)	
Yes	13 (59.1)
No	9 (40.9)
House-Brackmann facial grading system (I grade)—no. (%)	22 (100.0)
Facial numbness score on the VAS (IQR)	1.00 (1.0−1.0)
Burke−Fahn−Marsden Dystonia Rating Scale (BFMDRS)—(median [IQR])	
BFMDRS-M (median [IQR])	15.00 [12.25, 16.00]
BFMDRS-D (median [IQR])	0.50 [0.00, 4.00]
BFMDRS-M subscale	
BFM-eye (median [IQR])	8.00 [6.50, 8.00]
BFM-mouse (median [IQR])	6.00 [4.00, 6.00]
Speech and swallowing (median [IQR])	0.50 [0.00, 2.75]
Neck (median [IQR])	0.00 [0.00, 0.00]

of symptoms was 27.00 months (IQR 12.00–48.00). The baseline data are shown in Table 1.

Primary endpoint

The BFMDRS scores gradually decreased and reached statistical significance at postoperative periods (1 week, 3, 6, and 12 months after surgery). The mean change in the total BFMDRS-M score at 12 months after surgery was 4.03 ± 2.52 compared to 13.77 ± 4.03 at baseline. This represents a mean improvement of 70.7% in the total BFMDRS-M movement scores 12 months after surgery, showing a significantly greater improvement.

We also analyzed the correlation between the BFMDRS-M score and both age and illness duration. Patients were divided into two groups based on age at onset (<55 or ≥55 years) and duration of illness (<2 years or ≥2 years). The mean improvement rates of the BFMDRS-M scores were analyzed 12 months after surgery. The results showed that the postoperative BFMDRS-M score was lower in patients aged <55 years and those with an illness duration of <2 years (Supplementary Figure 2).

Secondary endpoint

At month 12 postoperatively, the mean BFMDRS-M sub-item movement scores were as follows: the score for "Eyes" was 2.52 ± 2.09, with an improvement rate of 65.6% (from the baseline score of 7.27 ± 1.32); the score for "Mouth" was 0.95 ± 1.09, with an improvement rate of 81.00% (from the baseline score of 5.00 ± 2.60); the score for "Speech/swallowing" was 0.60 ± 0.88, with an improvement rate of 60% (from the baseline score of 1.50 ± 1.82); and the score for "Neck" was 0.00 (the same as the baseline score, 0.00; Table 2 and Figure 3).

The median total BFMDRS-D score was 0.70 ± 1.17 at 12 months after surgery compared to 1.86 ± 2.21 at baseline. According to the SF-36, the patients' quality of life improved significantly at 12 months after surgery (Figure 4). This indicates that the surgery alleviated the symptoms of dystonia. After the surgery, patients were able to resume their daily activities and lifestyle.

Safety

Adverse events related to the treatment (as determined by the principal investigator) included facial paralysis and facial numbness.

Seven patients reported facial paralysis after surgery, with facial paralysis classified as House-Brackmann (HB) Grade II. After therapy with oral tablets (mecobalamine, vitamin B12, Salvia, nimodipine, and prednisone), two patients recovered to normal within 3 months, and two patients recovered to normal within 6 months. However, three patients continued to experience facial paralysis at HB Garde II 12 months after surgery. Only one patient reported facial numbness after surgery, and this patient recovered to normal within 12 months.

Changes in blink reflex (BR) monitoring of intracranial stimulation and stim-electromyography (stim-EMG) were recorded before and after the combing process. The median decrease in the R2 amplitude of the BR (BR-R2) was 38% (IQR 3–48). The median decrease in the wave amplitude of the stimulated EMG (Stim-EMG) was 41% (IQR 33–47).

The relationship between the degree of decrease in the wave amplitude of the actual intraoperative blink reflex R2 and stim-EMG and the postoperative BFMDRS-M scores was analyzed.

TABLE 2 Primary, secondary, and safety outcomes at 12 months.

Outcome	Before surgery ($N = 20$)	After surgery (1 year; $N = 20$)	P
Primary outcome			
Burke–Fahn–Marsden Dystonia Rating Scale (median [IQR])			
BFMDRS-M	15.0 (11.5–16.0)	4.0 (2.0–6.0)	<0.001
Secondary outcomes			
BFMDRS-M subscale (median [IQR])			
BFM-eye	7.27 (1.32)	2.52 (2.09)	<0.001
BFM-mouse	5.00 (2.60)	0.95 (1.09)	<0.001
Speech and swallowing	1.50 (1.82)	0.60 (0.88)	0.052
Neck	0.0 (0.0)	0.0 (0.0)	NaN
BFMDRS-D	1.86 (2.21)	0.70 (1.17)	0.042
MOS item short-form health survey (SD)			
General health	55.0 (48.8–61.3)	70.0 (60.0–80.0)	<0.001
Physical functioning	55.0 (48.8–86.3)	85.0 (58.8–96.3)	0.002
Role-physical	25.0 (0.0–37.5)	50.0 (43.8–75.0)	<0.001
Role-emotional	33.0 (0.0–100.0)	67.0 (33.3–100.0)	0.002
Social functional	50.0 (37.5–62.5)	75.0 (50.0–75.0)	<0.001
Bodily pain	100.0 (100.0–100.0)	100.0 (100.0–100.0)	0.15
Vitality	50.0 (45.0–75.0)	75.0 (53.8–80.0)	0.001
Mental health	63.3 (52.5–67.5)	66.7 (66.7–71.7)	0.003
Safety outcomes			
House-Brackmann facial grading system—no. (%)			0.036
I	20 (100)	17 (85)	
II	0 (0)	3 (15)	
Facial numbness score on the VAS (median [IQR])	1.05 (0.21)	1.00 (0.00)	0.347

The results showed that, as the blink reflex and stim-EMG wave amplitudes decreased during the surgical procedure, the BFMDRS-M scores of the patients also decreased (Supplementary Figure 3A).

We analyzed the relationship between the declining rate of stim-EMG wave amplitude and facial paralysis, as assessed by the House-Brackmann facial grading system. The results indicated that, as the stim-EMG wave amplitude declined, the incidence rate of facial paralysis increased. We also analyzed the relationship between the decline in BR-R2 wave amplitude and the incidence rate of facial numbness. The results showed that, as the BR-R2 wave amplitude declined, the incidence rate of facial numbness increased. It is worth mentioning that, when the BR-R2 and stim-EMG wave amplitudes decreased by more than 45%, patients were more susceptible to symptoms of facial numbness and facial paralysis (Supplementary Figure 3B).

Discussion

MS is a functionally disabling disease, characterized primarily by blepharospasm and oromandibular dystonia. The onset of MS typically occurs between the ages of 30 and 70 years (with a mean age of 55.7 years) (1, 8). The prevalence of MS is estimated to be ~36–117 per million people (9). Persistently abnormal contraction of the facial muscles can lead to visual impairment and even functional blindness, as well as difficulties in chewing, swallowing, and speaking, severely affecting patients' quality of life.

The exact etiology and pathogenesis of MS remain unclear; however, various hypotheses have been proposed:

1) Dopaminergic and cholinergic hyperactivity (1, 10),
2) dysfunction of the basal ganglia and thalamus leads to an imbalance of dopamine, anticholinergic, and γ-amino acids, resulting in the dysregulation of neural excitation and inhibition (1, 8), and
3) environmental triggers and genetic predisposition cause plastic changes and reduced cortical inhibition (1).

Despite the unclear pathogenesis of MS, patients with MS exhibit similar clinical manifestations, including varying degrees of eyelid and facial muscle twitching, blinking difficulties, and frequent facial involuntary movements (2, 8). A study by Schwingenschuh et al. found that the R2 recovery cycle was significantly disinhibited in patients with MS (11). Additionally,

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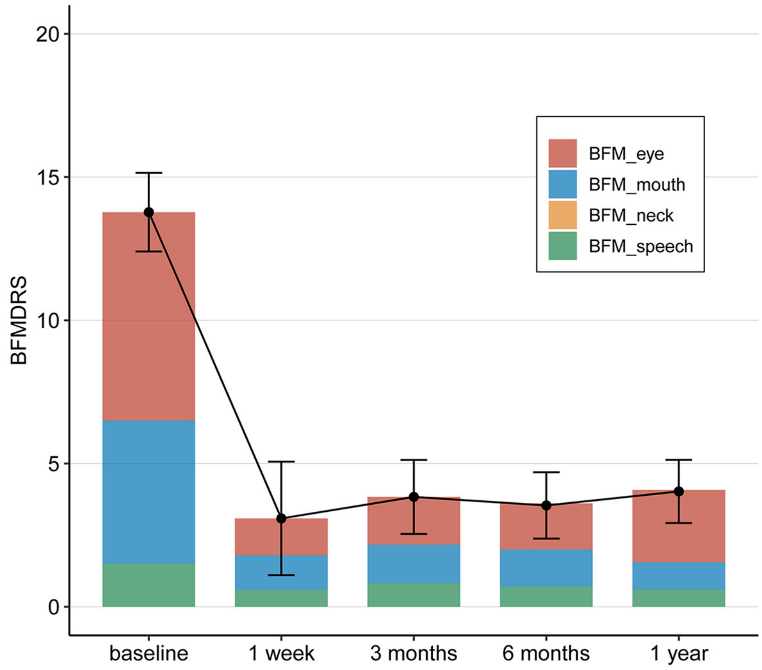

FIGURE 3
The changes in BFMDRS-M pre-operation and 1 week, 3, 6, and 12 months post-operation.

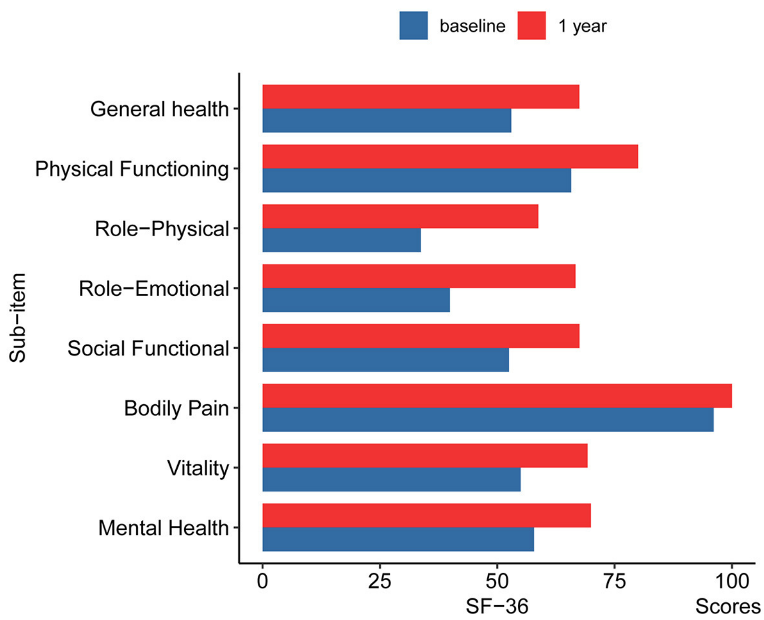

FIGURE 4
The changes of SF-36 in pre-operation and 12 months post-operation. GH, General health; PF, Physical Functioning; RP, Role-Physical; RE, Role-Emotional; SF, Social Functional; BP, Bodily Pain; VT, Vitality; MH, Mental Health.

a clinical, electrophysiological study by Akalin et al. found that patients with MS had the highest mean R2 amplitude and duration values compared to the healthy control group (12). All of these previous studies have shown that the blink reflex circuit is abnormally excited in patients with MS (5).

Based on the observation of abnormal hyper-excitability in the BR circuit, our team developed a new surgical approach called BTFC. This novel treatment aims to improve the abnormal spasticity of facial muscles in patients with MS to reduce the abnormal hyper-excitability of the BR circuit by combing the facial and trigeminal nerves. In a follow-up study involving 20 patients with MS, the total BFMDRS-M score decreased by 70.7% at 12 months after surgery, indicating that BTFC can effectively reduce the symptoms of patients with MS. The degree of improvement in motor symptoms was comparable to that achieved with DBS (6).

However, DBS surgery has several disadvantages, including a long treatment period and the necessity of implanting foreign objects, such as batteries and electrodes, which increases the risk of infection and rejection (7).

As the extent of nerve combing increases during surgery, the degree of symptomatic relief of MS improves, but the risk of facial and trigeminal nerve injury also increases simultaneously. Therefore, balancing the surgical outcome with the risk of facial and trigeminal nerve injuries is important. In our study, we found that reducing the amplitude of intraoperative BR-R2 and facial nerve stim-EMG by 30–45% provided an effective and safer range. Amplitude decreases of <30% were insufficient to achieve satisfactory surgical results, while amplitude decreases of more than 45% increased the risk of postoperative facial paralysis and facial numbness.

Nevertheless, the optimal degree of nerve combing through electrophysiology remains challenging. One patient experienced mild facial numbness after surgery but returned to normal within 12 months. Additionally, 35% (7/20) of the patients had Grade II mild facial palsy symptoms after surgery. After treatment with methylcobalamin and vitamin supplements, facial nerve function returned to normal in most patients (57.1%) within 12 months after surgery, which may also be attributed to the natural recovery process of the facial nerve. Although a few patients continued to experience mild facial palsy symptoms, these symptoms did not have a significant negative impact on their daily lives. This finding also highlights the importance of minimizing the degree of nerve combing to reduce complications.

We also found that BTFC showed varying rates of symptomatic improvement among different patients. Specifically, the improvement of MS was more pronounced in patients with a disease duration of <2 years compared to those with more than 2 years. A study on pallidal-DBS for MS indicated that the course of the disease was negatively associated with postoperative outcomes. Patients with a shorter disease duration experienced a faster onset and longer duration of postoperative effects, and shorter disease duration predicted better clinical outcomes (13). This finding is consistent with our findings.

Younger patients with MS appeared to have better outcomes after surgery. Similarly, a study on DBS in the treatment of MS showed that younger patients with shorter durations of symptoms had better clinical outcomes (13). However, the limited number of cases in this study suggests that more research is needed to completely understand the factors influencing prognosis.

In addition, the nerve combing technique has been widely employed in treatments for other disorders. Our previous studies have demonstrated that combing. the trigeminal or facial nerves effectively and safely treats intractable trigeminal neuralgia and facial spasms (3, 4). Posterior spinal nerve rhizotomy (SPR) can be used to treat limb spasticity by adjusting patient's muscle tone so that the spastic muscles become normal. However, the severed nerve in SPR cannot regenerate, and excessive severance can cause irreparable damage (14, 15). In contrast, nerve combing reduces nerve excitability without completely dissecting the nerve. It is safer under electrophysiological monitoring, making it a useful procedure for patients with limb spasticity and cerebral palsy.

Conclusion

Our study showed that BTFC is an effective and safe treatment for MS. In particular, it provides a new alternative for patients who have failed to respond to medications, botulinum toxin injections, and DBS. Consequently, BTFC is recommended as a second-line treatment option for this disease.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Xinhua Hospital (No. XHEC-C-2020-029). The participants provided their written informed consent to participate in this study.

Author contributions

TY: Conceptualization, Data curation, Investigation, Methodology, Software, Validation, Writing – original draft, Writing – review & editing. HW: Conceptualization, Data curation, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. YT: Conceptualization, Investigation, Validation, Writing – review & editing. HZ: Conceptualization, Investigation, Validation, Writing – review & editing. XC: Investigation, Validation, Writing – review & editing. YS: Investigation, Writing – review & editing. BW: Investigation, Validation, Writing – review & editing. WZhu: Investigation, Validation, Writing – review & editing. PZ: Investigation, Validation, Writing – review & editing. XZ: Investigation, Validation, Writing – review & editing. JZho: Investigation, Validation, Writing – review & editing. XW: Investigation, Validation, Writing – review & editing. XF: Investigation, Validation, Writing – review & editing. JZhu: Data curation, Funding acquisition, Investigation, Methodology, Software, Validation, Writing – review & editing. WZha: Data curation, Funding acquisition, Investigation, Methodology, Software, Validation, Writing – review & editing. SL: Data curation, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2024.1410531/full#supplementary-material

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Interposition versus transposition technique in microvascular decompression for trigeminal neuralgia secondary to vertebrobasilar dolichoectasia: a systematic review and pooled meta-analysis

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Introduction: Limited data are available comparing the interposition and transposition techniques for microvascular decompression (MVD) in patients with trigeminal neuralgia (TN) secondary to vertebrobasilar dolichoectasia (VBD); this study aims to review current findings on TN associated with VBD and compare the interposition and transposition techniques in terms of surgical morbidity and patient outcomes.

Methods: Following the PRISMA guidelines, PubMed/Medline, Web of Science, and SCOPUS databases were searched to identify studies reporting patients undergoing MVD for TN secondary to VBD. The studies were divided into two groups, interposition and transposition, based on the microvascular decompression technique used. Studies not reporting the diagnostic criteria, included less than five cases, or were not available in English were excluded.

Results: Fourteen eligible papers were retrieved, of which five studies reported cases undergoing the interposition technique, eight studies for the transposition technique, and one study reported cases from both groups. Data including preoperative and postoperative BNI class, comorbidities, and postoperative complications were retrieved to analyze and compare the two techniques in terms of efficacy and long-term outcomes in treating TN secondary to VBD.

Conclusion: Both interposition and transposition techniques for MVD yield high rates of pain relief in patients with TN secondary to VBD. While both approaches demonstrate similar efficacy, the interposition method is associated with a lower rate of long-term complications. Further research, preferably through randomized prospective studies, is needed to refine surgical strategies and improve patient outcomes.

KEYWORDS

microvascular decompression, vertebrobasilar dolichoectasia, trigeminal neuralgia, interposition, transposition

Introduction

Trigeminal neuralgia (TN) is a common chronic pain disorder characterized by recurrent episodes of electric shock-like or stabbing pain affecting the dermatomal distribution of trigeminal nerve branches (1, 2). Between 80 and 90% of the cases of TN are caused by a neurovascular conflict where the trigeminal nerve is compressed by an adjacent artery or a vein, with the superior cerebellar artery being the most implicated vessel (1, 3). Less commonly TN is secondary to vertebrobasilar dolichoectasia (VBD), a rare cerebrovascular abnormality characterized by an ectatic, elongated, and tortuous vertebrobasilar artery (VBA) complex (4). These abnormal vessels may sometimes compress, directly or indirectly—thorough displacements of adjacent vessels (5)—the root of the trigeminal nerve resulting in TN (6). Recent published studies report VBD-induced TN accounting for 2–7.7% of all cases of TN (1, 7–10).

At present, there is a global consensus that surgical intervention through microvascular decompression (MVD) is recommended for drug-resistant TN when an offending vessel causing neurovascular compression can be identified. In VBD-induced TN cases, given the unusual anatomy due to the wide and abnormally located vertebrobasilar artery complex, surgical risks are higher. Two techniques can be considered to address this condition: the interposition method and the transposition method. The former represents the standard MVD approach, routinely used in cases of classical TN due to neurovascular conflict; it requires the insertion of implants between the nerve and the offending vessel. The latter entails repositioning the VBA complex using various materials such as aneurysm clips, biomedical glues, Prolene sutures, tapes, and titanium plates. To date, current literature on this topic is scarce, with only one available study that directly compares the two techniques. The purpose of this systematic review and meta-analysis is to review current findings on TN associated with VBD and compare the two techniques in terms of surgical morbidity and postoperative outcomes.

Materials and methods

Search strategy

The systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (11) to investigate the outcomes of Microvascular decompression in patients with trigeminal neuralgia secondary to vertebrobasilar dolichoectasia (VBD) and compare the interposition technique to the transposition technique. A comprehensive literature search of PubMed, Web of Science, and Scopus was performed on for studies published in English from January 1991 to February 2024. Our systematic review was registered and accepted in PROSPERO database with the following ID: CRD42024523971. The keywords and the detailed search strategy are reported in Supplementary File 1. After searching the three databases, all results were collected. Duplicates were removed using Rayyan software (12). All remaining articles were then fully screened by 3 reviewers (FZ, VR, RC); a senior author (FS) resolved discrepancies.

Data extraction

From each study, the following data were extracted: author/s; year of publication; study design, number of patients enrolled; demographic data; mean follow-up time; patient comorbidities; reported prevalence of VBD-induced trigeminal neuralgia; trigeminal neuralgia characteristics (side and branches involved); additional vessels compressing the trigeminal nerve in addition to the VBA; postoperative complications (transient and permanent); preoperative BNI; postoperative BNI and BNI at last follow up.

Statistical analysis

Meta-regression and meta-analysis of proportions with binomial distribution were used to assess the effect of MVD transposition and interposition post-operatively and at the last follow-up. The pooled prevalence of BNI was calculated using the inverse variance method, adopting fixed effects models if the tests met the hypothesis of homogeneity, or random effects model otherwise (13). Heterogeneity across the included studies was analyzed using the Q test and the I^2 index (values of 25, 50, and 75% are taken as low, medium, and high heterogeneity, respectively) (14). Subgroup analyses were performed by the intervention type. A forest plot was used to present the pooled prevalence. The leave-one-out sensitivity test was used to confirm that the findings were not driven by any single study. In addition, Egger's tests were used to detect potential publication bias by examining the funnel plot symmetry. The odds ratio (OR) for the development of postoperative complications in both cohorts, including 95% confidence intervals (CI), was calculated. A p-value <0.05 indicated statistical significance. Statistical analyses were performed using STATA18 software.

Quality scoring

Three authors (FZ, VR, and RC) independently assessed the risk of bias for each included study using the Risk of Bias In Non-randomized Studies—of Interventions (ROBINS-I) tool (15). The quality of evidence for outcomes was assessed by the Joanna Briggs Institute (JBI) critical appraisal checklist (16).

Outcomes

The primary outcomes of this systematic review and meta-analysis were the following: (1) to determine the prevalence and clinical features of TN secondary to VBA, and (2) to analyze the different surgical strategies and related clinical outcomes and complication rate. We compared the efficacy of interposition and transposition methods by assessing the Barrow's Neurological Institute (BNI) grade (17) (Table 1) post-operative and at last follow-up. BNI grades I–II were considered adequate pain relief, whereas BNI grades III–V indicated pain recurrence.

Results

Literature review

The search strategy yielded 160 results. After the removal of duplicates, articles were screened by title and abstract for relevance. The remaining articles were then screened via full text (see the PRISMA diagram shown in Figure 1). Studies meeting the defined criteria were included for quantitative analysis. The characteristics of the individual studies are presented in Table 2. Fourteen studies including 306 patients with trigeminal neuralgia secondary to VBD were analyzed in this review. All included studies presented a retrospective single-center design. The exclusion criteria were the following: (1) studies with less than five patients; (2) case reports; (3) review articles; (4) technical notes; (5) studies published in languages other than English with no available English translations; (6) case series not dealing with trigeminal neuralgia caused by VBA conflict; (7) case series with no specific data on surgical steps performed. Furthermore, we only included studies in which VBD was defined according to specific diagnostic criteria as first proposed by Ubogu and Zaidat (18): basilar artery (BA) or vertebral artery (VA) diameter > 4.5 mm, deviation of any portion >10 mm from the shortest expected course, BA length > 29.5 mm or intracranial VA length > 23.5 mm, BA bifurcation above the suprasellar cistern or any BA portion lying adjacent to the margin of the clivus or dorsum sellae (19).

TABLE 1 Barrow Neurological Institute (BNI) pain intensity score (17).

Score	
I	No trigeminal pain, no medication
II	Occasional pain, not requiring medication
III	Some pain, adequately controlled with medication
IV	Some pain, not adequately controlled with medication
V	Severe pain or no pain relief

Demographic data and risk factors

In our meta-analysis, the reported prevalence of vertebrobasilar dolichoectasia (VBD) among patients who underwent microvascular decompression (MVD) for trigeminal neuralgia ranged from 2 to 7% with a mean prevalence of 4%.

The mean age of patients varied between 54 and 68 years, with males comprising 53% (95% CI: 47–59%) of the cohort. Hypertension was reported in 59% (95% CI: 52–68%) of the patients. The right side was affected in 43% (95% CI: 37–48%) of patients, with the V2 branch being the most frequently involved, accounting for 82% (95% CI: 78–87%) of cases. The most common clinical presentation was the

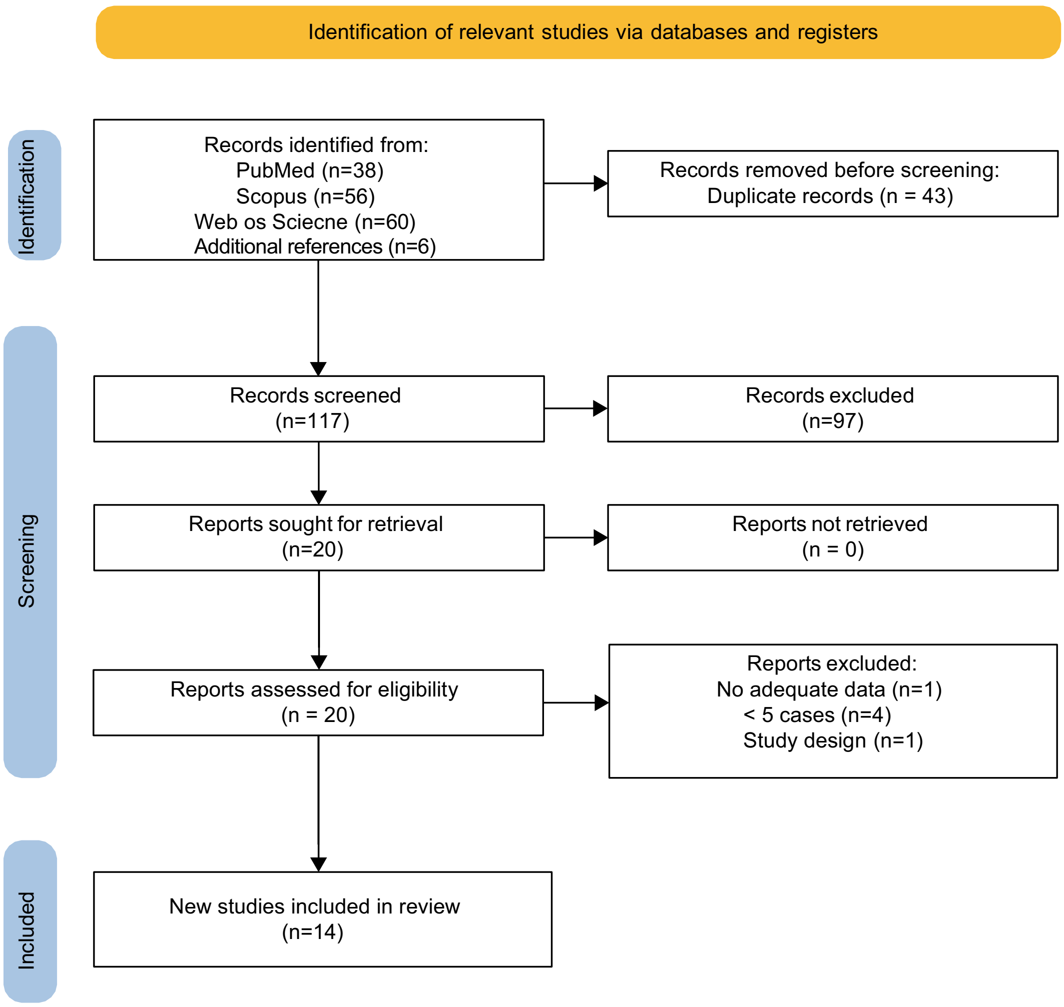

FIGURE 1
PRISMA diagram showing the details of the systematic search of the literature.

TABLE 2 Summary of the studies included in the meta-analyses.

References	Study design	Type of intervention	M/F	Follow-up (mean, months)
Zheng et al. (5)	R	VBA transposition	31/30	24.5
Amagasaki et al. (25)	R	VBA transposition	12/20	37.9
Inoue et al. (20)	R	VBA transposition	13/13	47
Liu et al. (21)	R	VBA transposition	9/13	22
Wang et al (22)	R	VBA transposition	9/14	32
Vanaclocha et al. (23)	R	VBA transposition	5/3	56.5
Linskey et al. (24)	R	VBA transposition	21/10	60
Yang et al. (10)	R	VBA transposition	5/5	
Honey and Kaufmann (29)	R	Interposition	1/1	68.3
		VBA transposition	9/2	
Yu et al. (6)	R	Interposition	21/9	76.67
Shulev et al. (26)	R	Interposition	4/10	66
Sun et al. (27)	R	Interposition	8/7	29.8
Ma et al. (9)	R	Interposition	8/3	22
El-Ghandour (28)	R	Interposition	6/4	93.6

involvement of both V2 and V3 branches (43, 95% CI: 37–48%). Detailed data are reported in Table 3.

Surgical approach and intraoperative findings

In our analysis, we found the retrosigmoid suboccipital to be the most frequently used approach for MVD. Following this approach, the dura mater is incised along the sigmoid and transverse sinuses, then, after a gradual release of cerebrospinal fluid (CSF) from the lateral cerebellar cistern, the cerebellum is retracted medially to facilitate exposure. The arachnoid membrane is then dissected to provide full visualization of the lower cranial nerves.

Other than vertebrobasilar artery (VBA) compression, additional vessels were found to be compressing the trigeminal nerve. The anterior inferior cerebellar artery (AICA) and the superior cerebellar artery (SCA) were the most frequently reported additional offending vessels, involved in 30% (95% CI: 25–36%) and 25% (95% CI: 20–30%) of cases, respectively. Detailed data are reported in Table 3.

There were eight studies reporting patients treated with the transposition technique (5, 10, 20–25), and five studies reporting on the interposition technique (6, 9, 26–28). One case series included patients treated with either technique (29). In the transposition group ($n = 224$), VBA repositioning was achieved using various materials including Teflon sling/roll/pads/felt, biomedical glue, aneurysm clips, Ivalon sponge, autologous muscle, and silicon sheet. In the interposition group ($n = 82$) pieces of Teflon between the trigeminal nerve and the vessel responsible for the neurovascular conflict were placed, without forcing the repositioning of the vessel.

TABLE 3 Demographic data and clinical characteristics.

	N of patients	%	95% CI
Males	162/306	52.94%	47–59%
Reported prevalence of TN secondary to VBD	304/7829	3.88%	3–4%
Comorbidities			
Hypertension	121/205	59.02%	52–66%
Type 2 diabetes	10/205	4.88%	2–8%
Stroke	7/205	3.41%	1–6%
Trigeminal neuralgia characteristics			
Right side involvement	131/306	42.81%	37–48%
V1 involvement	63/306	20.59%	16–25%
V2 involvement	252/306	82.35%	78–87%
V3 involvement	202/306	66.01%	61–71%
V1V2	27/306	8.82%	6–12%
V1V3	1/306	0.33%	0–1%
V2V3	131/306	42.81%	37–48%
V1V2V3	26/306	8.50%	5–12%
VII involvement			
Hemifacial spasm	16/306	5.23%	3–8%
Vessel responsible for compression			
AICA	93	30.39%	25–36%
SCA	77	25.16%	20–30%
Vein	31	10.13%	7–14%
PICA	18	5.88%	3–9%
Trigeminocerebellar artery	2	0.65%	0–2%

Interposition vs. transposition: clinical outcomes and postoperative complications

The pooled analysis (Figure 2) demonstrated that the interposition approach resulted in post-operative Barrow Neurological Institute (BNI) grades I-II in 97% (95% CI: 84–100%, $I^2 = 59.5\%$, $p = 0.03$) of cases, compared to 98% (95% CI: 93–100%, $I^2 = 27.5\%$, $p = 0.22$) with the transposition approach. At the last follow-up, BNI I-II was observed in 95% (95% CI: 78–100%, $I^2 = 68\%$, $p = 0.01$) of patients treated with interposition and 96% (95% CI: 90–99%, $I^2 = 29.5\%$, $p = 0.20$) of those treated with transposition (Figure 3). After assessing the comparability of the two patient groups and stratifying by intervention type, the meta-regression estimated a BNI I-II rate of 96% for both the interposition group (95% CI: 71–98%) and the transposition group (95% CI: 77–98%) (Figure 4).

However, the interposition group showed a significantly lower pooled complication rate compared to the transposition group (4.88% vs 17.41%; OR 0.24, 95% CI 8-70%, $p = 0.009$). Early postoperative complications in the interposition group included facial weakness (10%, 95% CI: 3-16%), facial hypoesthesia (2%, 95% CI: 0-6%), and hearing impairment (2%, 95% CI: 0-6%). Notably, all cases of facial weakness resolved, while facial hypoesthesia and hearing loss persisted at the last follow-up.

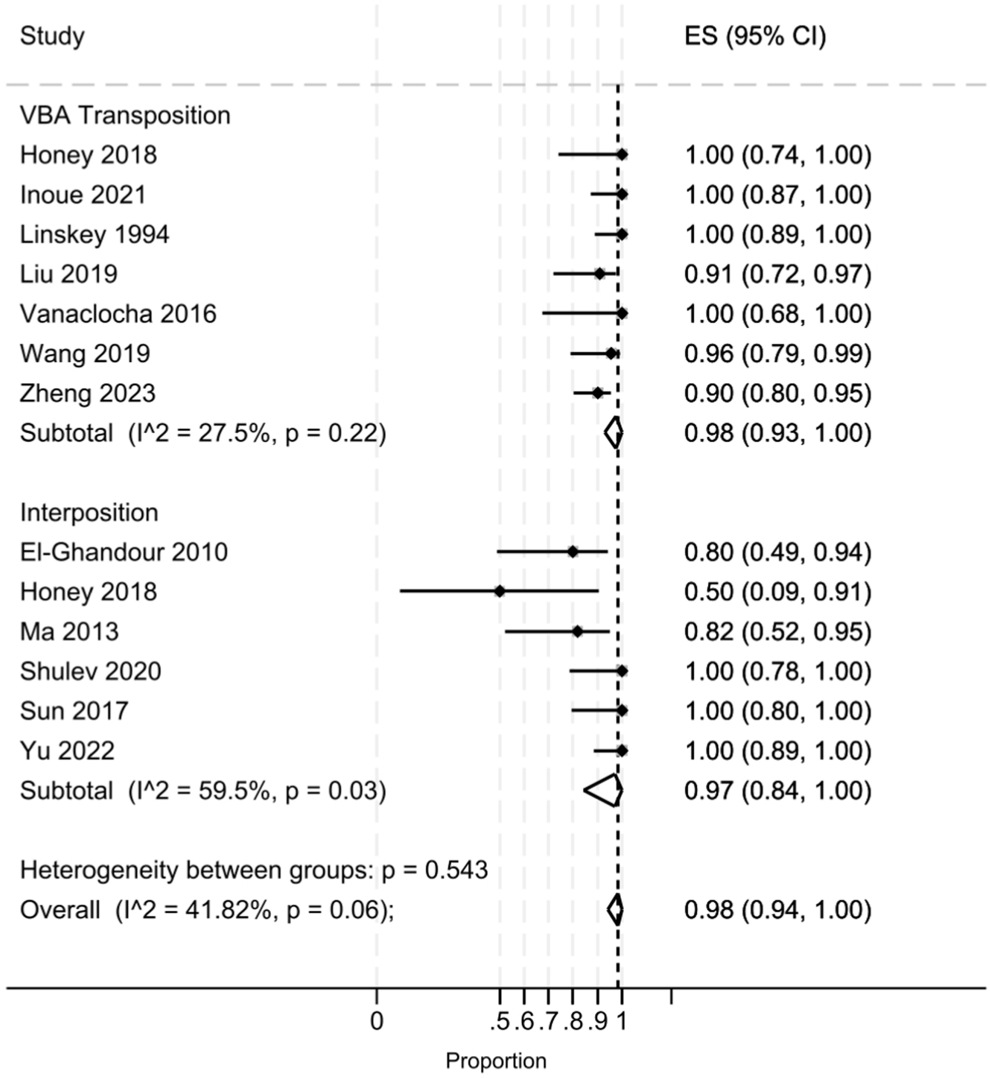

FIGURE 2
Forest plot detailing the pooled rate and 95% confidence intervals for the rate of post-operative BNI I-II in the VBA transposition group and the Interposition group.

In contrast, the transposition group had higher rates of complications: fifteen patients (7%, 95% CI: 3–10%) experienced permanent facial hypoesthesia, and seventeen patients (8%, 95% CI: 4–11%) reported permanent hearing impairment. Additionally, nine patients developed postoperative meningitis (4%, 95% CI: 1–7%). Details on the rate of postoperative complications are shown in Table 4.

Discussion

Vertebrobasilar dolichoectasia (VBD; from the Greek dolicho, "elongated," and ectasia, "dilated") is an uncommon cause of trigeminal neuralgia (TN). It refers to a vascular abnormality characterized by expansion, elongation, and tortuosity of the vertebrobasilar system. Di Carlo et al. previously performed a meta-analysis and systematic review on VBD-related TN (30), and more recently, we published an updated narrative review on the topic (31). However, neither of these works included a quantitative comparison of the interposition and transposition techniques. The current study aims to address that gap by directly comparing these surgical approaches and evaluating their outcomes.

Epidemiology and clinical characteristics

The etiopathogenesis of VBD is still largely unknown, but evidence points toward a multifactorial process combining congenital vascular wall abnormalities with acquired factors related to atherosclerosis (32, 33). Our analysis found that 52.94% of the population were males, and hypertension was present in 59.02% of cases. These findings align with the literature, indicating that patients with VBD-related TN are more likely to be older males with a history of hypertension, diabetes, hyperlipidemia, and myocardial infarction (6, 8, 23, 24, 28, 34). Addressing these risk factors postoperatively may improve long-term outcomes and potentially delay or prevent pain recurrence to a certain extent, though further research is needed to confirm this statement (5).

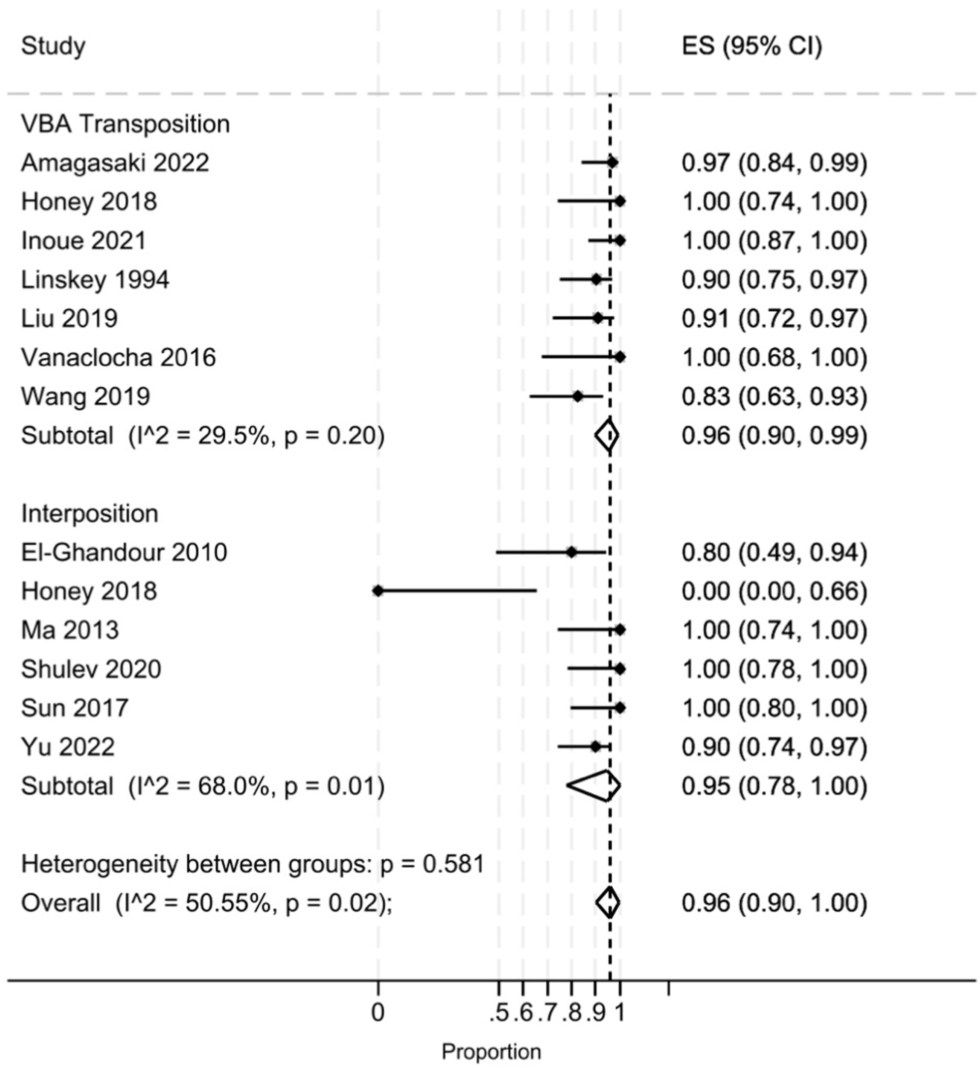

FIGURE 3
Forest plot detailing the pooled rate and 95% confidence intervals for the rate of BNI I-II in the VBA transposition group and the Interposition group at last follow-up.

Our study found that the left side was more frequently affected (57.19%), consistent with previous findings (30). Left predominance may be related to hemodynamic and anatomical factors, as blood flow and shear stress are higher in the left VA than the right one (since the left subclavian artery, from which the VA arises, originates directly from the aortic arch), resulting in an asymmetric blood flow to the basilar artery with subsequent elongation and curvation of the VBA complex toward the weaker vertebral artery (6).

The V2 and V3 branches of the trigeminal nerve were affected in most cases (82.35 and 66.01%, respectively), due to the compression from below, leaving the rostral V1 branch intact. VBD-related TN often showed multiple vessels contributing to the neurovascular conflict: in 30.39% of cases, an AICA+VBA combination was found, while SCA + VBA was found in 25.16% of patients.

Clinical outcomes and surgical technique

Microvascular decompression (MVD) is the most effective surgical option for classic TN refractory to medical treatment (35–38). However, when the compression is secondary to VBA dolichoectasia, there is no universally accepted method for isolating the offending vessel. Generally, two approaches are performed: the interposition method and the transposition method. The transposition method theoretically reduces the risk of adhesion and granuloma formation at the decompression site, which are key factors in the recurrence of symptoms post-MVD. However, this method is often more time-consuming, complex, and potentially hazardous compared to the interposition method. The interposition method, which involves placing patches between the REZ and the offending vessels, is relatively straightforward and effective in relieving nerve compression. Despite some support for the interposition method, many experts believe it may result in inadequate decompression, thus diminishing the efficacy of MVD.

Our pooled analysis indicated that the transposition group had slightly higher rates of postoperative pain relief (considered as post-operative BNI score of 1–2) than the interposition group. However, this finding may be influenced by the higher heterogeneity of the interposition group in the included studies (I^2 59.5 and 27.5% in the interposition and transposition group, respectively, $p = 0543$). Indeed,

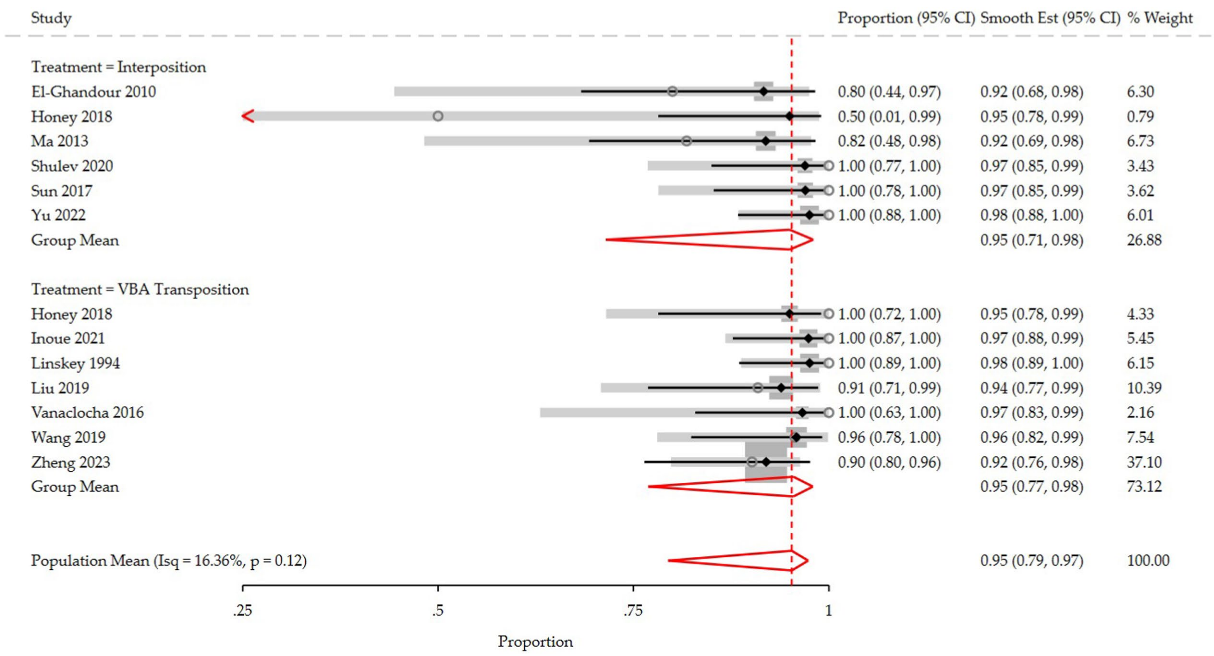

FIGURE 4
Forest plot detailing the meta-regression rate and 95% confidence intervals for the rate of post-operative BNI I-II in the VBA transposition group and the Interposition group.

the meta-regression analysis revealed an identical post-operative BNI group mean score (96%) for both techniques, suggesting they are comparable in terms of immediate pain relief.

In the study by Chai et al. (8), the authors compared the transposition and interposition techniques and found that the transposition group was associated with significantly better outcomes in terms of post-operative BNI score and pain-recurrence rate. They attributed these findings to several factors: given that in VBD the offending vessel is larger than AICA, SCA, and other vessels usually involved in classic TN, the interposition technique requires an increased amount of Teflon to achieve optimal decompression, posing a risk of applying additional pressure from excessive material used; additionally, the transposition technique can directly address the pulsatile transmission of the dolichoectatic VBA, which is believed to contribute to TN development and recurrence.

Despite these advantages, the transposition method is associated with higher postoperative complication rates. We found permanent facial hypoesthesia in 7% of cases and permanent hearing impairment in 8% at the last follow-up. It is also worth noting that the dolichoectatic arteries generally present with atherosclerosis, abnormal course, increased diameter, low elasticity, and limited mobility. These factors significantly increase the complexity of the surgery, particularly during vessel displacement, posing potential risks such as plaque dislodgement, rupture of branch vessels, and vasospasm (26).

Strength and limitations

Our study has some limitations. The included articles were only small, retrospective, and single-institution case series and the reported data were incomplete in many of these. Follow-up ranged from 1 year up to 15 years, which may not provide a homogeneous long-term perspective. Additionally, the interposition group had fewer cases and greater heterogeneity across the included studies compared to the transposition group. This variability complicates direct comparison of data and necessitates caution when interpreting results. Despite these limitations, our study is the only meta-analysis comparing the interposition and transposition techniques for VBD-related TN, providing valuable insights into their relative efficacy and complications.

Future research should focus on larger, prospective studies with standardized reporting to better compare these techniques and refine surgical strategies to improve patient outcomes.

Conclusion

Vascular compression is a frequent and treatable cause of essential trigeminal neuralgia. Even in the rare and complex case of a dolichoectatic vertebrobasilar artery, the microsurgical decompression method can provide excellent long-term outcomes in patients with TN who do not respond to medication. In our revision study, interposition and transposition groups revealed an identical post-operative BNI group mean score (96%) suggesting they are comparable in terms of immediate pain relief. However the transposition group is associated with higher postoperative complication rates.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

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TABLE 4 Postoperative complications.

	Interposition group				Transposition group			
	Raw data	(%)	CI 95%	Number of articles	Raw data	(%)	CI 95%	Number of articles
POSTOPERATIVE COMPLICATIONS								
CN IV deficit								
(Transient)	2	2,44%	0% - 6%	6	5	2,23%	0% - 4%	9
(Permanent)	0	0,00%		6	0			9
CN VI deficit								
(Transient)	1	1,22%	0% - 4%	6	15	6,70%	3% - 10%	9
(Permanent)	0	0,00%		6	1	0,45%	0% - 1%	9
Facial hypothesia								
(Transient)	0	0,00%		6	5	2,23%	0% - 4%	9
(Permanent)	2	2,44%	0% - 6%	6	15	6,70%	3% - 10%	9
Facial weakness								
(Transient)	8	9,76%	3% - 16%	6	8	3,57%	1% - 6%	9
(Permanent)	0	0,00%		6	5	2,23%	0% - 4%	9
Hearing loss/impairment								
(Transient)	0	0,00%		6	1	0,45%	0% - 1%	9
(Permanent)	2	2,44%	0% - 6%	6	17	7,59%	4% - 11%	9
Cerebellar Ataxia								
(Transient)	0	0,00%		6	4	1,79%	0% - 4%	9
(Permanent)	0	0,00%		6	1	0,45%	0% - 1%	9
Taste hypoestesia								
(Transient)	0	0,00%		6	0			9
(Permanent)	0	0,00%		6	0			9
Meningitis								
	0	0,00%		6	9	4,02%	1% - 7%	9
CSF leakeage								
	0	0,00%		6	1	0,45%	0% - 1%	9
Supratentorial acute subdural hematoma		2,44%						
	0	0,00%		6	1	0,45%	0% - 1%	9
TOTAL (Permanent)	4	4,88%	0% - 10%	6	39	17,41%	12% - 22%	9

Author contributions

FS: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – review & editing. FZ: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. VR: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. FB: Data curation, Formal analysis, Investigation, Resources, Writing – original draft. RC: Data curation, Investigation, Writing – original draft. MV: Conceptualization, Funding acquisition, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2024.1474553/full#supplementary-material

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Immediate consecutive microvascular decompression for bilateral classical trigeminal neuralgia

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Background: Classical trigeminal neuralgia (TN) is characterized by sudden, severe facial pain, typically resulting from a neurovascular conflict affecting the trigeminal nerve. In rare cases, both nerves are affected simultaneously causing bilateral TN (BTN), increasing the complexity of the treatment. Microvascular decompression (MVD) is a well-established treatment for TN; however, the experience with immediate consecutive bilateral MVD procedures is limited and requires further evaluation.

Objective: To evaluate the safety and efficacy of immediate consecutive bilateral MVD in patients with severe BTN compared to non-consecutive bilateral MVD procedures.

Methods: A retrospective analysis was conducted on 15 patients with BTN who underwent bilateral MVD. The data on clinical presentation, surgical technique, perioperative findings, complications, and follow-up outcomes of three cases of BTN treated with consecutive bilateral MVD surgeries were analyzed and compared to 12 who received separated procedures. Moreover, a detailed presentation of the three cases of consecutive MVD is provided to illustrate clinical decision-making, surgical nuances, and individual outcomes.

Results: Both groups achieved significant pain relief ($p < 0.001$) without notable differences in Barrow Neurological Institute (BNI) pain intensity score ($p = 0.305$), indicating that both approaches were equally effective. The consecutive MVD group experienced a shorter total surgical duration ($p = 0.025$), while postoperative complications were comparable ($p = 0.077$), mostly transient with no major adverse events or mortality. At the last follow-up, the patients remained pain-free without recurrence of TN symptoms.

Conclusion: Consecutive bilateral MVD is a safe and effective option, comparable to non-consecutive procedures for treating BTN. This approach provides a viable alternative for patients with severe bilateral symptoms or when medical constraints limit the possibility of two separate surgeries. Further studies with larger cohorts and extended follow-up periods are needed to support these results.

KEYWORDS

bilateral trigeminal neuralgia, microvascular decompression, neuropathy, facial pain, neurovascular conflict

1 Introduction

Trigeminal neuralgia (TN) is a syndrome characterized by sudden, paroxysmal episodes of severe facial pain involving one or more branches of the trigeminal nerve (cranial nerve V, CN V) (1). This facial pain is often triggered by innocuous stimuli, causing significant discomfort and functional impairment in daily activities (2). The pathogenesis of classical TN is described as a neurovascular conflict (NVC) between the CN V and adjacent blood vessels (1). Generally, TN affect one side of the face and rarely occurs in both sides. Bilateral TN (BTN) is rare in clinical practice, with an incidence ranging from 0.6 to 5.9% of all TN cases (3).

Treatment options for BTN comprise those for unilateral TN (UTN) and include pharmacotherapy, percutaneous destructive procedures, gamma-knife radiosurgery, and microvascular decompression (MVD) (2). A thorough evaluation of each patient's specific characteristics is necessary to select the most appropriate treatment. The MVD surgery has been shown to provide superior long-term outcomes with minimal complications and low morbidity and mortality rates compared to ablative procedures (1, 2, 4). The aim of MVD is to relieve pressure on the nerve by carefully separating the affected CN V from the compressing blood vessels, and strategically placing an autologous or artificial insulating material, thereby reducing or eliminating the pain associated with TN (5–7).

In cases of classical BTN, two MVD surgeries are typically performed with a recovery period between them (8, 9). However, in some instances, the severity of bilateral pain may require performing the second surgery without delay. This article presents three cases of patients with BTN who underwent MVD via two immediate consecutive bilateral craniotomies and compares the clinical data and outcomes with those of patients who received two separate MVD procedures for BTN.

2 Materials and methods

2.1 Study design

This retrospective, single-center study aimed to evaluate the safety and efficacy of immediate consecutive MVD for classical BTN. For comparison, clinical data and outcomes were analyzed against non-consecutive MVD procedures. Data were collected from clinical and surgical records, and statistical analyses were performed to identify differences between the two surgical approaches.

2.2 Inclusion criteria

From January 2011 to July 2024, a total of 2,166 patients with classical TN were treated at our clinic, with 143 (6.6%) presenting with BTN. During this period, we performed 85 MVD surgeries on 70 patients with BTN. Among these, 15 patients underwent bilateral MVD, including three who received consecutive surgeries. These three patients were selected for consecutive procedures due to the severity of their bilateral symptoms and resistance to pharmacological or other surgical treatments. Informed consent was obtained from all three patients, and the surgical interventions received approval from the institutional review board prior to the procedures.

2.3 Preoperative procedure

Each patient underwent a clinical evaluation by a multidisciplinary team including neurosurgeons, internists, and anesthesiologists to assess their suitability for surgery. Preoperative assessments included a comprehensive neurological examination, laboratory tests (lipid profile, thyroid function, glucose levels, etc.), and an evaluation of comorbidities and overall health status. Additionally, an imaging 3D-FIESTA MRI was performed to identify vascular contact with the cisternal portions of both CN V. The imaging data were used to plan the surgical approach and anticipate potential complications, such as prominent bony structures.

2.4 Surgical procedures

Patients were positioned in the lateral decubitus position with a 45° head rotation to allow optimal access to the cerebellopontine angle. The surgical intervention commenced with a retrosigmoid craniotomy on the side with the lower potential risk of complications, as determined by preoperative imaging and clinical evaluation. The surgical approach involved careful exploration of the cerebellopontine angle to identify and separate vascular structures in contact with the CN V. Teflon pads were meticulously placed to insulate the nerve from compressing vessels, while any conflicting veins were coagulated and resected when necessary.

Once decompression was achieved on the first side, the craniotomy was closed, and the patient was repositioned to allow access to the contralateral side. A second retrosigmoid craniotomy was then performed, employing the same technique. In cases where a prominent suprameatal tubercle obstructed visualization, bone drilling was performed to enhance the microsurgical view. Throughout the procedures, total intravenous anesthesia was maintained.

2.5 Postoperative evaluation

Postoperatively, 3D reconstructed CT scans were obtained to confirm the correct placement of the Teflon pads and to identify potential complications, such as pneumocephalus. Patients were closely monitored for adverse effects, and clinical follow-up was conducted for a minimum of 6 months. In addition, a long-term follow-up plan has been established, with evaluations every 6 months for a minimum of 3 years to assess sustained pain relief, detect potential recurrence, and monitor for late complications.

2.6 Statistical analysis

A statistical analysis was conducted to compare clinical and surgical data between consecutive and non-consecutive MVD surgeries for BTN. Independent samples t-tests or Mann–Whitney *U* tests were employed to compare variables such as age, surgical duration, and complication rates, depending on normality assessed by the Shapiro–Wilk test. Differences in Barrow Neurological Institute (BNI) pain intensity scores and symptom duration between groups were analyzed using the Mann–Whitney *U* test, while pre- and postoperative changes in BNI scores within groups were evaluated using the Wilcoxon signed-rank test. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS Version 25 (IBM® SPSS® Statistics, Chicago, IL, United States).

3 Results

3.1 Case 1

A 60-year-old Mexican woman presented to our clinic with a 20-year history of episodic, electric shock-like pain in the right V1, V2, and V3 branches of the CN V, and similar left facial pain in the V2 and V3 branches for the past 2 years. Initially, the patient sought dental care, which led to the extraction of four molars. Subsequently, she was treated by neurologists who diagnosed her with BTN and managed her condition with pharmacotherapy, including 1,200 mg/day of carbamazepine and 50 mg/day of dexketoprofen. However, due to the long history of pharmacological treatments and the current high doses of medication, the patient reported persistent side effects, including nausea, dizziness, and vomiting. She had no history of prior surgical interventions.

During the clinical examination, severe bilateral facial pain was triggered by touch and eating. Her body mass index (BMI) was 26. A 3D-FIESTA MRI demonstrated vascular contact over the cisternal portion of both CN V (Figure 1A). Laboratory tests revealed slightly elevated cholesterol and triglyceride levels, along with elevated TSH and reduced free T4 and T3. The patient indicated being under treatment with 20 mg/d of atorvastatin and 50 mcg/d of levothyroxine to manage her comorbidities. Four months after the initial consultation, the patient's bilateral pain had become disabling, severely affecting her ability to swallow and eat. Given the worsening condition, intolerable medication side effects, and the patient's financial limitations, two consecutive MVD procedures were suggested. After discussing the risks and benefits, bilateral surgery was approved by the patient, her family, and authorized by the hospital's ethics committee. The patient's physical health was assessed by our team of internists and anesthesiologists, who evaluated her potential response to anesthesia and the risk of cardiac and respiratory complications. Following a comprehensive evaluation, it was concluded that she was in suitable condition to undergo both consecutive procedures.

Initially, a right MVD was performed. During the procedure, the superior cerebellar artery (SCA) and an unnamed vein were identified compressing the CN V (Figure 1B). The artery was gently separated from the nerve, and a Teflon pad was interposed. The vein was coagulated and resected. Immediately after closing the right approach, the patient was repositioned to expose the left side for a second, consecutive retrosigmoid approach. Upon opening the dura, a suprameatal tubercle approximately 3 mm in size obstructed the surgical view (Figure 1C). Drilling of this bony structure was necessary until a redundant SCA and another unnamed vein could be identified and separated using Teflon felts (Figure 1D). The suprameatal tubercle was not detected on the presurgical MRI (Figure 1A).

Postoperatively, a CT scan with 3D reconstruction was performed (Figures 1E,F). The patient reported hypoesthesia on the right side and paresthesia, otic fullness, and tinnitus on the left side. All these adverse events were transient. There were no major complications. Pain relief was immediate on both sides, with continued satisfactory results at 6 months of follow-up.

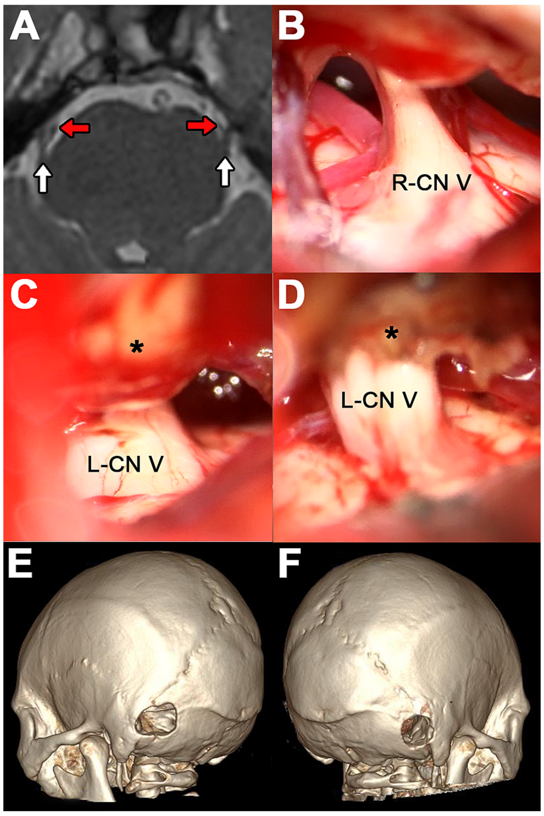

FIGURE 1
Case 1. (A) Axial 3D-FIESTA MRI at the level of the pons. The white arrows indicate the cisternal portion of CN V and the red arrows the contact vessels. (B) Surgical exploration on the right side showing SCA as the culprit vessel. (C) Suprameatal tubercle (asterisk) obstructing visualization of the left CN V. (D) Left-sided surgical exploration showing drilled suprameatal tubercle (asterisk) and redundant SCA as the offending vessel. (E,F) 3D reconstruction CT scan showing left and right retrosigmoid craniotomy, respectively.

3.2 Case 2

A 58-year-old Chilean woman presented with an eight-year history of TN on the left side, involving only the V2 division. Over the past 3 years, she developed pain in the V2-V3 distribution on the contralateral side. The patient initially consulted a dentist who extracted a molar and was subsequently seen by a neurologist who diagnosed her with BTN. The patient reported an allergy to carbamazepine and was instead prescribed pregabalin and amitriptyline. These medications controlled her pain for the past 2 years with progressively increasing doses. Recently, she experienced severe pain crises, which were managed with tramadol. Two years ago, she underwent a left-sided radiofrequency thermocoagulation which only controlled the pain for 3 months.

During clinical examination, severe bilateral pain was triggered by touch and exposure to cold and wind, with more frequent pain episodes on the right side. Her BMI was 24. Laboratory tests showed no remarkable abnormalities. However, her blood pressure was elevated (151/93 mmHg), and she reported being under treatment with losartan 50 mg/d. Furthermore, the Beck Depression Inventory (BDI-2) revealed moderate depression. A 3D FIESTA MRI revealed vascular contact over the cisternal portion of both CN V and a > 6 mm prominence of the petrosal surface of the right temporal bone was also identified (Figure 2A). The patient was prescribed pregabalin 150 mg/d and duloxetine 60 mg/d.

Given the MRI finding on the right side, which could complicate or prolong the surgery, it was decided to explore the left side first to ensure at least one successful MVD. During the initial procedure, the SCA and a circumflex vein were separated from the nerve by interposing Teflon felts (Figure 2B). Upon contralateral exploration, a large suprameatal tubercle exceeding 6 mm was encountered, obstructing the microsurgical corridor to the cisternal segment of the CN V. This required the drilling of the bony structure, which extended the surgical time by 75 min more than expected (Figure 2C). When the neurovascular conflict could be identified, the CN V was being contacted by a redundant AICA and SCA (Figure 2D). These vessels were gently transposed, and two Teflon pads were placed to insulate the nerve.

During the postoperative evaluation, the patient reported persistent headache, vertigo, right-sided hypoesthesia and left-sided tinnitus. A postoperative CT scan revealed a mild pneumocephalus located at the right anterolateral cistern of the brainstem, likely resulting from the extended drilling of the suprameatal tubercle (Figure 2E). The pneumocephalus was managed with 72 h of strict supine rest, hyperhydration and supplemental oxygen. Bilateral pain relief was achieved following the surgery, and the patient remains pain-free during the 6 months of follow-up. All complications were transient, and her emotional state has improved since the intervention.

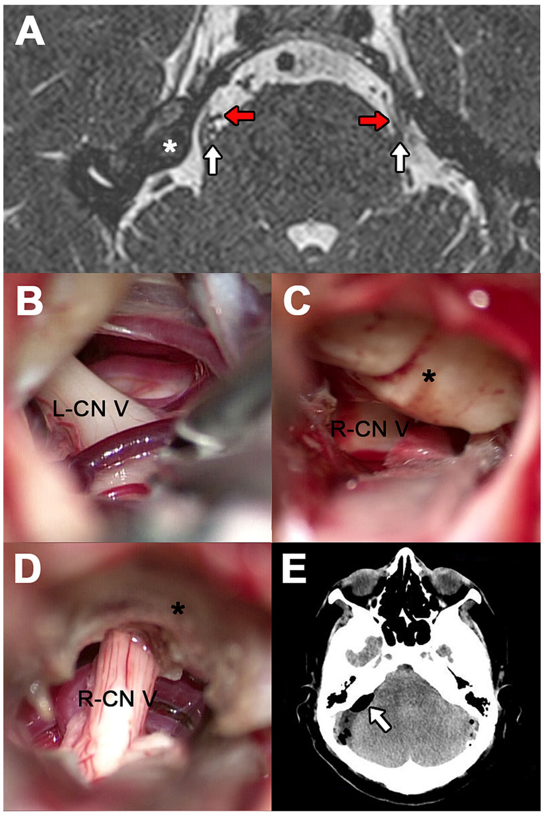

FIGURE 2
Case 2. (A) 3D-FIESTA MRI showing both CN V at the level of the pons (white arrows). The red arrows indicate the contact vessels and the asterisk shows a lobulated osseous prominence of the right petrosal surface. (B) SCA and a circumflex vein over the left CN V. (C) Prominent suprameatal tubercle (asterisk) obstructing the clear visualization of the CN V. (D) Redundant AICA compressing the CN V revealed after drilling the suprameatal tubercle (asterisk). (E) Postoperative cranial CT scan. The arrow indicates the pneumocephalus in the right anterolateral cistern of the brainstem.

3.3 Case 3

A 54-year-old Mexican woman was admitted to our clinic after experiencing seven consecutive days of severe pain crises that required hospitalization. She reported a two-year history of neuropathic pain characterized by electrical and burning sensations affecting the left V1, V2, V3, and right V3 branches of CN V. Bilateral pain began 3 years prior, with the onset occurring almost simultaneously, differing by only a few weeks. Initially, she consulted a dentist who extracted three molars. Her treatment regimen, prescribed by a neurologist and an algologist, included oxcarbazepine 1800 mg/d, pregabalin 300 mg/d, duloxetine 60 mg mg/d and tapentadol 100 mg/d. No previous surgical interventions were reported.

During the clinical examination, severe bilateral pain was triggered by any contact with the face and presented with the same intensity on both sides. Her BMI was calculated to be 22. Laboratory tests indicated slightly elevated glucose, cholesterol, and triglyceride levels. The patient was managing type 2 diabetes mellitus and dyslipidemia with metformin 850 mg/d and atorvastatin 10 mg/d, respectively. A 3D-FIESTA MRI revealed vascular contact with the cisternal portions of both CN V (Figure 3A).

Two consecutive craniectomies were conducted to decompress the left and then the right CN V. On the left side, the neurovascular conflict involved the SCA and a pontine vein (Figure 3B). On the right side, the offending vessels were the SCA and a tributary vein to the superior petrosal vein complex (SPVC; Figure 3C). The arteries were separated from the nerve, and Teflon pads were interposed. The vein was coagulated and resected. Both explorations revealed severe thickening of the arachnoid membranes with a viscous consistency, which was meticulously excised, increasing the difficulty of the microsurgery (Figure 3D). The altered arachnoid tissue was stained with hematoxylin and eosin (H&E), which showed evidence of fibrosis and microcalcifications (Figures 3E,F).

Postoperatively, the patient reported tinnitus on the right side, while the left side exhibited grade II facial paralysis, ear fullness, and hypoesthesia. All complications were transient, with no major complications occurring. At the four-month follow-up, pain had completely resolved on the right side. On the left side, the patient reported occasional, less intense pain that did not require medication.

3.4 Comparison between consecutive and non-consecutive bilateral MVD for classical BTN

To further evaluate the effectiveness and safety of immediate consecutive MVD, we compared its outcomes with those of patients who underwent two non-consecutive MVD surgeries for classical BTN at our center ($n = 12$; Table 1).

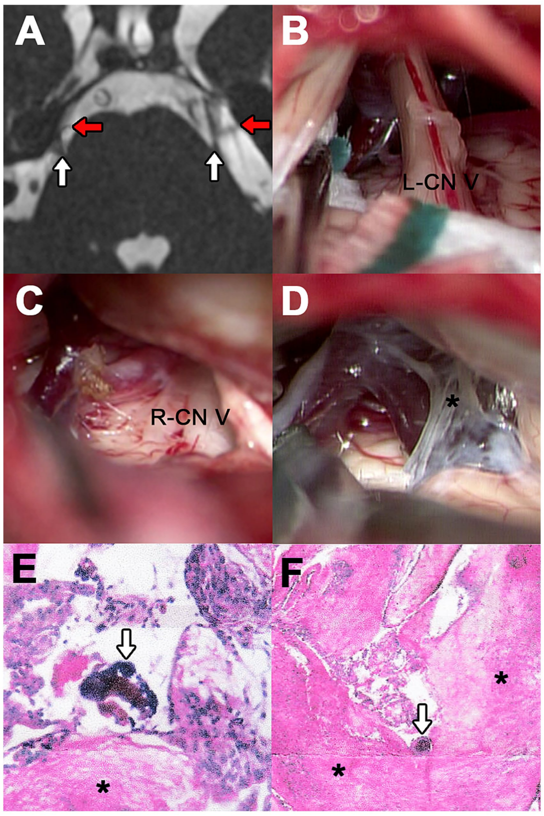

FIGURE 3
Case 3. (A) 3D-FIESTA MRI demonstrating both CN V at the level of the pons (white arrows). The red arrows point to the vessels making contact. (B) Surgical exploration on the left side showing SCA and a pontine vein. (C) Right neurovascular conflict caused by SCA and a vein tributary to the SPVC. (D) Right findings of altered arachnoid (asterisk) with a viscous consistency during the examination. (E,F) Results of hematoxylin and eosin staining of left and right arachnoid samples, respectively. The asterisk shows the area with fibrosis and the arrow indicates macrocalcifications.

The mean age of patients who underwent consecutive bilateral MVD was 57.7 years, while the mean ages for patients who had two separate MVD procedures were 52.8 years for the first procedure and 55.8 years for the second procedure. No significant differences in age were observed between patients undergoing consecutive MVD and those undergoing the first ($p = 0.32$) or second ($p = 0.69$) non-consecutive surgeries. The median duration of TN symptoms on the first operated side was 10 years for patients in the consecutive group and 11.7 years for those in the non-consecutive group ($p = 0.292$). Prior to the surgery of the second operated side, the duration of pain was 4.3 years for patients in the consecutive group and 2.3 years in the non-consecutive group ($p = 0.268$). Notably, contralateral pain developed in 66.6% of patients after their initial MVD with an average onset of 2.7 years. Additionally, in patients with non-consecutive surgeries, the average interval between the two procedures was 2.9 years. The mean operative time for consecutive MVD was 296.7 min, while the mean of combined operative time for both procedures in the non-consecutive group was 343.3 min, indicating a shorter total surgical time for consecutive procedures ($p = 0.025$).

Postoperative complications were assessed before discharge. The median number of complications was comparable between groups, with an average of 4.3 in the consecutive group and 3.3 in the non-consecutive group ($p = 0.077$). At 6 months the after surgery, pain outcomes of all patents could be evaluated using the BNI pain intensity scale (10). Both groups demonstrated significant improvement in BNI scores after surgery ($p < 0.001$). However, there was no significant difference in pain relief between the consecutive and non-consecutive MVD groups ($p = 0.305$), suggesting that both approaches can be equally effective in controlling pain in patients with BTN.

4 Discussion

Classical BTN is characterized by paroxysmal, electric shock-like pain on both sides of the face, typically affecting areas innervated by the CN V. The neurovascular conflict hypothesis is widely accepted for explaining the pathogenesis of classical TN. According to this theory, chronic compression of the CN V by abnormal blood vessel trajectories at the root entry zone (REZ) leads to inflammation and demyelination of the nerve root. This compression results in a "short circuit" of membrane potential, causing neuropathic pain triggered by innocuous stimuli (11, 12). Additionally, it has been described that patients with BTN have smaller posterior cranial fossae and cerebellopontine cistern volumes compared to healthy controls. This reduced volume is associated with an overcrowded posterior fossa, leading to a higher incidence of neurovascular conflict that ultimately may induce BTN (12).

The diagnosis of both BTN and UTN primarily relies on patient history and is supported by appropriate imaging studies (13). Clinical and imaging evaluations are essential not only for diagnosing TN but also for excluding secondary causes, such as tumors or multiple sclerosis (MS). The incidence of BTN accounts for 0.6 to 5.9% of all TN cases (3, 8). At our center, BTN has an incidence of 6.6% among cases of classic TN; however, this incidence rises to 8.7% when secondary and idiopathic TN cases are considered. Bilaterality is significantly more common in patients with a familial history of TN compared to those with UTN, suggesting a potential predisposition to symptomatic neurovascular compression in certain individuals and families (8, 14). Additionally, MS is associated with a higher incidence of BTN, with reports indicating that 4–10% of BTN patients also present MS (15, 16). However, none of the patients in our study showed evidence of MS during clinical examination, nor were they aware of any family history of TN.

Pharmacological treatment is the first-line option for managing both UTN and BTN. However, when medications fail to provide long-term pain control or cause intolerable side effects, surgical intervention should be considered. Various surgical approaches have been proposed for the treatment of these conditions, including ablative procedures, which offer quick pain relief but have limited long-term effectiveness (2, 17). MVD is another surgical technique to treat compressive neuropathies that directly addresses the underlying cause of symptoms. As a non-ablative surgery, MVD can preserve CN V function, thereby increasing pain control rates, and decreasing the risks of complications, recurrence rates, and the need for repeated interventions compared to ablative surgeries (3, 12, 17, 18). The success rate of MVD for UTN at 1-year follow-up is high (80–90%)

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TABLE 1 Characteristics of patients who underwent non-consecutive (1–12) and consecutive (A-C) MVD surgeries for BTN.

Case	Sex	Age at surgery		Years of symptoms / Affected side		Years between surgeries	Pre-surgical BNI score		Duration of surgery (min)		Surgical findings		Number of postoperative complications		Post-surgical BNI score	
		1st surgery	2nd surgery	1st surgery	2nd surgery		1st surgery	2nd surgery	1st surgery	2nd surgery	1st surgery	2nd surgery	1st surgery	2nd surgery	1st surgery	2nd surgery
1	F	54	58	7/L	2/R	4	V	V	161	144	ST, A	V, A	1	1	I	II
2	F	62	63	8/L	0.3/R	0.5	V	IV	137	153	SCA, V, A	SCA, V, A	1	2	I	I
3	F	34	37	2/R	0.25/L	2.6	IV	IV	166	193	V, A	SCA, V, A	1	3	I	I
4	F	71	73	33/L	15/R	2.5	V	V	199	224	SCA	SCA, V	2	2	I	I
5	F	55	55	10/L	15/R	0.4	V	V	145	156	SCA, V, A	SCA, A	2	1	I	I
6	F	26	30	2/L	1/R	3.6	V	IV	174	178	SCA, V, A	SCA, ST	2	1	II	II
7	F	76	81	15/L	7/R	4.7	V	V	206	118	V	SCA, V, A	1	1	I	I
8	M	43	46	2/L	0.5/R	3.3	IV	IV	182	158	SCA, AICA, V, A	SCA, V, A	3	2	I	I
9	F	51	51	10/L	9/R	0.3	V	V	136	150	V, A	SCA, A	3	2	II	II
10	F	41	45	4/R	0.5/L	3.6	IV	V	146	203	AICA, V, A	SCA, A	1	1	I	I
11	F	61	64	20/R	0.6/L	3.4	V	IV	235	220	SCA, V, A	SCA, V, A	3	2	III	II
12	F	60	66	23/R	0.5/L	6	V	V	184	152	SCA, V, A	SCA, A	1	2	II	III
A	F	60		20/R	2/L	0	V	V	295		SCA, V, A	SCA, V, A, ST	1	**3**	**I**	**I**
B	F	58		8/L	3/R	0	V	V	315		AICA, V	SCA, AICA, ST	2	3	I	I
C	F	54		3/L	3/R	0	V	V	280		SCA, V, A	SCA, V	3	1	I	II

F, Female; M, Male; L, Left; R, Right; SCA, Superior Cerebellar Artery; AICA, Anterior Inferior Cerebellar Artery; V, Vein; A, Altered Arachnoid; ST, Suprameatal Tubercle; BNI, Barrow Neurological Institute pain intensity score: I (no pain, no medication required), II (occasional pain, not requiring medication), III (persistent pain, adequately controlled with medication), IV (some pain, not adequately controlled with medication), V (severe pain/no pain relief).

(9), and is generally recommended as the primary surgical option in cases of classical TN when the patient's overall condition is favorable. In contrast, ablative approaches are considered for atypical cases of TN, when there is an absence of neurovascular compression, when the patient faces increased perioperative risks, or when MVD has failed (19).

Similar to UTN, MVD can be a safe and effective treatment of BTN (12). However, the utility of performing separated MVD for primary BTN has been evaluated in only three studies, all of which were case series (8, 9, 14). In Pollack's study involving 35 BTN patients over 14 years, good or excellent results were achieved on 89% of the treated sides, and 74% maintained good or excellent pain relief during a mean follow-up of 75 months (8). Tacconi and Miles reported poorer responses in 16 BTN cases treated over 14 years, requiring further medical management and additional ablative procedures, possibly due to including patients with idiopathic BTN and TN associated with MS or Charcot–Marie–Tooth disease (14). Zhao et al. described 13 BTN cases treated with MVD over a two-year period, achieving good or excellent symptom control on 92.3% of the treated sides; among these, nine patients underwent contralateral MVD within 1 year with excellent outcomes (9). In BTN patients, contralateral surgery is recommended at least 3 months after the initial MVD (12). However, Tun et al. reported performing two separate MVD procedures on an older BTN patient with a two-week interval, the shortest period reported at the same institution. The patient did not experience any complications during follow-up (17).

Only two previous reports mention having performed bilateral MVD consecutively (8, 14). However, neither provided detailed information on the intervention, perioperative management or follow-up. It is mentioned that consecutive bilateral MVD is a feasible and reasonable option when the MRI shows bilateral contact, and the pain on both sides is equally severe, such that treating only one side would not reduce the medication or improve the patient's quality of life (14). Recently, a report described the possibility of decompression on both sides through a single unilateral approach. The authors performed bilateral MVD using a unilateral craniectomy in two patients with an enlarged superior trigeminal nerve space, successfully identifying and releasing both neurovascular conflicts. However, they indicated that not every BTN patient could be treated this way due to anatomical limitations (3).

Based on our experience, a thorough preoperative physiological evaluation should precede consideration of a double procedure. Ensuring the absence of significant metabolic conditions or comorbidities that could complicate surgery is crucial. Patients should ideally undergo this approach at their optimal weight to minimize anesthetic and obesity-related risks. Our three patients were relatively young and healthy, with manageable comorbidities and no significant contraindications to surgery. Additionally, other palliative surgical and non-surgical options were discussed with the patients. The decision for surgery was made jointly by the patient, their family, the hospital ethics committee, and an expert medical team, who evaluated the patient's health status and potential surgical risks. On the other hand, it is also important to consider the patient's economic situation. By performing two consecutive interventions, the patient undergoes a single process for anesthesia, hospitalization, transportation, and recovery, thereby reducing overall costs.

Bilateral pain typically occurs asynchronously, with one side often more symptomatic than the other. Generally, the side with the most severe pain is treated surgically first (12). However, after treating the more symptomatic side, contralateral symptoms often become more disabling over time, necessitating continued high-dose medication (8). In such cases, patients might benefit from an immediate consecutive MVD. As with unilateral MVD, a criterion for surgery is the confirmation of vascular contact on the nerve via MRI (9). Imaging studies can also help identify findings that may increase surgical complexity. In the second case, a prominent right suprameatal tubercle was identified on the preoperative MRI, prompting us to operate on the opposite side first. While it is generally recommended to address the more symptomatic side first, we suggest prioritizing the side with fewer risks and requires shorter surgical time. This strategy aims to ensure at least one successful MVD and provides additional time to address the more complex side. Operating on the more complicated side first could result in the second surgery being postponed due to complications or unforeseen findings. In this instance, drilling of the suprameatal tubercle extended the surgical time and resulted in a pneumatocele, underscoring the importance of minimizing intradural exposure and avoiding prolonged CSF drainage during microsurgery. In the third case, thickened arachnoid tissue was observed on both sides, complicating vessel and nerve manipulation. This altered tissue might contribute to neurovascular conflict by forming adhesions with adjacent structures, necessitating its careful removal. The etiology of this alteration remains unclear; however, the presence of fibrosis and microcalcifications suggests the involvement of a chronic inflammatory process (20).

Some authors are reluctant to perform an early second MVD due to reports of contralateral symptom resolution following unilateral MVD. It has been suggested that bilateral symptom relief may occur when the contralateral vessel is displaced during the removal of the ipsilateral offender or when CSF release during surgery leads to separation of neurovascular contact (9). However, there are also reports of early and late iatrogenic contralateral TN after MVD for unilateral TN (21, 22). Achieving bilateral pain relief in a single surgical session can benefit patients by avoiding two separate procedures with their associated risks and complications, reducing patient costs, preventing two recovery periods, and avoiding prolonged unnecessary pain. While the aim of this study is to support the safety and efficacy of consecutive MVD, the small sample size and short follow-up period limit the generalizability of the findings. Nonetheless, this study provides a foundation for further research. Increasing the cohort size and extending the follow-up period in future studies will be essential to confirming the effectiveness and safety of this approach in patients with severe bilateral pain who meet the optimal criteria, such as good overall health, appropriate weight, and a diagnosis of classic BTN.

5 Conclusion

The cases presented herein demonstrate the feasibility and effectiveness of performing two immediate consecutive MVD surgeries for the treatment of synchronous classical BTN. Our results support that, when patients are appropriately selected based on their clinical profile and imaging studies, this approach can provide significant pain relief with minimal complications in a specialized center. This approach may be particularly viable for patients with severe bilateral symptoms or other constraints that prevent two separate surgeries. Nevertheless, larger case series and extended follow-up studies are necessary to further support the safety and long-term efficacy of this surgical strategy.

Data availability statement

The datasets presented in this article are not readily available because of ethical and privacy restrictions. Requests to access the datasets should be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Comité de Ética en Investigación, Hospital Angeles Morelia. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MS-L: Writing – review & editing, Writing – original draft. MR-G: Writing – review & editing, Methodology. PM-L: Methodology, Writing – review & editing, Validation. OC-R: Writing – review & editing, Supervision. YT-T: Writing – review & editing, Data curation, Methodology. AG-S: Project administration, Writing – review & editing. AS-P: Conceptualization, Writing – review & editing. AM-R: Investigation, Software, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Efficacy analysis of electroacupuncture plus TDP in the treatment of peripheral facial paralysis: a systematic review and meta-analysis

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Objective: This study intends to carry out a systematic review and meta-analysis of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis.

Methods: CNKI, VIP, Wanfang, PubMed, Embase and Cochrane databases were searched for literatures on randomized or quasi-randomized controlled trials of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis, and the references of the included studies were searched. Meta-analysis was performed using Stata15.0 software after risk of bias, quality assessment, and data extraction of the included articles by two reviewers independently.

Results: Fifteen articles were finally included, with approximately 1,568 participants (920 in the treatment group and 648 in the control group). Meta-analysis showed that the effective rate of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis was not significantly different from other treatment methods ([$RR = 1.05$, 95%CI (0.97, 1.12), $p = 0.226$]), and the recovery rate was better than other treatment methods ([$RR = 1.14$, 95%CI (1.05, 1.24), $p = 0.002$]). Subgroup analysis showed that when stratified by the inclusion of minors in the study population, it was observed that in studies including minors, the combination of electroacupuncture and TDP therapy demonstrated superior efficacy in treating peripheral facial paralysis compared to other therapeutic modalities [OR = 1.14, 95% CI (1.03, 1.25), $p = 0.011$]. Conversely, in studies where the population comprised solely adults, no significant difference was found between the combination therapy and other treatments [OR = 1.15, 95% CI (0.99, 1.33), $p = 0.059$]; whether electroacupuncture alone or other treatment methods, the recovery rate of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis was better than other methods.

Conclusion: Electroacupuncture combined with TDP is superior to other treatment methods in the treatment of peripheral facial paralysis.

KEYWORDS

peripheral facial paralysis, electroacupuncture, TDP, meta-analysis, complementary therapies

1 Introduction

Peripheral facial paralysis, also known as idiopathic facial nerve palsy and Bell's palsy, represents a prevalent neuropathy of the facial nerve (1). Clinically, it primarily manifests as impaired motor function of the facial muscles on the affected side, with incomplete or complete paralysis of the expression muscles on the affected side (2). Peripheral facial paralysis is considered a self-limiting condition, with a favorable prognosis if diagnosed and treated promptly and accurately (3). Research indicates that approximately two-thirds of patients may experience abnormal regeneration of the facial nerve, often accompanied by synkinesis and crocodile tears. Poor recovery of facial muscle control in some patients can lead to facial deformity and pain (4).

Various treatment modalities are available for peripheral facial paralysis, including symptomatic treatment in Western medicine (5, 6), external treatment in traditional Chinese medicine (7–9), and combination therapies (10, 11). Electroacupuncture is a commonly used external treatment, supported by evidence from some review studies (8, 12). However, existing research often focuses on the influence of electroacupuncture parameters such as waveform, frequency, and intervention timing on the treatment of peripheral facial paralysis. TDP (Teding Diancibo Pu) therapy, also known as the "Magic Lamp" or "Infrared Therapeutic Apparatus" (13), is a domestically developed electromagnetic spectrum therapy device in China. TDP emits micron-level electromagnetic waves, exerting effects such as promoting blood circulation, relieving stasis, and alleviating pain. The elements generated by TDP radiation can enhance endogenous enzyme activity, promote metabolism, and boost immunity. Additionally, TDP irradiation can increase the content of endorphins in the body, alleviating pain (14).

In recent years, numerous studies have focused on the use of electroacupuncture combined with TDP therapy for the treatment of peripheral facial paralysis. However, the results of these studies have been inconsistent due to variations in sample sizes and differences in study design (15–17). Additionally, there is a lack of robust evidence regarding the comparative efficacy of electroacupuncture combined with TDP therapy versus standalone electroacupuncture, conventional Western medications, or acupuncture in the treatment of peripheral facial paralysis. Therefore, this study aims to conduct a systematic review and Meta-analysis of randomized controlled trials on the use of electroacupuncture combined with TDP therapy for the treatment of peripheral facial paralysis. This evaluation will provide evidence-based support for the clinical implementation of electroacupuncture combined with TDP therapy in treating peripheral facial paralysis.

2 Materials and methods

2.1 Literature search strategy

A systematic search was conducted in PubMed, EMBASE, Cochrane Library, CNKI, VIP, and Wanfang databases for studies on the use of electroacupuncture combined with TDP therapy for peripheral facial paralysis published up to April 29, 2024. The search terms in Chinese included "peripheral facial palsy," "facial neuritis," "Bell's palsy," "Bell's facial paralysis," "idiopathic facial neuritis"; "electroacupuncture"; "TDP," "hot lamp," "magic lamp," "electromagnetic wave," and "infrared." The search terms in English included "Bell's Palsy," "peripheral facial palsy," "facial paralysis," "facial neuritis"; "electroacupuncture"; and "TDP."

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) study type: randomized controlled trials published in Chinese or English; (2) subjects: patients diagnosed with peripheral facial paralysis with detailed diagnostic criteria; (3) interventions: electroacupuncture combined with TDP therapy; the control group receiving other treatments such as standalone electroacupuncture, conventional Western medications, or acupuncture; and (4) outcomes: clinical efficacy including overall response rate and cure rate, facial nerve function score, facial disability index score, and adverse effects.

Exclusion criteria: (1) studies that were duplicate reports or from which valid data could not be extracted; (2) case reports, reviews, and conference abstracts; and (3) animal or cadaver studies.

2.3 Information extraction and quality evaluation

Two independent investigators meticulously screened the literature and extracted data in strict accordance with the inclusion and exclusion criteria. In cases of disagreement, discussions were held to reach a consensus. The extracted data included the first author, year of publication, geographical background, sample size, intervention measures, and outcome indicators.

The modified Jadad scale (18) was employed to evaluate the quality of the literature. This scale assesses literature quality based on the randomization method, whether allocation concealment was present, the correct implementation of blinding, and the description of withdrawals and dropouts. Mention "random," "random allocation" and "random grouping" and so on, and score 1 point; If the use of' double-blind' is mentioned as 1 point, the double-blind method is correctly described as 2 points; The reasons and cases of withdrawal and loss of follow-up in each group were reported, and the number of cases was 1 point. Studies scoring 4–7 points were considered high-quality research, those scoring 1–2 points were deemed low-quality, and studies scoring 0 points were excluded from the research. The quality evaluation was conducted independently by two researchers, and any discrepancies were resolved through discussion to determine the final score.

2.4 Statistical analysis

Meta-analysis was performed using Stata15.0 statistical software. For categorical data, the effect size was estimated using the risk ratio (RR) and its 95% confidence interval (CI). For continuous data, the standardized mean difference (SMD) and its 95% CI were utilized. The I^2 statistic was used to evaluate heterogeneity due to non-threshold effects. Specifically, when $I^2 \geq 50\%$, the DerSimonian and Laird random-effects model was employed for meta-analysis; when $I^2 < 50\%$, the fixed-effects model was used.

3 Results

3.1 Literature screening results

A total of 741 articles were retrieved for this study. After removing 240 duplicate articles, 215 articles were excluded based on their titles and abstracts for being irrelevant. The remaining 286 articles were subjected to full-text screening, resulting in the inclusion of 15 articles in the meta-analysis. The literature screening process and results are depicted in Figure 1.

3.2 Basic information of included studies

A total of approximately 1,744 participants were included in all studies (1,008 in the treatment group and 736 in the control group). Table 1 summarizes the basic characteristics of the included studies. The study subjects were all from China. In 13 studies, the intervention for the treatment group was electroacupuncture combined with TDP (15–17, 19–27), while in two studies, the intervention was electroacupuncture point-through-point combined with TDP (28, 29). The control group interventions varied and included electroacupuncture (16, 19, 21–23, 25), acupuncture (15, 20), acupuncture combined with electroacupuncture (15, 20), Western medicine (17, 24), TDP therapy (26), electroacupuncture point-through-point (27), and acupuncture combined with TDP therapy (30). The majority of studies included participants who were minors ($N=11$) (15–17, 21, 22, 24–27, 29, 30), while the remaining studies focused exclusively on adult subjects ($N=4$) (19, 20, 23, 28).

3.3 Assessment of the quality of included studies

To evaluate the quality of the studies included, we utilized the Jadad scale. Detailed findings are presented in Table 2. The specific scores of the 15 included studies are as follows: there were 2 studies rated as high-quality literature with scores ranging from 4 to 7, both scoring 4 points. Thirteen studies were classified as low-quality literature with scores ≤3, including 2 studies scoring 3 points, 8 studies scoring 2 points, and 3 studies scoring 1 point. Generation of random sequences: Two studies employed randomization and described the correct randomization methods, while eight studies used randomization but did not describe the methods. Randomization concealment: Two studies only mentioned using random number methods or random number tables for random allocation but did not indicate whether this method prevented clinicians and participants from predicting the allocation sequence. Usage of blinding: None of the studies mentioned whether blinding was used.

3.4 Meta-analysis results

3.4.1 Efficiency rate

All included studies reported the overall efficacy rate. Heterogeneity test analysis indicated no statistical heterogeneity among the 15 studies ($p=1.00$, $I^2=0\%$), thus employing a fixed-effects model for pooled analysis. Meta-analysis results (Figure 2) revealed no significant difference in overall efficacy rate between electroacupuncture combined with TDP treatment for peripheral facial paralysis and other treatment modalities [$OR=1.05$, 95%CI (0.97, 1.12), $p=0.226$]. Sensitivity analysis was conducted to assess the stability of the study

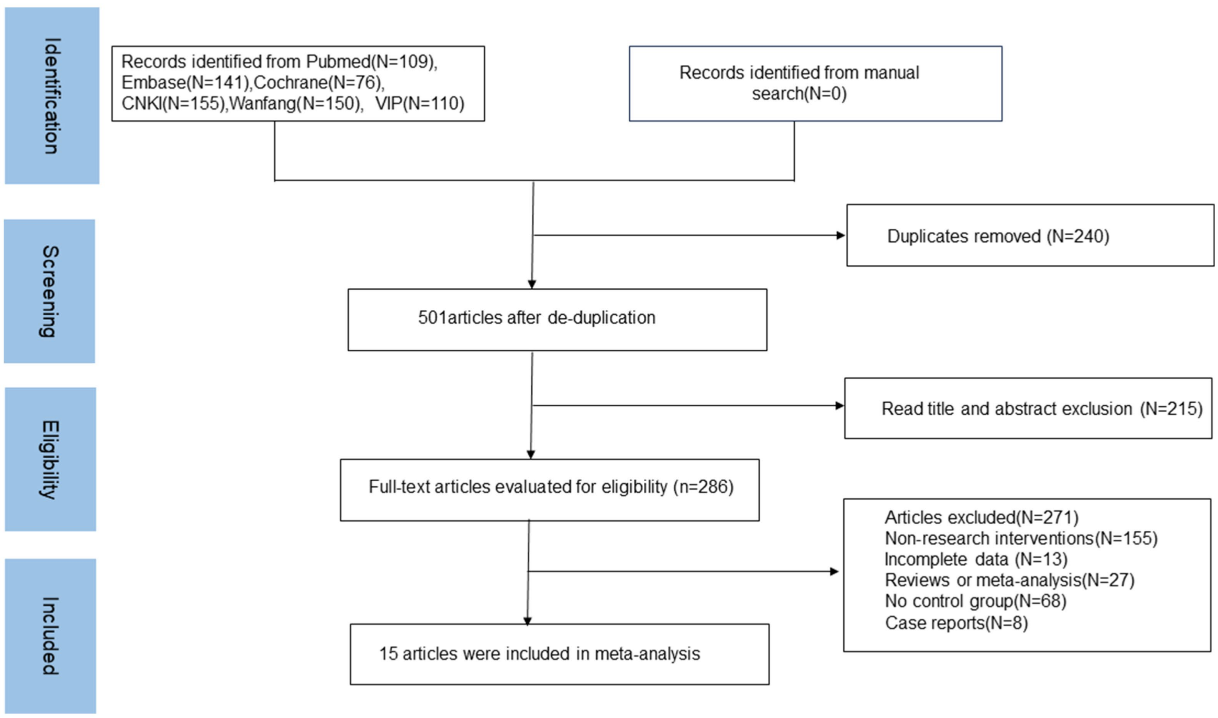

FIGURE 1
Literature screening flowchart and results.

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TABLE 1 Basic characteristics of the 15 included studies.

Author	Year	Area	Treatment group			Control group			Outcome
			Sample size	Age	Intervention	Sample size	Age	Intervention	
Xiao Huizhong	1990	Fujian Province	36	–	Electroacupuncture + TDP	36	–	Electroacupuncture	①②
Che Juan	1993	Heilongjiang Province	180	20 ~ 40	Electroacupuncture + TDP	40	20 ~ 40	Acupuncture	①②
Zhu Qiufen	1994	Gansu Province	90	10 ~ 59	Electroacupuncture + TDP	80	10 ~ 59	TDP	①②
Wu Hongbo	1998	Fujian Province	132	21 ~ 68	Electroacupuncture + TDP	68	21 ~ 68	Electroacupuncture	①②
Qiu Xiaolong	2006	Zhejiang Province	38	15 ~ 80	Electroacupuncture + TDP	43	15 ~ 80	Acupuncture + TDP	①②
Zhang Guangli	2008	Hunan Province	50	13 ~ 72	Electroacupuncture point-through-point + TDP	50	15 ~ 69	Electroacupuncture point-through-point	①②
Tian Qiang	2009	Guizhou Province	18	1 ~ 50	Electroacupuncture + TDP	22	7 ~ 60	Electroacupuncture	①②
Xin Yuwen	2010	Guangdong Province	65	3 ~ 75	Electroacupuncture + TDP	30	5 ~ 76	Western medicine	①②
Chang Xueli	2011	Henan Province	50	27.26 ± 15.78	Electroacupuncture + TDP	22	26.87 ± 16.25	Acupuncture	①②
Cao Fadong	2012	Henan Province	85	19 ~ 68	Electroacupuncture + TDP	85	20 ~ 69	Electroacupuncture	①②
Hu Jiaqian	2013	Zhejiang Province	48	3 ~ 70	Electroacupuncture + TDP	44	14 ~ 73	Electroacupuncture	①②
Wu Lei	2013	Chongqing	88	3 ~ 7	Electroacupuncture + TDP	88	3 ~ 7	Acupuncture + TDP	①②
Zou Yan	2014	Zhejiang Province	30	15 ~ 55	Electroacupuncture + TDP	30	18 ~ 59	Electroacupuncture + acupuncture	①②
Li Shujuan	2015	Hebei Province	76	16 ~ 72	Electroacupuncture + TDP	76	14 ~ 69	Electroacupuncture	①②
Ge Xiaohang	2016	Henan Province	22	22 ~ 78	Electroacupuncture point-through-point + TDP	22	18 ~ 71	Electroacupuncture point-through-point	①②

TDP, Teding Dianci Pu; ①: Efficacy rate, ②: Cure rate.

TABLE 2 Quality assessment of included studies.

Author	Year	Random	Randomization concealment	Blind	Withdrawal/loss to follow up	Total score
Xiao Huizhong	1990	0	0	0	1	1
Che Juan	1993	1	0	0	1	2
Zhu Qiufen	1994	1	0	0	1	2
Wu Hongbo	1998	1	0	0	1	2
Qiu Xiaolong	2006	1	0	0	1	2
Zhang Guangli	2008	1	0	0	1	2
Tian Qiang	2009	2	1	0	1	4
Xin Yuwen	2010	1	0	0	1	3
Chang Xueli	2011	0	0	0	1	1
Cao Fadong	2012	2	0	0	1	3
Hu Jiaqian	2013	0	0	0	1	1
Wu Lei	2013	2	0	0	1	3
Zou Yan	2014	1	0	0	1	2
Li Shujuan	2015	1	0	0	1	2
Ge Xiaohang	2016	2	1	0	1	4

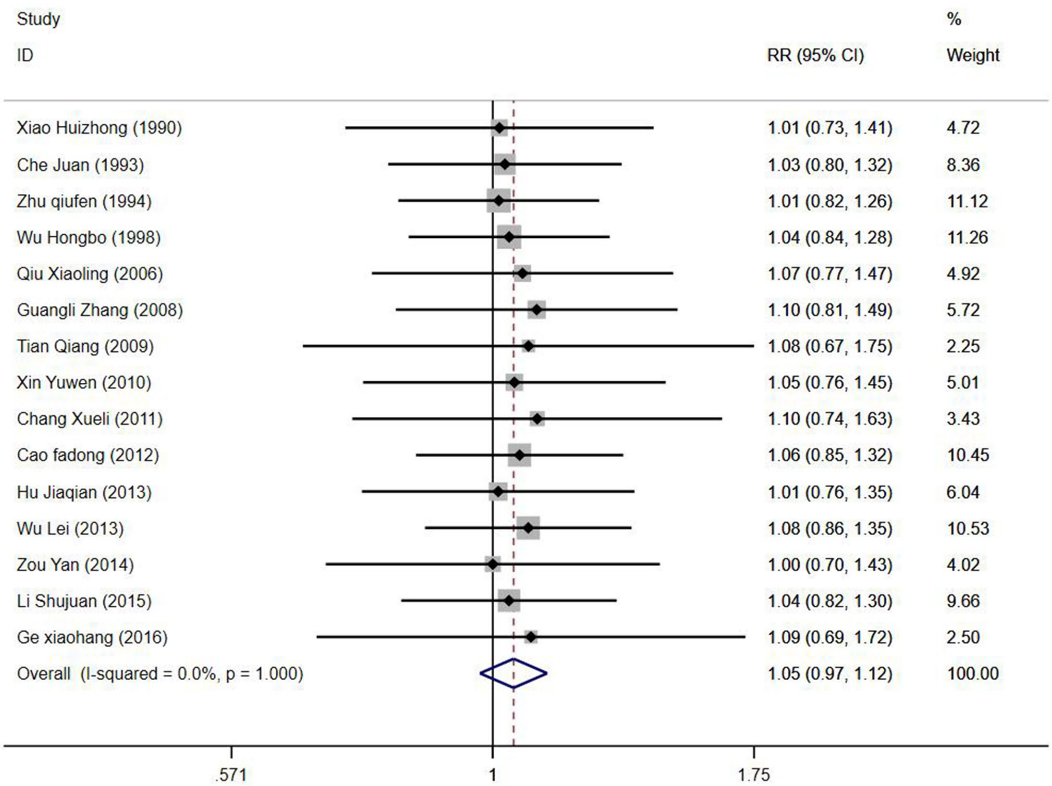

FIGURE 2
Systematic review and meta-analysis of efficacy rate.

findings. The results (Figure 3) indicated no significant changes, suggesting stability. Additionally, Egger's test ($T = 0.98$, $p = 0.345$) and funnel plot results revealed no apparent publication bias (Figure 4). Stratification based on factors such as the inclusion of minors and whether electroacupuncture was used as a control intervention showed no significant variations in study outcomes (Figure 5).

3.4.2 Cure rate

All included studies reported both cure rate and efficacy rate. Consequently, our study pooled the results for the cure rate. Heterogeneity testing revealed no statistical heterogeneity among the 15 studies ($p = 1.00$, $I^2 = 0.966\%$). Therefore, a fixed-effect model was employed for the combined analysis. The Meta-analysis results

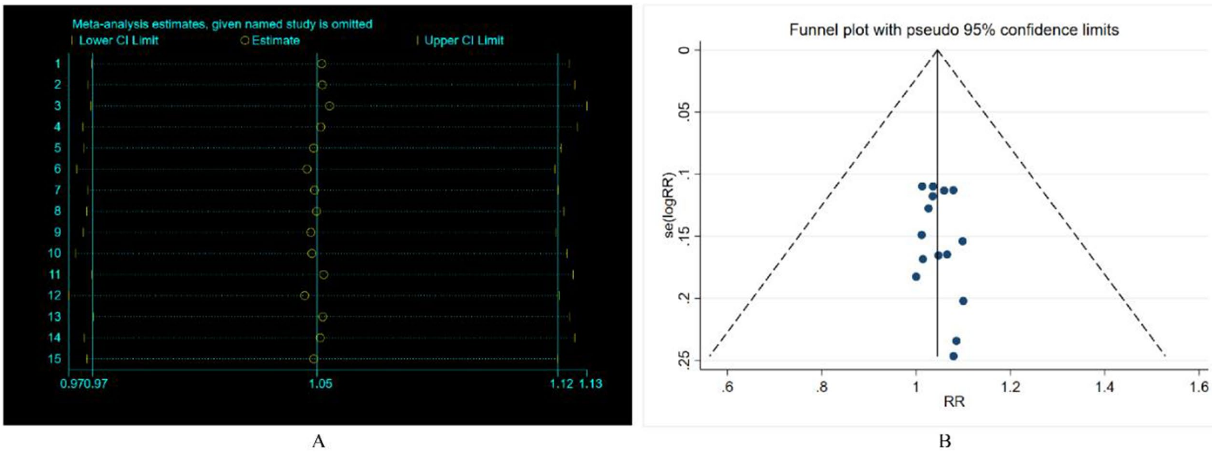

FIGURE 3
Sensitivity analysis and funnel plot of efficacy rate.

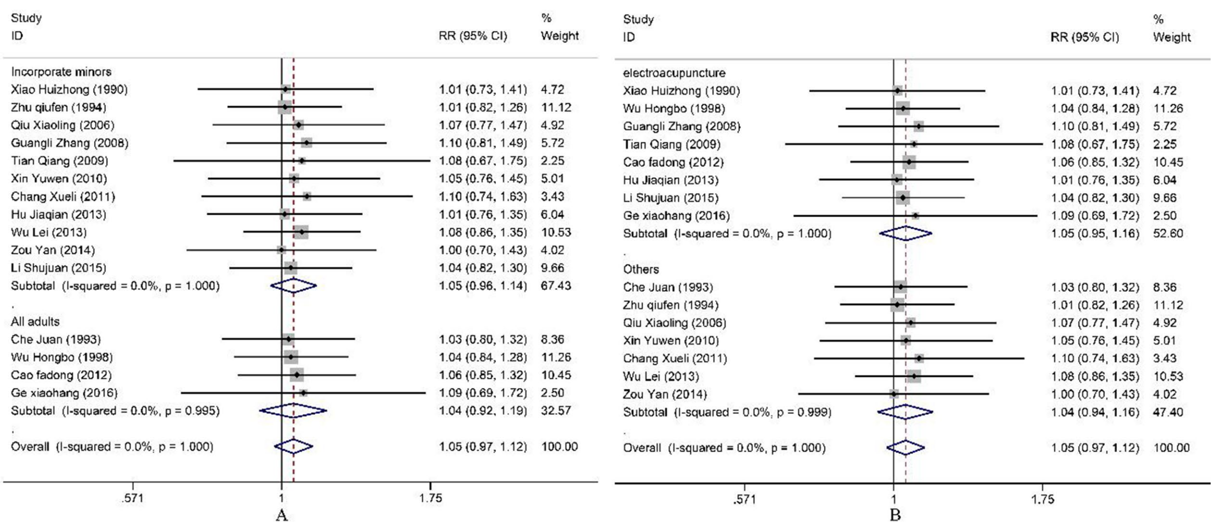

FIGURE 4
Subgroup analysis.

(Figure 5) demonstrate that electroacupuncture combined with TDP therapy significantly outperformed other treatment methods in terms of cure rate [$OR = 1.14$, 95%CI (1.05, 1.24), $p = 0.002$]. To assess the robustness of these findings, a sensitivity analysis was conducted (Figure 6). The results indicate that there were no significant changes, suggesting that the results are stable. Additionally, Egger's test ($T = 1.42$, $p = 0.180$) and the funnel plot results revealed no significant publication bias (Figure 6). When stratified by the inclusion of minors in the study population, it was observed that in studies including minors, the combination of electroacupuncture and TDP therapy demonstrated superior efficacy in treating peripheral facial paralysis compared to other therapeutic modalities [$OR = 1.14$, 95% CI (1.03, 1.25), $p = 0.011$]. Conversely, in studies where the population comprised solely adults, no significant difference was found between the combination therapy and other treatments [$OR = 1.15$, 95% CI (0.99, 1.33), $p = 0.059$] (Figure 7). Stratification based on whether the control group interventions included electroacupuncture did not alter the results significantly. Regarding the rate of marked improvement, electroacupuncture combined with TDP therapy was superior to both monotherapy [$OR = 1.13$, 95% CI (1.01, 1.26), $p = 0.032$] and other therapeutic methods [$OR = 1.15$, 95% CI (1.02, 1.30), $p = 0.020$].

4 Discussion

Peripheral facial paralysis is an inflammatory disorder induced by various etiologies that result in facial nerve impairment. Presently, the incidence rate of peripheral facial paralysis in China ranks sixth among all neurological disorders, with approximately 3 million cases annually (31), surpassing the annual incidence rate of 20 per 100,000 in Western countries (32).

In contemporary clinical practice, the predominant therapeutic approach for patients with peripheral facial paralysis involves pharmacological treatment. However, medication cycles typically

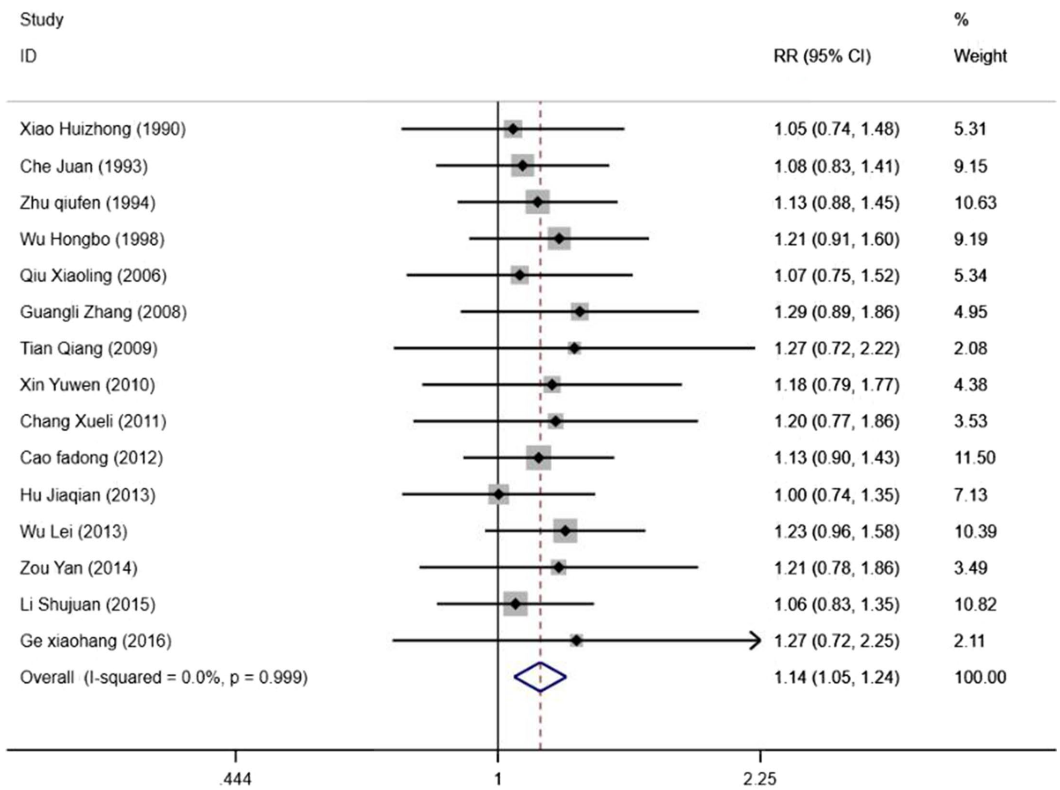

FIGURE 5
Systematic overview and meta-analysis of cure rate.

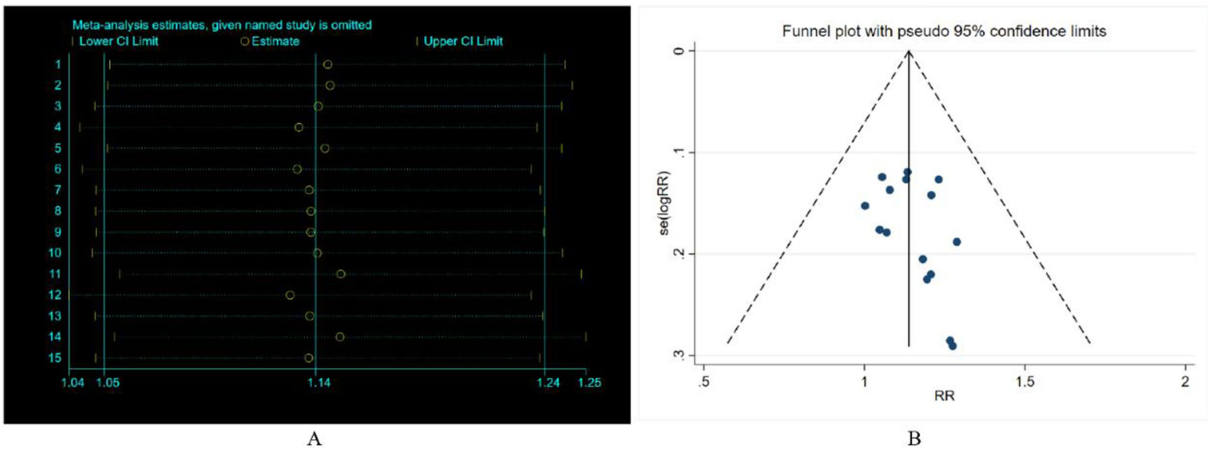

FIGURE 6
Sensitivity analysis and funnel plot of cure rate.

require a longer recovery time, with poorer outcomes and prognosis for quality of life. In comparison, external treatments in traditional Chinese medicine exhibit significant therapeutic advantages in the clinical treatment of peripheral facial paralysis (33–35). Electroacupuncture demonstrates considerable benefits over conventional Western medicine (36) and acupuncture alone (30). Furthermore, the thermal effects generated by TDP electromagnetic waves have biological effects such as enhancing metabolism, improving microcirculation in lesioned tissues, reducing inflammation, providing analgesic effects, and boosting immunity (37). TDP has been proven to have significant therapeutic effects in many clinical fields, with its application becoming increasingly widespread. Therefore, this study aims to conduct a systematic review and meta-analysis of randomized controlled trials on electroacupuncture combined with TDP for the treatment of peripheral facial paralysis, to evaluate the effectiveness of electroacupuncture combined with TDP in treating peripheral facial paralysis.

The findings of this study indicate that the efficacy rate of electroacupuncture combined with TDP therapy for treating peripheral facial paralysis shows no significant difference when

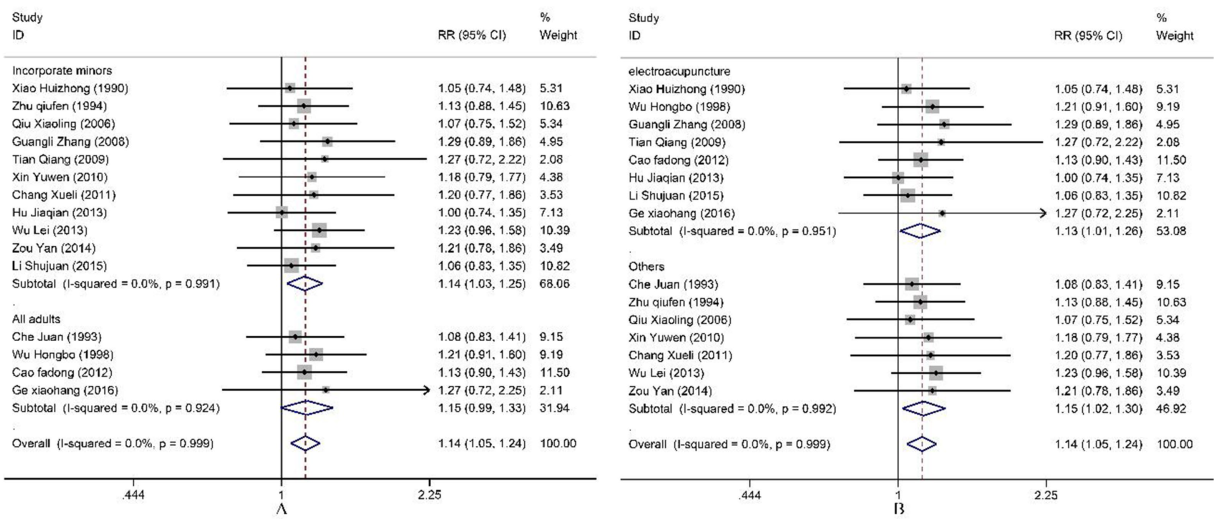

FIGURE 7
Subgroup analysis of cure rate.

compared to other therapeutic methods. This consistency in results persists across various subgroups. There is a certain heterogeneity in this study, which is mainly caused by the different measures of the control group, the inconsistent evaluation criteria of curative effect and the small sample size. Notably, the recovery rate for peripheral facial paralysis treated with electroacupuncture combined with TDP therapy surpasses that of other methods. Subgroup analysis further reveals that, among pediatric populations, the recovery rate for electroacupuncture combined with TDP therapy is superior to other treatments. Regardless of whether the comparison is with standalone electroacupuncture or alternative therapies, the recovery rate for electroacupuncture combined with TDP therapy remains higher. However, it is crucial to note that the methodological quality and reporting standards of the included studies are generally low, and the sample sizes are limited, which constrains the overall reliability of this systematic review. In this sense, large randomized controlled trials with higher quality requirements need to be conducted to validate the efficacy of electroacupuncture combined with TDP in the treatment of peripheral facial palsy.

There are several limitations inherent in this study. Firstly, both the treatment and control groups utilized electroacupuncture for peripheral facial paralysis; however, there was no description of the waveform or timing of the electroacupuncture application. Variations in waveform (38, 39) and timing (40, 41) can significantly impact the efficacy of treatment for peripheral facial paralysis. Secondly, the control group was subjected to multiple therapeutic interventions, which may have confounded the results and affected their generalizability. The sample size of the included research is small, and the research results may lack representativeness. Furthermore, none of the included studies employed blinding techniques, potentially introducing a degree of bias into the findings. It is suggested that large-scale, high-quality randomized controlled trials should be carried out in future research, and stricter blind method and randomization procedures should be included. In addition, it is suggested that the measurement of the results should be further standardized.

5 Conclusion

Meta-analysis showed that the effective rate of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis was not significantly different from other treatment methods, and the recovery rate was better than other treatment methods. Subgroup analysis showed that the recovery rate of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis was better than other methods in the minor population; whether electroacupuncture alone or other treatment methods, the recovery rate of electroacupuncture combined with TDP in the treatment of peripheral facial paralysis was better than other methods.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

H-WG: Writing – original draft, Writing – review & editing. Q-CX: Writing – original draft, Writing – review & editing. Z-HL: Writing – original draft, Writing – review & editing. WC: Writing – original draft, Writing – review & editing. YL: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2024.1450312/full#supplementary-material

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Machine learning to predict radiomics models of classical trigeminal neuralgia response to percutaneous balloon compression treatment

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Background: Classic trigeminal neuralgia (CTN) seriously affects patients' quality of life. Percutaneous balloon compression (PBC) is a surgical program for treating trigeminal neuralgia. But some patients are ineffective or relapse after treatment. The aim is to use machine learning to construct clinical imaging models to predict relapse after treatment (PBC).

Methods: The clinical data and intraoperative balloon imaging data of CTN from January 2017 to August 2023 were retrospectively analyzed. The relationship between least absolute shrinkage and selection operator and random forest prediction of PBC postoperative recurrence, ROC curve and decision -decision curve analysis is used to evaluate the impact of imaging histology on TN recurrence.

Results: Imaging features, like original_shape_Maximum2D, DiameterRow, Original_Shape_Elongation, etc. predict the prognosis of TN on PBC. The areas under roc curve were 0.812 and 0.874, respectively. The area under the ROC curve of the final model is 0.872. DCA and calibration curves show that nomogram has a promising future in clinical application.

Conclusion: The combination of machine learning and clinical imaging and clinical information has the good potential of predicting PBC in CTN treatment. The efficacy of CTN is suitable for clinical applications of CTN patients after PBC.

KEYWORDS

machine learning, nomogram, percutaneous balloon compression, trigeminal neuralgia, prognosis

Introduction

Classic trigeminal neuralgia (CTN) is a spontaneous pain sensation that occurs in the trigeminal nerve region, and the clinical manifestation is mainly paroxysmal electric shock-like or pinprick-like recurrent pain, CTN is a type of chronic pain that excludes secondary causes such as tumors, multiple sclerosis, or arteriovenous malformations affecting the trigeminal nerve. CTN is characterized by sudden, severe, electric shock-like pain or tingling in the distribution of one or more branches of the trigeminal nerve (1). The exact cause of CTN is not fully understood, but it is usually associated with vascular compression of the trigeminal nerve root. This compression leads to demyelination of the nerve fibers, resulting in abnormal electrical conduction and hypersensitivity. CTN usually affects the side of the face with pain and may be triggered by daily activities such as chewing, talking, or touching the face. CTN is relatively rare, with an incidence of about 4–12 per 100,000 people per year. It is more common in women and is usually seen in individuals over the age of 50 (2, 3).

Surgical treatments for CTN include microvascular decompression (MVD), PBC, radiofrequency thermocoagulation and gamma knife radiation therapy. Each approach carries its unique risk–benefit profile, with treatment selection influenced by factors such as the patient's financial situation, age, comorbidities, as well as patient and physician preferences (3, 4). At present, the anticonvulsants carbamazepine and oxcarbamazepine are the main drugs to treat TN, but medication can bring side effects including drowsiness, dizziness, skin rash, etc. Not only that, often patients will not be able to achieve the therapeutic dose of the medication or medication dosage should be considered for surgical treatment (1, 3). MVD is presently the preferred surgical intervention for trigeminal neuralgia when there is evident vascular nerve compression. However, it poses significant challenges to the surgeon and is associated with potential postoperative complications. These complications include exacerbated pain, cerebrospinal fluid leakage, intracranial infections, and other severe adverse events, which can ultimately result in patient mortality (4, 5). Among them, PBC is effective in relieving pain in many CTN patients. Studies have reported initial pain relief rates of 80–90%. The procedure is particularly valued for its rapid pain relief and relatively low risk of serious complications, also to treat patients with recurrence (6, 7). Therefore, clinicians are increasingly using PBC for patients who cannot tolerate other surgical methods (5). However, pain recurrence is common, and different recurrence rates are reported in the literature. Some patients may require repeat surgery to maintain pain relief. And common side effects of PBC include facial numbness, which may be temporary or permanent. Among the less common complications, patients may also experience bite muscle weakness, corneal numbness leading to keratitis, or numbness from anesthesia (painful numbness), infection, bleeding, or damage to surrounding structures (8). Therefore, Each approach carries its unique risk–benefit profile, with treatment selection influenced by factors such as the patient's financial situation, age, comorbidities, as well as patient and physician preferences. Therefore, there is a need to develop a predictive tool to assess which patients are likely to achieve long-term remission from PBC before surgery, which will help in planning follow-up care and other interventions as necessary. This proactive approach could improve the sustainability of treatment benefits.

Radiomics is the use of data representation algorithms to extract and analyze image structural features from medical images provide detailed quantification of phenotypic and tissue heterogeneity, including tumors, allowing for a more precise and comprehensive assessment of disease (9–11). Machine Learning (ML) has revolutionized medical imaging by improving the ability to predict treatment outcomes for a wide range of diseases. By analyzing complex patterns in imaging data, ML algorithms can provide insights that inform personalized treatment plans and improve prognostic accuracy (12). PBC is a surgical procedure in which a needle is viewed through the cheek into the foramen ovale to compress the trigeminal ganglion using an intraoperative lateral fluoroscopic film. During the operation, the side perspective sheet shows the position of the balloon and the correct pear -shaped shape is considered the key to the success of the operation (13). Previous studies have shown that factors such as TN therapeutic effects and imaging features, and balloon shapes, volume and compression time may be related (14). Despite many scholars' attempts to define the shape of the pear, the criteria for becoming a pear shape are still not uniform in the current position. Studies have reported the correlation analysis between clinical factors and the therapeutic efficacy of trigeminal neuralgia treatment (15). Most previous studies mainly focused on the comparative study of clinical data, ignoring the predictive value of imaging histology as well as histomorphology in disease progression. The predictive value of intraoperative balloon morphology imaging histological features for postoperative recurrence of TN is unclear.

In this study, patient clinical information and imaging histology morphological features based on intraoperative balloon x-ray were extracted, a predictive model for postoperative recurrence of TN was constructed by multifactorial logistic regression analysis, RF algorithms, a nomogram based on the columns of clinical risk factors and imaging histology features was established (16, 17). In conclusion, patients with CTN have considerable variability in their response to treatments such as percutaneous balloon compression (PBC). Our personalized prediction in this study could help identify which patients are most likely to benefit from PBC, thereby improving the overall success of the intervention.

Methods

The study systematically collected clinical and intraoperative imaging data from patients with TN who underwent PBC between January 2017 and March 2023. Follow-up assessments were performed via telephone to monitor for TN recurrence. Inclusion criteria comprised patients aged 18 years or older diagnosed with primary TN, with complete clinical and imaging materials. The exclusion standards include the history of the surgical medical history of the previous microvascular decompression (MVD) or the glycerol root cutting (PGR) surgery (PGR) surgery, incomplete clinical or imaging records, secondary TN, recurrence TN, and patients who cannot be followed up after discharge (18).

In addition, pertinent clinical information, including collected clinical data, was obtained from the patient's hospital medical record department. This information encompasses a comprehensive array of clinical data, including: age, gender, duration of facial pain, location of the affected side of the pain, trigeminal neuralgia typology, NRS score, evaluation of the efficacy of carbamazepine, balloon morphology, trigeminal nerve cardiac reflexes, facial numbness, weakness in mastication, keratitis, and score of the severity of compression. Clinical manifestations such as postoperative surgical response were confirmed and recorded by a Hao Mei imaging surgeon. Finally 117 patients were included in the study.

Surgical procedure

All the procedures are consistent with what our team has done before (18). And analysis of the degree of vascular compression is performed post-procedure.

Compression severity score

We define level I as mild blood vessels, and II and III levels are defined as severe blood vessels. Level I indicates that there are no blood vessels around the nerve or there are blood vessels around the nerve but there is no direct contact. Grade II indicates that the trigeminal is oppressed by blood vessels, but not to the extent that it causes distortion. Grade III is when a blood vessel compresses the trigeminal nerve, causing distortion. In the criteria of (18, 19).

TN staging

Diagnosis was based on the International Classification of Headache Disorders (19). The TN classification is based on the standards formulated by the International Pain Research Association.

Outcome assessment

Through the standardized telephone follow-up after the patient was discharged, the pain relief level was evaluated using the Barrow Institute of Neurology (BNI) Standard (I-V) (20, 21). We classify the BNI to II-III, indicating that the pain relieves it, and the BNI is graded to IV-V, indicating that the pain relief is invalid.

Image segmentation and feature extraction

Intraoperative cranial X-ray images of randomly selected patients were evaluated for inter-observer agreement for feature extraction. Haematoma contouring was done manually by 2 experienced radiologists (film readers 1 and 2) independently without knowledge of clinical data. The reproducibility of inter-observer outlining of the region of interest (ROI) was evaluated using the intragroup correlation coefficient (ICC). ICC value>0.75 is considered to be a good and consistent instruction, using 3D Slicer software (Version 4.13) to extract the historical characteristics of all images. Image pre-processing, including noise removal, contrast enhancement and image smoothing, to improve image quality. Use thresholding, morphological operations, original_shape_maximum2DiameterRow: This is the length of the balloon in the direction of the maximum diameter. This can be determined by calculating the maximum distance between all pairs of points inside the balloon. original_shape_Elongation: This is the aspect ratio of the balloon and is used to describe how flat the balloon is. It can be determined by calculating the length of the long and short axes of the balloon (22).

Imaging histological feature screening and model construction

One-way analyses were performed using R software, and clinical traits and imaging histologic features that were statistically different in a single factor were included in random forest (RF) tree model Screening important features and LASSO regression analysis for removing overfitting. RF parameter settings and validation. n_estimators: number of trees, usually 1000. max_depth: tree depth to avoid overfitting. 5 samples needed for re-splitting. Minimum number of samples for leaf nodes, increasing reduces overfitting. max_features: number of features considered per split, use sqrt(n_features). Cross-validation: k-fold cross-validation ($k = 5$) is used to assess the model's generalization ability. The importance of each feature is assessed using Random Forest and the most important features are selected. Model performance was assessed using metrics such as R^2 and MSE (23). LASSO regression: alpha is the penalty parameter, usually chosen through cross-validation. Normalize the data to ensure features are comparable. Cross-validation is used to select the optimal alpha value and to assess model performance. Examine residual plots to assess model fit (24). Calibration curves and DCA were used to assess the credibility of the model, and ROC curves (area under the ROC curve is greater than 0.5 and the diagnostic test has some diagnostic value) were used to validate the diagnostic ability of the model.

Statistical analysis

Use R software for statistical analysis and data processing. Count data were expressed as percentages, while measurement data were presented as mean ± standard deviation. Group comparisons were conducted using t-tests or chi-square tests.

Results

The study is depicted in Figure 1 as illustrated in Figure 2. LASSO and random forest algorithms were employed to select the most relevant radiomic features. Build nomogram for individual assessment, and then analyze the ROC curve and decision curve analysis to verify the reliability of the model.

Clinical characteristics

A total of 117 patients diagnosed with Classical Trigeminal Neuralgia were included in the study, Among them, 43 men, 74 women, an average age of 69.11 (age is 48 to 95 years old). Table 1 summarizes the clinical characteristics of patients.

Among these patients, 16 cases were categorized into the ineffective group in the training set, while 101 cases were classified into the effective group. There are no statistical differences in the two groups of patients in the age, duration of symptoms, accumulated sides, digital evaluation meters (NRS), trigeminal nerve reflexes, facial numbness, and keratitis (Table 1).

Univariate analysis for TN outcome

The relationship between the clinical characteristics of one -way logic regression and the prognosis of TN is adopted. As shown in Table 2, we noticed a significant correlation between the treatment effect between the trigeminal nerve division and the training concentrated drug TN ending ($p < 0.05$). Females accounted for the majority of patients who relapsed, and TTN strategy division is an important prediction indicator immediately relieved (or 0.70, 95%CI 0.51 ~ 0.94; or 0.71, 95%ci 0.51 ~ 0.95).

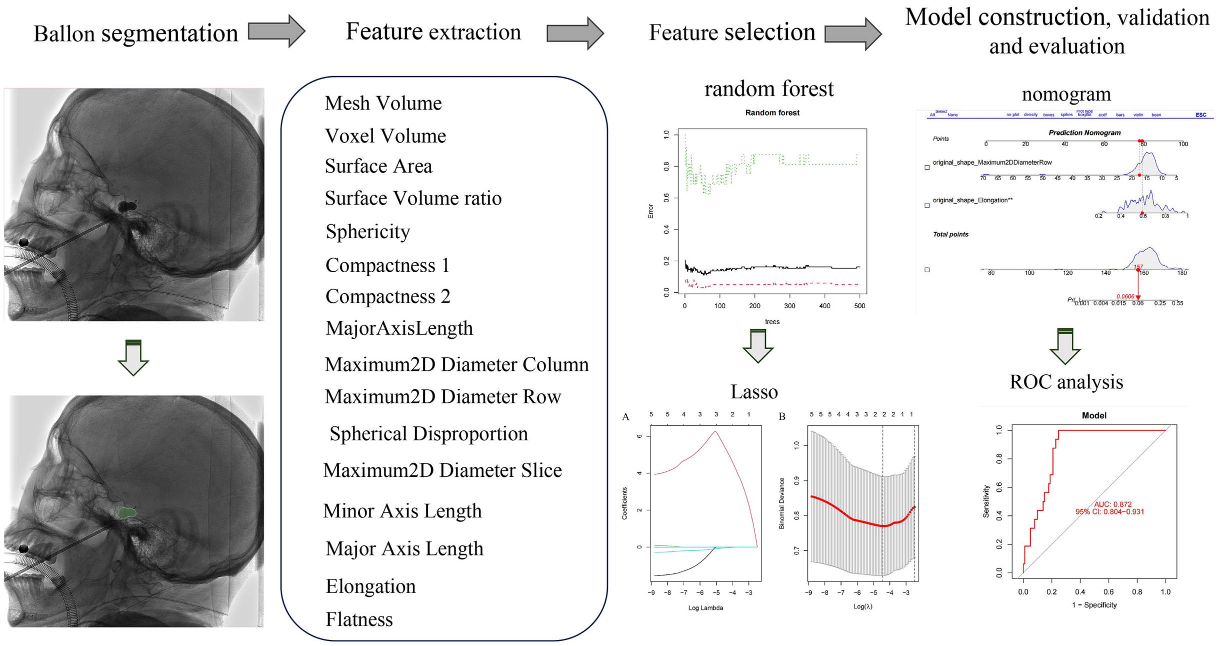

FIGURE 1
The overall workflow of our study. The ROI was manually drawn on the lateral plain film. Radiomic features were extracted from the radiographs to quantify their shape characteristics. LASSO and random forest algorithm were used to select radiomic features. A nomogram was created for individualized assessment, followed by ROC curve and decision curve analysis.

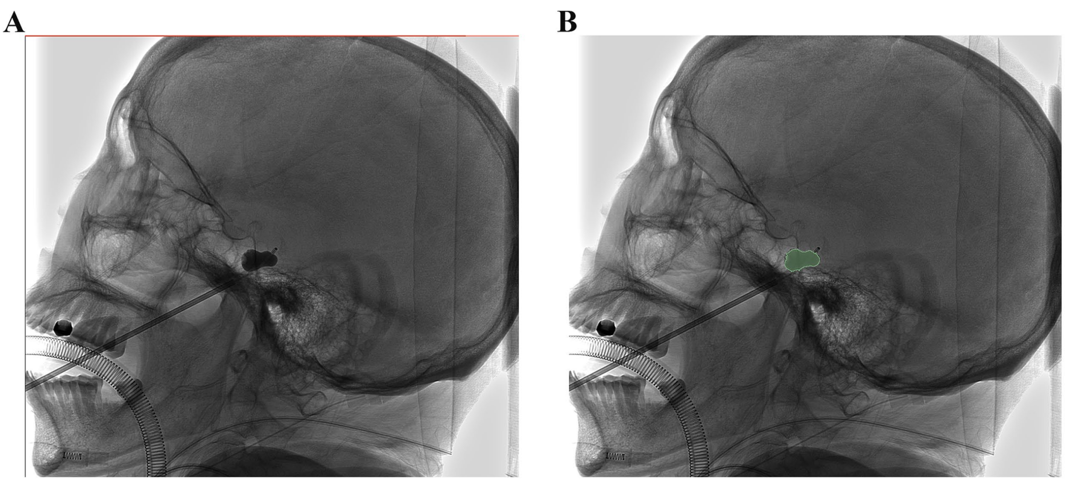

FIGURE 2
Image morphological feature extraction: **(A,B)** The ROI was manually drawn on the lateral plain film. Radiomic features were extracted from the radiographs to quantify their shape characteristics.

Machine learning to build diagnostic models and validation

Initially, three radiomics features were differentially extracted from the depicted ROIs. The inter-observer ICC ranged from 0.751 to 0.997, indicating good reproducibility of these features. Subsequently, the best radiomics features were identified from the ROI through mRMR and random forest (RF) tree model screening important features, as illustrated in Figures 3A,B. We performed a lasso Add a penalty function to keep compressing the coefficients so as to streamline the model to avoid covariance and overfitting (Figures 4A,B). The ROC curves of each feature in the model are shown, and their AUC values are:

original_shape_Maximum2D DiameterRow, original_shape_Elongation were screened to predict the prognostic prediction of TN for PBC treatment with the areas under the roc curves being. 0.812, 0.874; and the predictive and under the ROC curve of the model is 0.872 (Figures 5A,B).

TABLE 1 Patient characteristics.

Characteristics	Ineffective group ($n = 16$)	Effective group ($n = 101$)	p
Age (year)	65.69 ± 10.849	69.69 ± 9.536	0.14
Symptom duration (months)	91.87 + 136.504	82.64 ± 116.866	0.70
Gender			0.937
Male	6 (37.5%)	37 (37.7%)	
Female	10 (62.5%)	64 (62.3%)	
Affected side			0.055
Right	13 (81.25%)	55 (77%)	
Left	3 (18.75%)	46 (23%)	
Trigeminal division			0.024
V1	0 (0%)	4 (3.96%)	
V2	7 (43.75%)	11 (10.89%)	
V3	1 (6.25%)	13 (12.87%)	
V1 + V2	5 (31.25%)	21 (20.79%)	
V1 + V3	0 (0%)	1 (0.99%)	
V2 + V3	1 (6.25%)	33 (32.67%)	
V1 + V2 + V3	2 (12.5%)	18 (17.82%)	
Compression severity score			0.50
No vessel near nerve or grade I	3 (18.75%)	20 (19.8%)	
Grade II or III	13 (81.25%)	81 (80.2%)	
Therapeutic effect of drugs			0.049
No response to medical treatment	12 (75.0%)	48 (47.52%)	
Multiple side effects on drugs	4 (25.0%)	53 (52.48%)	
Intraoperative trigeminal cardiac reflex			0.266
No	3 (18.75%)	68 (67.33%)	
Yes	13 (81.25%)	33 (32.67%)	
Postoperative complications			
Facial numbness			0.20
No	6 (37.5%)	57 (56.44%)	
Yes	10 (62.5%)	44 (43.56%)	
Keratitis			0.40
No	13 (81.25%)	90 (89.11%)	
Yes	3 (18.75%)	11 (10.89%)	

TABLE 2 Univariate and multivariate logistic analyses of prognostic risk factors for TN.

Variable	Univariate logistic analysis				Multivariate logistic analysis			
	OR	(95% CI)		*p* value	OR	(95% CI)		*p* value
Sex	1.04	0.33	3.03	0.9				
Age	0.96	0.91	1.01	0.14				
Affected side	0.28	0.06	0.92	0.055				
Trigeminal division	0.70	0.51	0.94	0.024	0.71	0.51	0.95	0.028
Compression severity score	0.78	0.36	1.68	0.5				
Intraoperative trigeminal cardiac reflex	2.10	0.63	9.63	0.3				
Facial numbness	2.16	0.74	6.77	0.2				
Therapeutic effect of drugs	0.30	0.08	0.93	0.049	0.31	0.08	0.97	0.058
Keratitis	1.89	0.39	7.06	0.4				

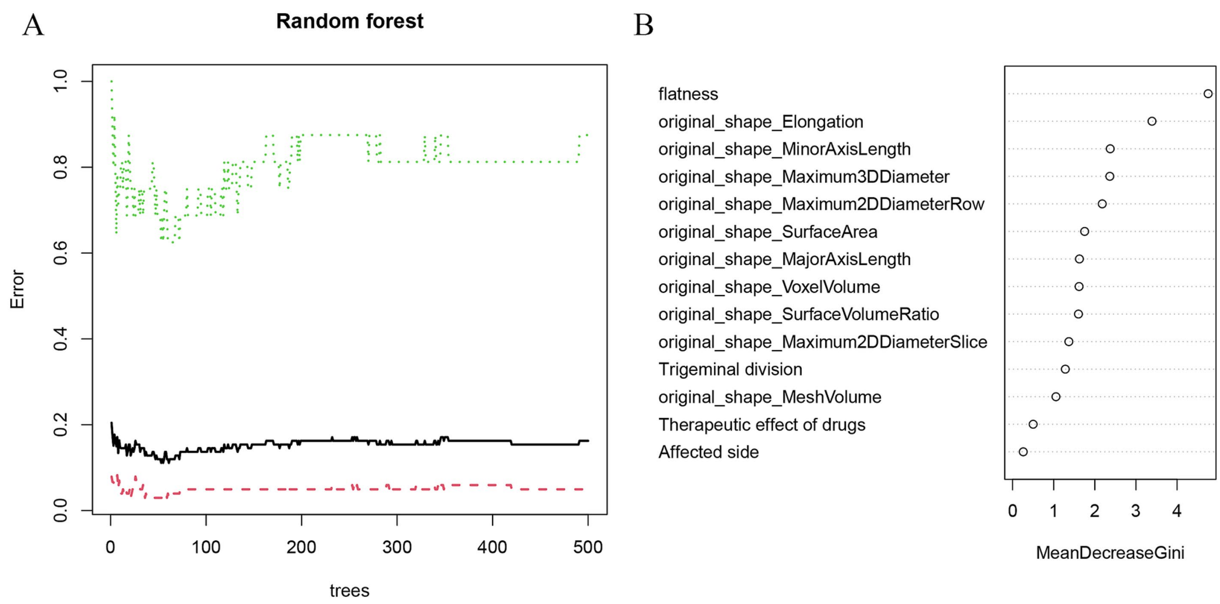

FIGURE 3
Random forest screening to predict the characteristic factors of recurrence. **(A)** The random forest algorithm showed the error between the relapse group and the control group. **(B)** Rank clinical-imaging morphological features according to importance scores.

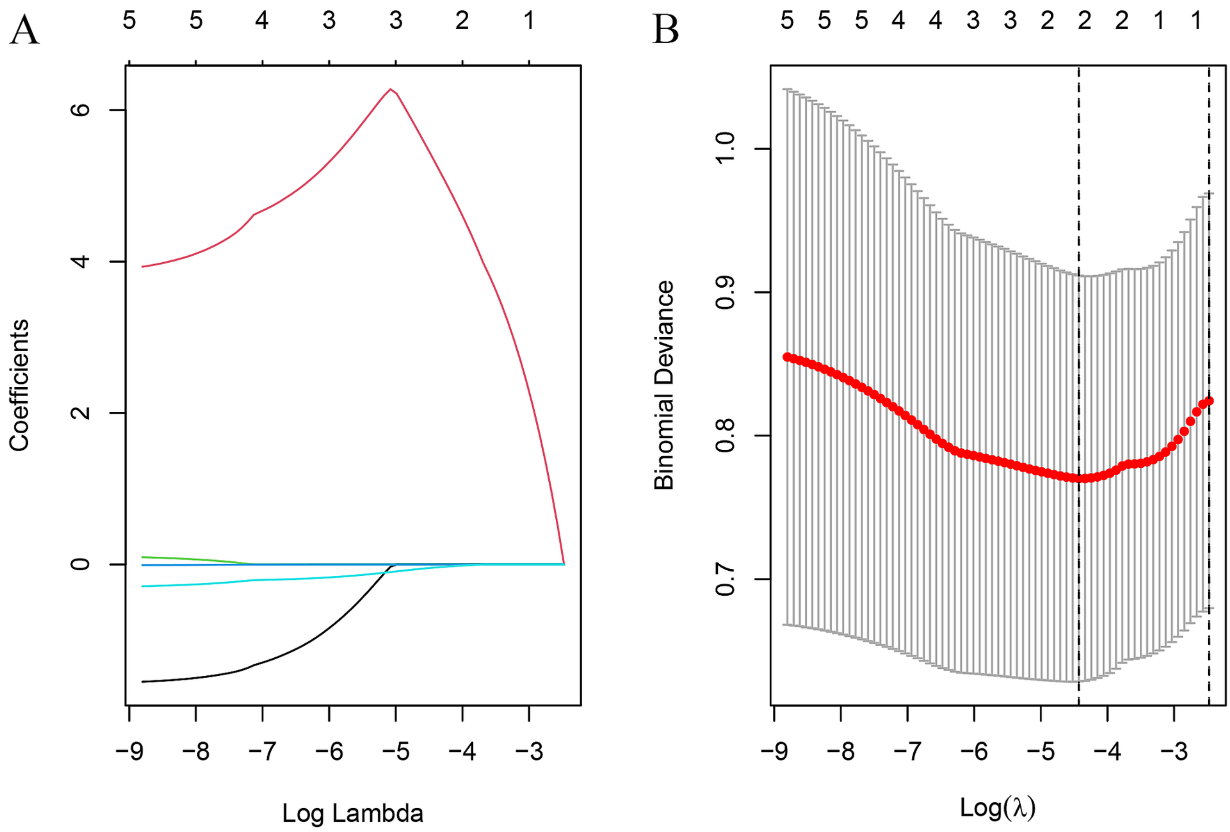

FIGURE 4
Texture feature selection using the least absolute shrinkage and selection operator (LASSO) logistic regression **(A)** The optimal tuning parameter (λ) was selected using 10-fold cross-validation in the LASSO regression model; **(B)** LASSO regression coefficient distribution.

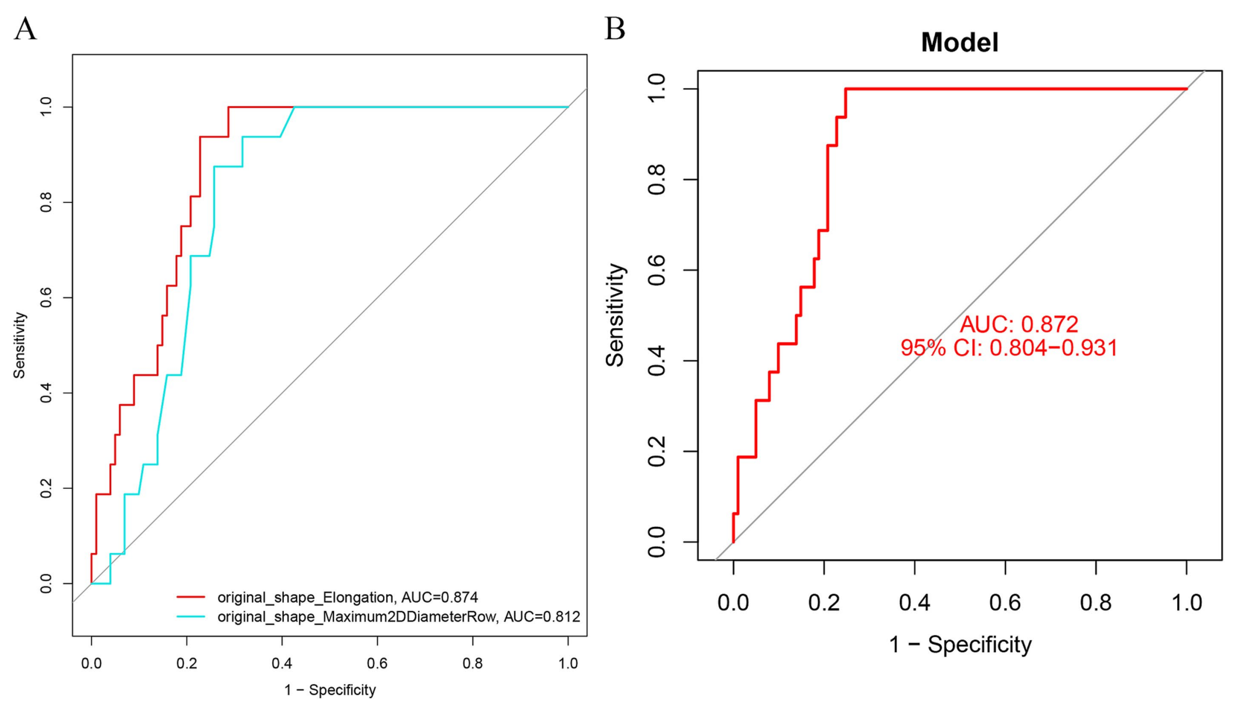

FIGURE 5
(A) ROC curve was used to analyze the prediction efficiency of image morphological feature model **(B)** ROC analysis of diagnostic model in training set. **(B)** ROC analysis of diagnostic model in validation set. AUC, area under the curve; subject operating characteristic curve (ROC); CI. Confidence Interval; LASSO, Least Absolute Shrinkage and Selection Operation.

4. Establishment of radiomics model

Imaging features from the RF model and lasso:original_shape_Maximum2DDiameterRow,original_shape_Elongation were incorporated to predict the risk of TN recurrence. A nomogram predicting the probability of effective regression after PBC in a typical TN patient was established (Figure 6A), and the calibration curve also shows the consistency of satisfactory (Figure 6B). The decision -making curve shows that the pillar diagram of the risk of effective results increases more benefits than the full or no scene (Figure 6C).

Discussion

Classical trigeminal neuralgia (TN) is characterized by sudden, severe, electric shock-like or stabbing pain in specific areas of the face, typically on one side and affecting the trigeminal nerve's V2 and V3 branches. These brief episodes, lasting seconds to minutes, can occur multiple times a day and are often triggered by routine activities like chewing, speaking, or touching the face (1, 4). However, due to the chronic onset of pain, when the pain is severe, it will seriously affect the patient's normal life and work (2). In recent years, PBC has become a common therapeutic option for the treatment of TN, which has a high success rate, simple technique, and relatively low risk, especially in elderly patients (25). PBC relieves trigeminal nerve pain by damaging myelinated axons involved in pain transmission, causing focal axonal injury and blocking abnormal discharge pathways (26). However, PBC has several disadvantages. Potential complications include facial numbness, which can be permanent, and sensory deficits. The procedure may also result in temporary or permanent jaw muscle weakness. Additionally, there is a risk of infection, bleeding, or hematoma at the puncture site. Over time, axonal myelin sheaths may regenerate, leading to pain recurrence (27). Previous studies indicate that PBC provides immediate postoperative pain relief in 82–97.1% of cases, lasting about 18–20 months (5, 28, 29).

Percutaneous balloon compression (PBC) stands as a minimally invasive procedure frequently employed to address trigeminal neuralgia (TN). Its mechanism involves compressing the trigeminal ganglion, thereby mitigating pain by impairing the nerve fibers responsible for pain signal transmission. Despite its effectiveness, PBC can lead to various complications. Among these, facial numbness emerges as the most prevalent. While indicative of successful trigeminal ganglion compression, persistent or severe facial numbness can significantly impact quality of life (13, 29, 30). Several previous studies have shown that clinical factors such as preoperative TN type, symptom duration, NRS, and TN nerve compression severity scores in patients with atypical pain affect the outcome of ablative procedures including GR and SRS, as well as the consequences of MVD procedures (13, 30, 31). The treatment of PBC in CTN patients is still largely dependent on subjective judgment (32, 33), and therefore there is a need to develop a validated method for predicting recurrence modeling after PBC. Leveraging radiomics could offer a non-invasive avenue to discern which patients are most likely to benefit from PBC by analyzing pre-procedure imaging data. Such an approach could pave the way for personalized treatment plans and improved outcomes in CTN patients.

Radiomics has substantial advantages over traditional structural imaging by artificial intelligence applications to develop predictive models (34–36). This integration significantly improves clinicians'

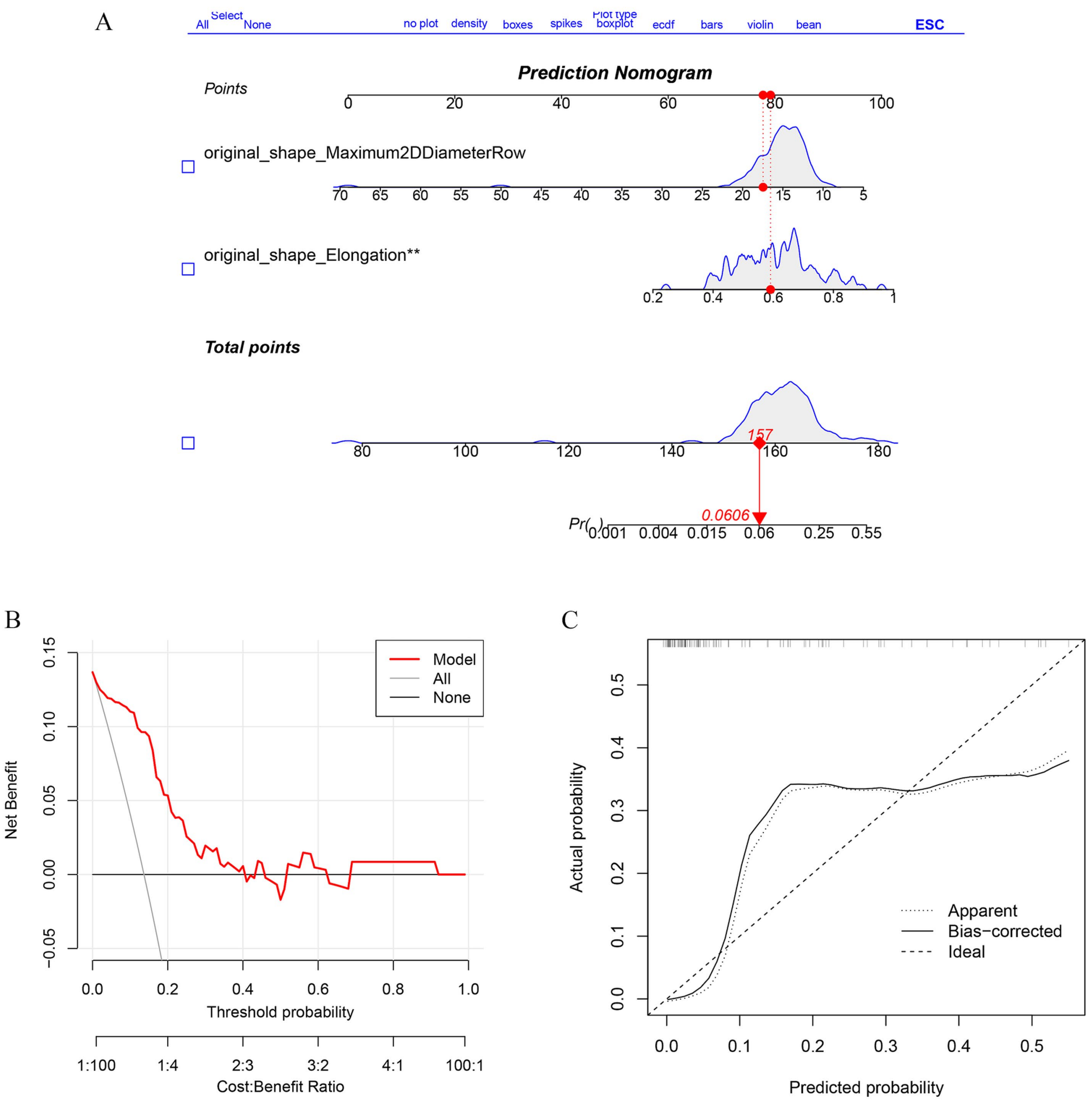

FIGURE 6
Establishment of Radiomics Model and performance verification. **(A)** Nomogram was constructed to predict the probability in recurrent trigeminal neuralgia progress. The values of each variable (Affected side, sex, Flatness, Major Axis Length) are summed to obtain a total score. **(B)** The calibration curves of the nomogram. **(C)** The DCA curve shows the clinical decision benefit of this model.

capacity to make evidence-based diagnoses and predict treatment efficacy. The response to treatments like PBC varies widely among patients with Classical Trigeminal Neuralgia (CTN). Individualized predictions can aid in identifying which patients are most likely to benefit from PBC, thereby improving the overall success of the intervention. By predicting treatment response, clinicians can select appropriate candidates for PBC, potentially avoiding invasive procedures for those unlikely to benefit (29, 37). In our study, we identified two crucial imaging features and developed an accurate prediction model utilizing LASSO and random forest algorithms. This model was specifically designed to predict the outcome of postoperative PBC in patients with CTN, achieving an AUC of 0.872, indicative of good performance. Furthermore, the calibration curve exhibited good agreement with the decision curve analysis (DCA) curve, suggesting potential clinical application. This imaging histology model could transform patient management. The model identifies high-risk patients by combining imaging and histological features with clinical factors. This risk assessment helps clinicians develop personalized treatment plans, offering early intervention or alternative options for those with a poorer prognosis. Treatment decisions can be made by identifying patients who are more likely to benefit, thereby optimizing the allocation of resources (38).

The clinical imaging histological model developed in this study predicted the efficacy of PBC in patients with trigeminal neuralgia (TN), but has limitations. The sample size was small and the data were derived from a single center, limiting the generalisability and applicability of the findings. The selection of imaging histological features may be limited by the accuracy and consistency of the imaging technology used. Future studies should focus on multi-center studies to validate the model. Combining clinical, genomic and other biomarker data improves the accuracy and reliability of predictive models. Examining patients' clinical and imaging characteristics over time allows for more precise and individualized treatment. By addressing these limitations, imaging genomics models can be enhanced, ultimately improving patient prognosis and outcomes.

Conclusion

The use of radiological features and machine learning models to predict treatment response in CTN is essential for personalized treatment planning. This approach is expected to optimize treatment outcomes and reduce adverse effects, as well as improve patient quality of life and cost-effectiveness. The subsequent construction of large-sample multicentre predictive modeling is expected to transform CTN management into a more precise and patient-centered practice, ultimately leading to better clinical outcomes and higher patient satisfaction.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the Medical Ethics Committee of Zhongnan Hospital of Wuhan University. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

JW: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. CQ: Conceptualization, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. YZ: Conceptualization, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. XW: Data curation, Formal analysis, Project administration, Supervision, Writing – original draft. DQ: Conceptualization, Investigation, Resources, Supervision, Writing – original draft. KC: Conceptualization, Investigation, Project administration, Resources, Writing – original draft. YC: Conceptualization, Investigation, Project administration, Resources, Writing – original draft. LS: Conceptualization, Investigation, Project administration, Resources, Writing – original draft. JY: Conceptualization, Investigation, Project administration, Resources, Writing – original draft. DX: Conceptualization, Investigation, Project administration, Resources, Writing – original draft. SC: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing, Writing – original draft. NX: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Intravenous fosphenytoin therapy for the rescue of acute trigeminal neuralgia crisis in pre- and post-neurosurgical patients: a retrospective observational study

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Background: There is no established treatment for the acute exacerbation of trigeminal neuralgia. We aimed to investigate the efficacy and safety of intravenous fosphenytoin for this disease.

Methods: We conducted a retrospective observational study of data from 41 patients with trigeminal neuralgia who received intravenous fosphenytoin therapy. Fosphenytoin diluted with physiological saline was administered intravenously at a loading dose of 9.8–20.7 mg/kg or at a dose of 7.5–9.5 mg/kg when maintenance therapy was needed. Pain was evaluated using a numerical rating scale (NRS), assessed immediately before administration (baseline) and at 2, 12, and 24 h after administration.

Results: The mean (± standard deviation) NRS score was 9.85 ± 0.69, 0.49 ± 1.47, 1.60 ± 2.19, and 3.46 ± 3.19 at baseline, 2, 12, and 24 h after administration, respectively ($p < 0.001$). Intravenous fosphenytoin therapy was effective for the acute exacerbation of trigeminal neuralgia regardless of whether it was administered during the perioperative period of microvascular decompression (MVD) or the type of drugs used concomitantly. Fosphenytoin was effective when re-administered ($n = 14$) or at a maintenance dose ($n = 2$). The adverse drug reactions observed were mild dizziness in six patients, abnormal auditory perception and thirst in three patients each, and somnolence, decreased SpO_2, and drug eruption in one patient each, all of which were transient.

Conclusions: Intravenous fosphenytoin therapy can immediately eliminate pain during acute exacerbation of trigeminal neuralgia and can be a useful therapeutic drug in emergency response or until elective treatment, such as MVD, is performed.

KEYWORDS

trigeminal neuralgia, acute exacerbation, fosphenytoin, phenytoin, numerical rating scale, microvascular decompression

1 Introduction

Trigeminal neuralgia is induced when a trigger zone is stimulated by activities of daily living, such as eating, tooth brushing, face washing, and talking, and is characterized by sudden unilateral pain attacks along the branches of the trigeminal nerve (1). The International Classification of Headache Disorders (3rd Edition) classifies trigeminal neuralgia into three categories. Typically, trigeminal neuralgia is associated with the compression of the trigeminal nerve by blood vessels. Secondary trigeminal neuralgia is caused by compression by a tumor or demyelination of the nerve (e.g., multiple sclerosis or brain infarction). The causes of idiopathic trigeminal neuralgia cannot be determined by examinations, such as electrophysiological tests and magnetic resonance imaging (2, 3). Various antiepileptics and other drugs are recommended for typical trigeminal neuralgia and idiopathic trigeminal neuralgia (primary trigeminal neuralgia) based on the results of a systematic review and other studies. For secondary trigeminal neuralgia, pharmacotherapy should be similar to that for primary trigeminal neuralgia, although evidence regarding this is sparse. Thus, currently, pharmacotherapy does not differ based on the type of trigeminal neuralgia (2).

Treatment guidelines (2, 4–6) recommend carbamazepine or oxcarbazepine as the first-line pharmacotherapy for trigeminal neuralgia, and carbamazepine is widely used in Japan. Baclofen and lamotrigine are recommended for second-line pharmacotherapy, although these agents are used off-label. Despite appropriate treatment with any of these pharmacotherapeutic strategies alone or in combination, intractable pain due to the acute exacerbation of trigeminal neuralgia develops in some patients. Occasionally, persistent pain attacks lasting for days or weeks occur during severe episodes. Microvascular decompression (MVD) and trigeminal nerve blocks are effective. However, performing these procedures in emergency medical care settings is challenging. These procedures are often performed electively, and the waiting time for MVD at our hospital is 5–30 days.

Oral agents are not suitable for pain relief during acute exacerbations. Japanese treatment guidelines recommend the following drugs as effective fast-acting analgesics, although the strength of the recommendation is low because no randomized controlled trials have been conducted (1).

- Local anesthetics such as lidocaine (administration route: eye instillation, nasal or oral route, injection into the trigger point, intravenous infusion, or nerve block) are used.
- Anticonvulsants such as phenytoin or fosphenytoin (intravenous infusion) are used.
- Serotonin agonists such as sumatriptan (subcutaneous injection or nasal route) are used.

Fosphenytoin is an anticonvulsant commonly used to treat status epilepticus. Fosphenytoin, a prodrug of phenytoin, is used to treat adverse reactions associated with phenytoin, such as injection site pain and phlebitis. It is rapidly converted in the plasma to its active form, phenytoin, in equivalent (equimolar) amounts and can be safely administered intravenously. Phenytoin blocks Na^+ channels by suppressing the influx of Na^+, after which depolarization of neurons and neurotransmission within axons are less likely to occur. Through this mechanism, phenytoin specifically suppresses only the abnormal frequency of discharge or "firing" of nerves and does not suppress normal, less frequent discharge activity of nerves. Carbamazepine is the first-line drug for the treatment of trigeminal neuralgia; therefore, voltage-dependent Na^+ channels are considered to be involved in the pathology of trigeminal neuralgia, and reports indicate that the firing of nerve potential is a cause of pain in trigeminal neuralgia (7, 8). Voltage-dependent Na^+ channels are thought to be involved in the mechanism of action of carbamazepine and fosphenytoin. The use of fosphenytoin for the acute exacerbation of trigeminal neuralgia has already been reported (9–11).

We have also used fosphenytoin off-label out of necessity for patients with acute exacerbation of trigeminal neuralgia for whom effective procedures such as MVD could not be performed in the emergency response and have previously reported some cases (12). Since then, we have accumulated more experience and obtained new findings, reported herein. In this study, we aimed to investigate the efficacy and safety of intravenous fosphenytoin as a therapy for the acute exacerbation of trigeminal neuralgia.

2 Methods

2.1 Study population

We included data from 41 patients who were diagnosed with typical trigeminal neuralgia and received intravenous fosphenytoin between September 2015 and November 2023 at Nakamura Memorial Hospital (Sapporo, Japan). We included patients with trigeminal neuralgia who were aged ≥18 years, of any sex, experiencing acute exacerbations, regardless of prior medication, MVD, nerve blocks, or gamma knife surgery. Patients with a history of allergy to fosphenytoin and those with serious arrhythmias, including sinus bradycardia and heart block, were excluded. The following facts were explained to the patients: there are risks of adverse drug reactions caused by fosphenytoin, such as dizziness, gait disturbance, nystagmus, dysarthria, ataxia, diplopia, sleepiness, palpitations, phlebitis, hypotension, and arrhythmia; the use of fosphenytoin is off label; and no other procedures are available for emergencies. The patients accepted these risks. Consent for participation in this study was obtained from all the patients. The study protocol was approved by the Ethics Committee of Nakamura Memorial Hospital (Approval No. 2024090201) and conformed to the Declaration of Helsinki and its later amendments.

2.2 Administration method

Fosphenytoin was diluted with physiological saline (0.9% NaCl) and administered intravenously using an infusion pump (50 mg/min). The loading dose was 9.8–20.7 mg/kg (750–1,200 mg/dose), and the maintenance dose was 7.5–9.5 mg/kg (422–750 mg/dose). Patients receiving fosphenytoin were observed by nurses,

Abbreviations: IHS, International Headache Society; MVD, Microvascular decompression; NRS, Numerical rating scale.

underwent electrocardiography, and received non-invasive blood pressure monitoring. They were instructed to rest in bed for 1 h after the procedure. The fosphenytoin used was Fostoin (750 mg), which is commercially available in Japan (Nobelpharma Co., Ltd., Tokyo, Japan).

2.3 Endpoints

Facial pain was evaluated using a numerical rating scale (NRS) to determine efficacy. The NRS is an 11-point scale of pain severity, ranging from 0 to 10, with 0 indicating no pain and 10 indicating the most severe pain experienced by the patient. Patients evaluated their pain. The NRS score was evaluated immediately before administration (baseline) and at 2, 12, and 24 h after administration.

The degree and frequency of adverse drug reactions that developed after intravenous fosphenytoin therapy, including dizziness, gait disturbance, nystagmus, dysarthria, ataxia, diplopia, sleepiness, palpitations, phlebitis, hypotension, and arrhythmia, were evaluated for safety. Moreover, clinical laboratory test data related to hepatic and renal functions, including creatinine, urea nitrogen, liver enzymes, and gamma-glutamyl transferase, were evaluated.

2.4 Statistical analyses

The NRS scores immediately before administration (baseline) and at each time point (2, 12, and 24 h) after administration were compared using a paired *t*-test. A *p*-value of <0.05 was considered statistically significant. The R software (version 4.4.0) was used for statistical analyses.

TABLE 1 Summary of patient characteristics and treatment history.

		N	41
Sex	Male	17	(41%)
	Female	24	(59%)
Age (years)	Mean ± SD	63.2 ± 16.4	
	Median (min, max)	68 (23, 88)	
Weight (kg)	Mean ± SD	58.3 ± 11.0	
	Median (min, max)	55.2 (36.2, 79.0)	
TN classification	Classical trigeminal neuralgia	41	(100%)
TN laterality	R	23	(56%)
	L	18	(44%)
TN distribution	V1	1	(2%)
	V2	19	(46%)
	V3	6	(15%)
	More than 1 branch	15	(37%)
Concomitant medication*	Na^+ channel blocker	31	(76%)
	Ca^{2+} channel α2δ ligand	19	(46%)
	Na^+ channel blocker and Ca^{2+} channel α2δ ligand	9	(22%)
	Two or more drugs	12	(29%)
	None	0	(0%)
Treatment history for TN (therapy)*	MVD	10	(24%)
	Nerve block	8	(20%)
	γ-knife	2	(5%)

Ca, calcium; L, light; Max, maximum; Min, minimum; MVD, microvascular decompression; Na, sodium; R, right; SD, standard deviation; TN, trigeminal neuralgia.
*Duplicates present.

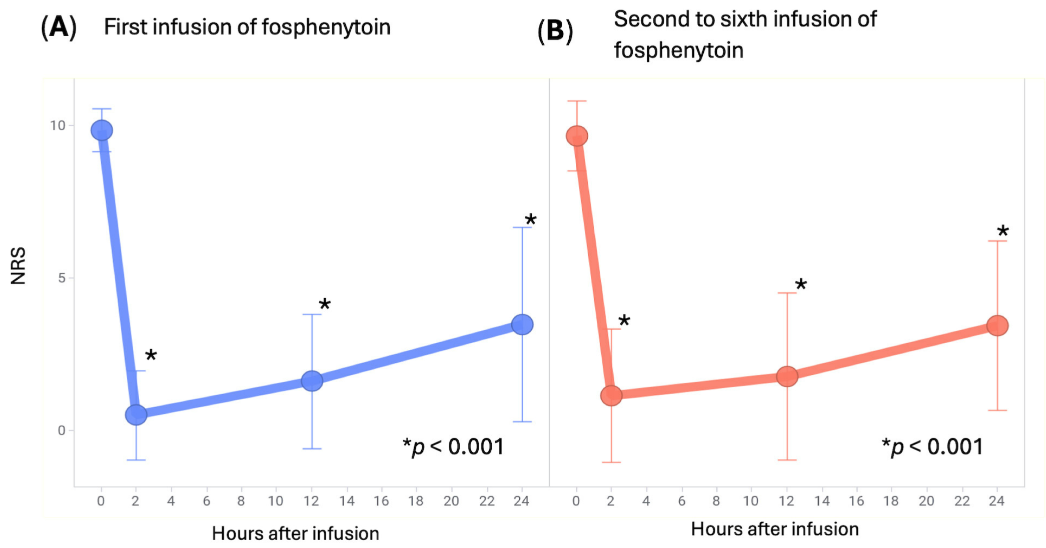
3 Results

Data from all 41 patients were included in this study and no data were excluded (clinical data of patients treated for trigeminal neuralgia crisis in Supplementary Table 1). Table 1 presents the summary of patient characteristics and treatment history. All patients were diagnosed with typical trigeminal neuralgia. The patients' mean age was 63.2 years (range, 23–88 years); 58.5% were female.

Intravenous fosphenytoin was administered 62 times in 41 patients. Ten of the 41 patients (24%) received it on two different occasions, and four patients (10%) received it on three or more different occasions (maximum: six occasions). Among the 62 courses of intravenous fosphenytoin therapy, 25 were administered to inpatients, 37 to outpatients, 11–10 outpatients who were hospitalized immediately (24%), and 16–9 emergency outpatients (22%).

Changes in NRS scores after fosphenytoin administration are depicted in Figure 1A. At baseline, the NRS score was, on average (±standard deviation), 9.85 ± 0.69 (range, 6–10). The NRS score was 0.49 ± 1.47 2 h after administration ($p < 0.001$), 1.60 ± 2.19 12 h after administration ($p < 0.001$), and 3.46 ± 3.19 24 h after administration ($p < 0.001$). Thus, NRS scores significantly decreased at all time points after administration compared to before administration, and the inhibitory effect on pain lasted for 24 h or longer after administration. The proportion of patients whose NRS score decreased by ≥50% compared to at baseline was 97.6% 2 h after administration and 76.9% 24 h after administration. In 82.9% of the patients, pain disappeared completely (NRS score = 0) 2 h after administration.

After the initial administration, 14 patients (a cumulative total of 21 patients) received intravenous fosphenytoin therapy multiple times on different occasions (Figure 1B). When fosphenytoin was administered multiple times (two or more), the NRS score was 9.67 ± 1.15 at baseline, 1.14 ± 2.20 ($p < 0.001$) 2 h after administration, 1.76 ± 2.76 ($p < 0.001$) 12 h after administration, and 3.42 ± 2.79 ($p < 0.001$) 24 h after administration. Thus, as with the initial administration, the NRS score significantly decreased at any time point after administration compared to baseline, and the inhibitory effect on pain lasted for 24 h or longer after administration. The proportion of patients whose NRS scores decreased by ≥50%



	(A) 2 h post-iv	(A) 12 h post-iv	(A) 24 h post-iv	(B) 2 h post-iv	(B) 12 h post-iv	(B) 24 h post-iv
No pain (NRS = 0)	82.9% (34/41)	50.0% (20/40)	25.6% (10/39)	66.7% (14/21)	61.9% (13/21)	23.8% (5/21)
50% reduction from baseline NRS	97.6% (40/41)	95.0% (38/40)	76.9% (30/39)	95.2% (20/21)	90.5% (19/21)	81.0% (17/21)

(/) Proportion of applicable patients

FIGURE 1
Changes in NRS scores after intravenous infusion of fosphenytoin. **(A)** Average NRS scores and standard deviation are shown for all patients (n = 41) who received the first infusion of fosphenytoin. **(B)** Average NRS scores and standard deviation are shown for patients (n = 14, 21 infusions in total) who received fosphenytoin infusion several times (except the first infusion). NRS, numerical rating scale.

compared to the baseline was 95.2% 2 h after administration and 81.0% 24 h after administration.

Changes in NRS scores after fosphenytoin administration according to the type of oral drug used to suppress trigeminal neuralgia crisis are shown in Figures 2A–C. Regardless of the type of oral drug used, intravenous fosphenytoin therapy had a similar effect on the acute exacerbation of trigeminal neuralgia. When intravenous fosphenytoin therapy was administered to seven patients in whom immediate pain relief was not achieved soon after MVD (within 1 week), pain relief was observed in all seven patients, similar to other patients (Figure 2D).

Changes in the NRS scores of two patients who received maintenance therapy because their NRS scores increased on the day after the initial dose was administered are depicted in Figure 3. After maintenance therapy, the patients' NRS scores decreased again.

The adverse drug reactions observed were mild dizziness in six patients, abnormal auditory perception and thirst in three patients each, somnolence, decreased SpO_2, and drug eruption in one patient each, all of which were transient. All the patients recovered within the same day without treatment. None of the patients experienced nystagmus or dysarthria as an adverse drug reaction. The patient who developed a drug eruption was allergic to several drugs. The patient received an intravenous injection of hydrocortisone sodium succinate and was cured within several hours of treatment. No adverse drug reactions that raised concerns were observed, and fosphenytoin was well-tolerated.

4 Discussion

The present study demonstrates the efficacy and safety of administering intravenous fosphenytoin therapy in reducing pain due to trigeminal neuralgia crisis in 41 patients. Regardless of whether it was administered during the perioperative period of MVD and the type of drugs used concomitantly, the inhibitory effect on pain lasted for 24 h or longer after administration. This therapy is effective for treating trigeminal neuralgia crisis on different occasions in the same patient. The findings of this study will contribute to the development of treatments for trigeminal neuralgia.

The pain associated with trigeminal neuralgia is considered one of the most intense types of pain. Pain is usually controlled by administering oral drugs, such as carbamazepine. However, some activities of daily living trigger sudden pain attacks. During attacks, patients may crouch with their hands on their faces and become unable to talk, eat alone, or drink. It is not uncommon for them to be rushed to the hospital. However, hospitals have no established or simple treatment. If a nerve block or emergency surgery, such as MVD, cannot be performed, there are no further options.

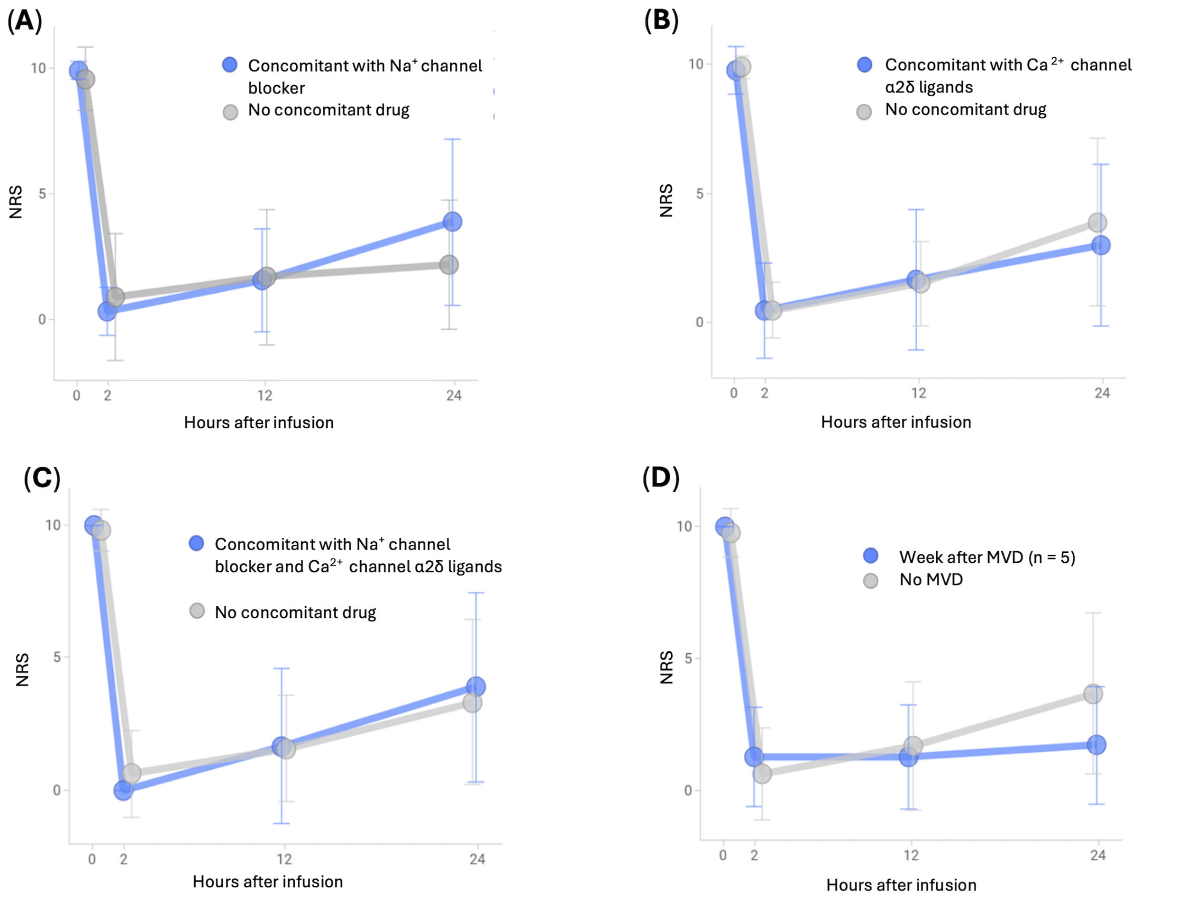


FIGURE 2
Changes in NRS scores after intravenous infusion of fosphenytoin in patients stratified by their background. **(A)** Average NRS scores and standard deviation for patients with or without oral Na^+ channel blockers. **(B)** Average NRS scores and standard deviation for patients with or without oral Ca^{2+} channel α2δ ligands. **(C)** Average NRS scores and standard deviation for patients with or without oral Na^+ channel blockers and Ca^{2+} channel α2δ ligands. **(D)** Average NRS scores and standard deviation for patients with or without MVD on the preceding day. MVD, microvascular decompression; NRS, numerical rating scale.

At our hospital, we have attempted to treat patients seeking emergency care with intravenous injections of the anticonvulsant fosphenytoin since 2015. For the 41 patients whose data have been accumulated to date, the NRS scores after fosphenytoin administration were significantly lower than the baseline NRS scores until at least 24 h after administration. The proportion of patients whose NRS score at 2 h after administration decreased by 50% or more compared to that at baseline (initial administration) was 97.6%, and the proportion of patients whose pain disappeared completely (NRS score = 0) was 82.9%, indicating that pain relief with this drug is effective and rapid. This effect persisted for 24 h or longer after administration.

Although few papers address managing acute TN crises, a systematic review and guidelines summarize the current evidence. They suggest that lidocaine can be administered via nasal spray, local nerve block, or intravenous infusion. There is some evidence supporting the use of botulinum toxin and a recommendation for subcutaneous sumatriptan to alleviate acute TN attacks. Intravenous lidocaine, phenytoin, and fosphenytoin are also proposed for inpatient treatment (13).

Andersen et al. (14) reported prospective observations of 15 patients who received intravenous fosphenytoin during the exacerbation of trigeminal neuralgia, and 60% (nine) of responders experienced a 50% decrease in pain intensity 24 h after administration. In line with these observations, our results are consistent with these reports, confirming that intravenous fosphenytoin therapy is an effective treatment for acute exacerbations.

Schnell et al. (15) investigated the intravenous administration of phenytoin and reported that it was administered to 18 patients with trigeminal neuralgia in an emergency room on 65 occasions and that immediate pain relief was observed in 89.2% of the cases. In contrast, our study indicates that IFT provides a superior and safer alternative for immediate TN crisis relief, with only mild adverse events such as dizziness, thirst, and abnormal auditory perception, which were transient, and the drug was well-tolerated and safe.

Interestingly, when fosphenytoin was administered soon after MVD (within 1 week) to seven patients in whom immediate pain relief was not achieved following MVD, pain disappeared in four patients, and the NRS score decreased from 10 at baseline to 2

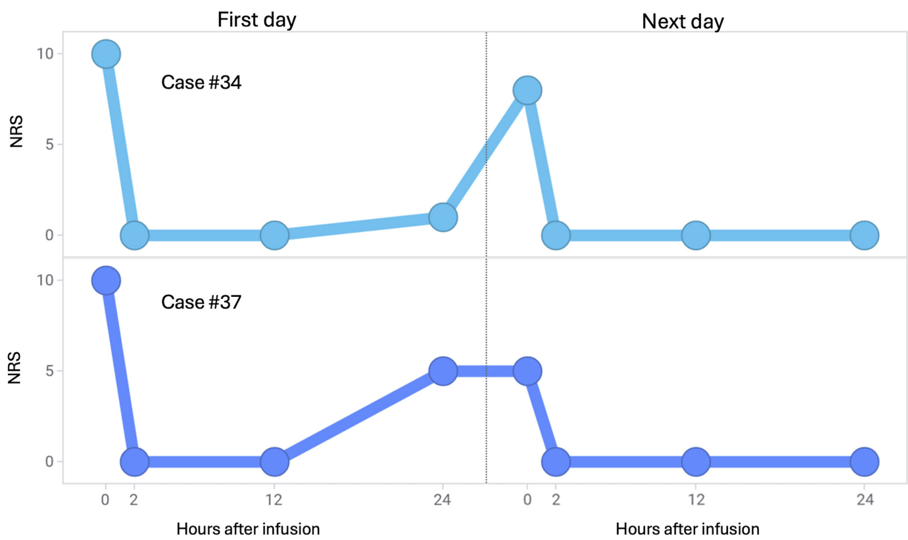


FIGURE 3
Changes in NRS scores after intravenous infusion of fosphenytoin for individual patients. (Upper panel) Case 34 was a 69-year-old woman who received fosphenytoin at a dose of 14.4 mg/kg on the first day and at the same dose on the next day. (Lower panel) Case 37 was a 50-year-old man who received fosphenytoin at a dose of 15.2 mg/kg on the first day and at 9.5 mg/kg on the next day. NRS, numerical rating scale.

in two patients, and from 10 at baseline to 5 in one patient 2 h after administration, indicating that the anxiety experienced by the patients who still had pain after surgery was successfully eliminated. Generally, the time to pain relief after MVD varies from individual to individual; it may be achieved immediately after surgery but may also take several weeks. The demonstration of the effect of this drug on pain relief after surgery indicates that the drug provides a measure to address remaining pain after surgery, which we consider encouraging for physicians.

In all patients whose data were included in this study, trigeminal neuralgia was managed by oral drugs such as Na^+ channel blockers or Ca^{2+} channel α2δ ligands, and the effect of fosphenytoin was not affected by the type of oral drug. Similar to carbamazepine, fosphenytoin is a Na^+ channel blocker. Therefore, acute exacerbation of trigeminal neuralgia in patients taking Na^+ channel blockers may have resulted in resistance. However, the results of this study refute this possibility and are clinically valuable in that fosphenytoin can be used without the need to ask patients about the type of oral drugs used for pain management.

Although fosphenytoin is clinically positioned as a therapeutic drug for acute exacerbation of trigeminal neuralgia, it cannot be expected that this drug will continue to be effective for 24 h or longer after administration. However, in the present study, when two patients received maintenance therapy because the pain relapsed on the day after this drug was initially administered, the maintenance therapy suppressed pain as well as the initial administration.

The mechanism by which fosphenytoin alleviates trigeminal neuralgia pain remains to be fully elucidated. Previous studies have suggested that cerebral blood flow (CBF) can be modulated by neurogenic and metabolic mechanisms (16, 17). Interestingly, phenytoin has demonstrated a protective hemodynamic effect on CBF (18), whereas a decrease in CBF has been observed during trigeminal ganglion stimulation, which mimics nerve hyperexcitability during paroxysmal attacks (19). These findings raise the possibility that changes in CBF may play a role in the mechanism by which fosphenytoin alleviates pain, potentially counteracting the hemodynamic effects of trigeminal nerve hyperactivity. Further investigations are warranted to confirm this hypothesis.

The present study has the following limitations, and the results must be interpreted cautiously. First, this was a retrospective study conducted at a single center with a single administration group. Therefore, bias may have been introduced in the results. Second, the loading and maintenance doses of this drug were set within the range of anticonvulsant doses, and pharmacokinetic investigations were not performed. Therefore, this issue could not be considered or discussed.

The results described above suggest that intravenous fosphenytoin therapy immediately eliminates pain during acute attacks of trigeminal neuralgia and that fosphenytoin can be a useful therapeutic drug in emergency response or until elective treatment, such as MVD, is performed. Therefore, verification of fosphenytoin in prospective studies is warranted.

5 Summary

This retrospective observational study investigated the efficacy and safety of intravenous fosphenytoin in the management of acute exacerbations of trigeminal neuralgia in pre- and post-neurosurgical patients. The study analyzed data from 41 patients, and pain was evaluated using a numerical rating scale (NRS). Fosphenytoin was diluted in physiological saline and administered intravenously. The mean NRS score was 9.85 before administration, 0.49 after 2 h, 1.60 after 12 h, and 3.46 after 24 h ($p<0.001$ for all), suggesting that treatment with intravenous fosphenytoin can rapidly eliminate pain during acute trigeminal neuralgia crisis.

Intravenous fosphenytoin therapy was also beneficial regardless of prior treatment, including microvascular decompression, nerve blocks, or gamma knife surgery, and was effective when administered on multiple occasions or as maintenance therapy. The adverse reactions were generally mild and transient and included dizziness, abnormal auditory perception, and somnolence. These findings suggest that intravenous fosphenytoin is a valuable emergency treatment option for trigeminal neuralgia, offering immediate pain relief and serving as a bridge to elective treatment. Further prospective studies are recommended to validate these results. This study aligns with *Frontiers in Neurology*'s focus on innovative therapeutic approaches for neurological conditions.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Nakamura Memorial Hospital (Approval No. 2024090201). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SN: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. HE: Data curation, Formal analysis, Methodology, Project administration, Writing – review & editing. BA: Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. YA: Formal analysis, Writing – review & editing. MO: Formal analysis, Visualization, Writing – review & editing. RN: Formal analysis, Resources, Writing – review & editing. KH: Visualization, Writing – review & editing. YS: Formal analysis, Supervision, Writing – review & editing. HN: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2024.1493274/full#supplementary-material

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The vagal rhizopathies

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Neurovascular compression of the tenth cranial nerve, the vagus nerve, can cause recognizable and neurosurgically treatable clinical conditions. This chapter will outline the clinical characteristics unique to vagus nerve compression and highlight both the definitive diagnostic protocol and neurosurgical treatment of these conditions. The vagus nerve has motor, sensory and autonomic components. Neurovascular compression of the motor component can cause hemi-laryngopharyngeal spasm (HELPS syndrome). Compression of the sensory component will cause a neurogenic cough called VANCOUVER syndrome – an acronym for Vagus Associated Neurogenic Cough Occurring due to Unilateral Vascular Compression of its Root. Both are caused by direct compression of the root of the tenth cranial nerve at the brainstem by a blood vessel and can be cured by microvascular decompression (MVD). Since the symptoms of choking and cough are common and blood vessels are often abutting the vagus nerve at the brainstem, it is vitally important to understand the definitive diagnostic protocol to avoid operating on false positives. Since the vagus nerve is far more susceptible to dysfunction during surgery than either the trigeminal or facial nerves, it is also important to understand the surgical nuances of this procedure.

KEYWORDS

microvascular decompression, vagus nerve (CN X), vagal rhizopathy, hemi-laryngopharyngeal spasm, VANCOUVER syndrome, vagal neuralgia, neurogenic cough

Introduction

Vascular compression of the 5th cranial nerve (trigeminal nerve) and 7th cranial nerve (facial nerve) can cause the classic features of trigeminal neuralgia and hemifacial spasm, respectively. This chapter describes the clinical features of a vascular compression of the 10th cranial nerve (vagus nerve). The vagus nerve has motor, sensory and autonomic components. The clinical features associated with a vascular compression of the motor and the sensory components can each be distinguished and have been previously published. The two resultant conditions are known as hemi-laryngopharyngeal spasm (HELPS syndrome) (1) and vagus associated neurogenic cough occurring due to unilateral vascular encroachment of its root (VANCOUVER syndrome) (2).

Hemi-laryngopharyngeal spasm (HELPS syndrome)

The motor fibers of the vagus nerve innervate the muscles of the pharynx and larynx. A vascular compression of this component of the vagus nerve can cause intermittent contractions of these muscles. This is similar to the hemifacial spasm that results from compression of the motor fibers within the facial nerve. The condition can be diagnosed by a combination of history, physical examination and special tests (1, 3, 4).

History

When the muscles of the pharynx are involved, the patient can localize the contractions to one side of their throat. When the muscles of the larynx are involved, the patient describes a non-lateralized general constriction of their airway. If both pharyngeal and laryngeal muscles are involved, the patient can lateralize their symptoms. The contractions are intermittent and patients are entirely normal between episodes. The contractions can last seconds to minutes and be very distressing for patients who can report difficulty breathing. There is no associated pain unless the condition has a concurrent glossopharyngeal neuralgia due to compression of the adjacent 9th cranial nerve (glossopharyngeal nerve) (5). The condition will typically progress over the years with the attacks becoming more frequent, lasting longer and severe. A unique aspect (also found in hemifacial spasm) is that the attacks of muscle contractions can occur while asleep.

The intermittent muscle spasms are associated with a cough. The cough is due to compression of the sensory fibers of the vagus nerve and will be described in detail below under VANCOUVER syndrome. We have never seen a patient with pure hemi-laryngopharyngeal spasm without a cough but one patient reported the motor contractions started before any coughing. We have seen patients with pure cough (see VANCOUVER syndrome below) without the muscles spasms of hemi-laryngopharyngeal spasm. Severe episodes of this coughing can produce unconsciousness. The likely etiology for unconsciousness is cough syncope rather than airway obstruction.

Patients can report other episodic symptoms due to contractions of muscles innervated by the vagus nerve. An intermittent "fat" tongue sensation may be due to pallatoglossus contractions; episodic vocal changes triggered by prolonged or loud talking may be due to intrinsic laryngeal muscle contractions and a globus sensation may be due to pharyngeal constrictors contraction.

The symptoms are refractory to the usual medications and treatments prescribed for episodic laryngospasm or chronic cough. Patients do not respond to proton pump blockers, speech therapy, psychotherapy, bronchodilators or antibiotics. The muscle contractions can be temporarily stopped by Botox injection into the correct muscles but will typically not respond to anti-neuralgia medications (like hemifacial spasm). The cough, however, may respond to anti-neuralgia medications (like trigeminal neuralgia).

Physical examination

In between episodes, the patient's examination is entirely normal. This often leads to the misdiagnosis of a psychogenic disorder. The patient's unpredictable, severe symptoms and typical difficulty with obtaining a diagnosis can lead to anxiety, depression and hostility toward medical workers thereby strengthening the psychogenic misdiagnosis.

During an attack, the patient is in extremus and fighting to breath. This may explain why there has not yet been a laryngoscopy reported during an attack. A portion of patients (approximately one-third) have a pathognomonic movement disorder of their vocal folds (4). This has been reported as a unilateral vocal fold twitch following vocalization. It is unique to hemi-laryngopharyngeal spasm and resolves following surgical cure. There are no other physical features between episodes remarkable for this condition except for the absence of any signs pointing to an alternate diagnosis.

Special tests

MRI must demonstrate a vascular compression of one of the vagus nerves. Imaging sequences are the same as for the other neurovascular compression syndromes (CISS or FIESTA). Care must be taken not to over diagnose the condition because asymptomatic patients can have a vessel on their vagus nerve up to 40% of the time (6). An MRI documented compression of the vagus nerve is therefore required but not sufficient for the diagnosis of hemi-laryngopharyngeal spasm. The compressing vessel is typically the posterior inferior cerebellar artery (PICA) with a 180-degree loop deflecting the vagus nerve. Three examples are shown in Figure 1. The vagus nerve rootlets are small enough to make their individual resolution difficult even with high field 3 T MRI. The looping PICA may show as two flow voids on a 2-dimentional axial plane of the MRI.

Laryngoscopy may show a pathognomonic ipsilateral twitch of the vocal fold following vocalization. An example has been published in the otolaryngology literature (4). This movement disorder appears to be unique to this condition and has not been previously reported. Unfortunately, not all patients demonstrate this finding. When it is present, however, it definitively points to the affected side.

Botulinum toxin (Botox) injected into the affected muscles will stop (or dramatically improve) the intermittent contractions but not the cough. Botox injected into the contralateral side will have no beneficial effect.

Diagnostic protocol

Patients with chronic, intermittent, medically refractory throat contractions and cough should be tested for a diagnosis of

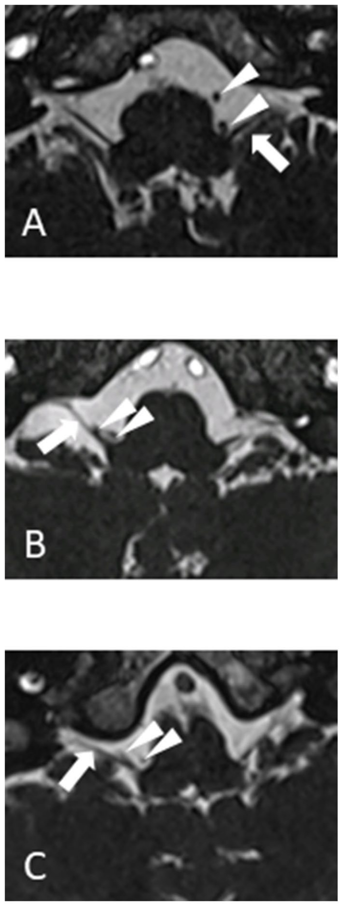

FIGURE 1
1.5 T MRI CISS sequences of three different patients **(A, B** and **C)** showing vagus nerve (arrow) and loop of PICA (arrowheads).

hemi-laryngopharyngeal spasm. The diagnostic protocol for patients who can lateralize their symptoms is shown in Figure 2A. If the MRI confirms a vascular compression on the same side as their symptoms, consideration can be given to offering microvascular decompression of the vagus nerve. The diagnostic protocol for patients who cannot lateralize their symptoms is shown in Figure 2B. Since those patients can not tell which side is affected (usually due to laryngeal muscles causing a circumferential sensation of choking) the beneficial effects of Botox must be used to locate the affected side. When Botox is injected into the symptomatic side, the episodic muscle contractions will be greatly diminished (typically 80% improved). The procedure is later repeated (once the effects of Botox have worn off after 3 months or more) on the contralateral side to confirm this is a unilateral benefit. The patient should have no benefit from the contralateral Botox. If the patient does improve with the contralateral Botox, then the condition is generalized, not unilateral, and can not be hemi-laryngopharyngeal spasm. There might be a theoretic patient with bilateral symptoms but that must be exceedingly rare (like bilateral hemifacial spasm).

Medical therapy

The motor contractions will be diminished with repeated Botox therapy into the affected muscles. This is similar to hemifacial spasm. The side effects of Botox therapy are related to the targeted muscles and include dysphagia and dysphonia. The cough may respond to anti-neuralgia medications such as Carbamazepine or Neurontin. The side effects of these medications are well described for trigeminal neuralgia and can include rash, sedation or cognitive slowing.

Surgical therapy

The definitive therapy for hemi-laryngopharyngeal spasm is microvascular decompression of the vagus nerve. The surgical approach is similar to that for exposing the 7th cranial nerve (hemifacial spasm) or the 9th cranial nerve (glossopharyngeal neuralgia). The most important aspect of the surgical approach is that the surgeon is familiar and comfortable with it. Our team has used the lateral position with the affected side up to facilitate the cerebellum falling away from the inside of the occipital bone (Figure 3A). Additional brain relaxation is facilitated with hyperventilation ($PaCO_2$ = 30 mmHg). The patient will have neuromonitoring of their eighth cranial nerve. The procedure begins using surgical loops and a retrosigmoid incision. The craniectomy is extended inferiorly to the horizontal portion of the occipital bone and laterally to the medial edge of the sigmoid sinus (the transverse sinus does not need to be exposed). The craniectomy is then widened superiorly and medially to permit easy access of instruments intradurally. The dura is opened in a curvilinear fashion, convex medially, with the base laterally toward the sigmoid sinus and turned to expose the cerebellum.

The operating microscope is then brought into play. After cerebrospinal fluid (CSF) is drained, the cerebellum can be mobilized medially and superiorly exposing the lateral wall of the posterior fossa. The exposure is slowly widened until the arachnoid over the lower cranial nerves is exposed. The arachnoid is then sharply dissected and additional CSF will be released. The spinal root of the 11th cranial nerve (accessory nerve) can be seen curving superiorly to join the multiple rootlets of the vagus nerve entering the jugular foramen. There are typically five or six separate rootlets of the vagus and then

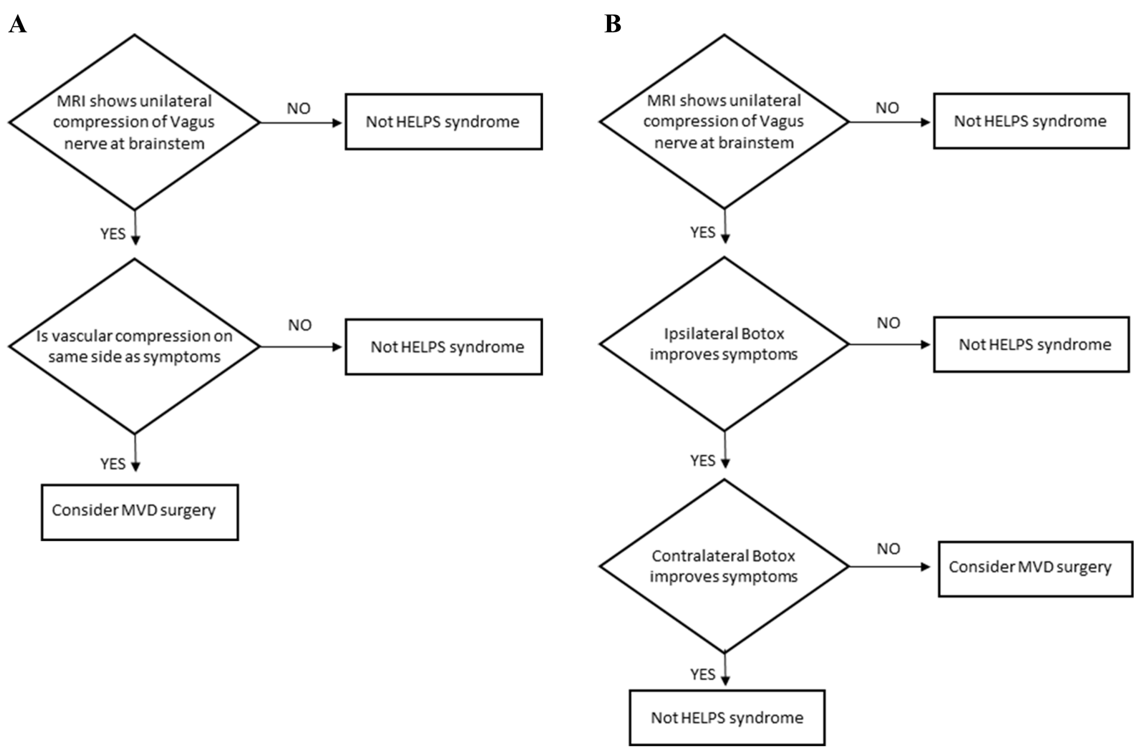

FIGURE 2
(A) Diagnostic protocol for hemi-laryngopharyngeal spasm in patients who can lateralize their symptoms. **(B)** Diagnostic protocol for hemi-laryngopharyngeal spasm in patients who cannot lateralize their symptoms.

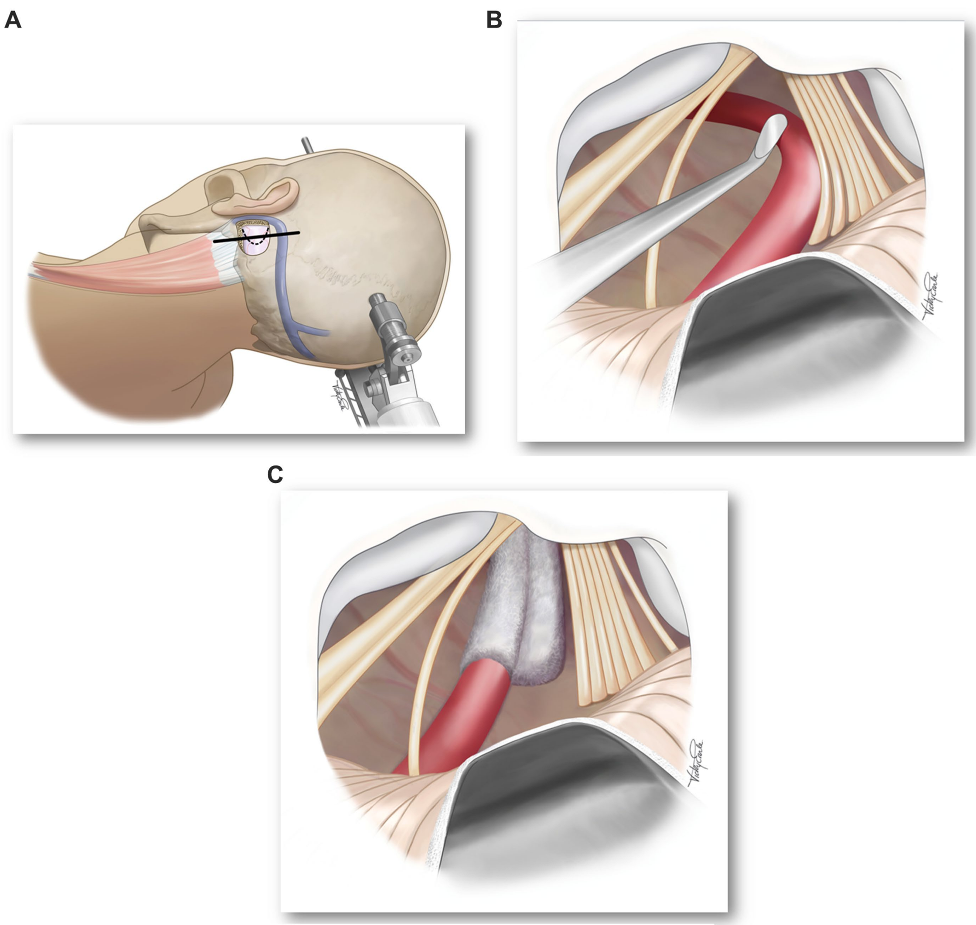

FIGURE 3
(A) Surgical position and location of skin (solid line) and dural (dotted line) incisions. **(B)** Microscope image showing compression of vagus nerve rootlets by a loop of the PICA. **(C)** Microscope image showing decompression of vagus nerve rootlets.

just rostral will be a single root (typically larger and whiter) of the 9th cranial nerve (glossopharyngeal nerve).

At this point, the vascular compression of the vagus nerve will be apparent (Figure 3B) and a decision should be made as to how best to move the vessel away and maintain its decompression (Figure 3C). The vagus nerve does not tolerate as much manipulation as the trigeminal nerve and is even more sensitive than the facial nerve. Excessive manipulation will cause post-operative dysphagia and dysphonia. Care should also be taken not to manipulate or compress the cranial root of the 11th cranial nerve as it controls laryngeal muscles and can result in an ipsilateral vocal fold paralysis. We prefer not to have any residual compression of the vagus nerve – not by the vessel or the Teflon pad.

The dura is closed watertight and methyl methacrylate used to refashion the craniectomy. The scalp is closed with running absorbable suture (2–0 Vicryl) in the fascia and a watertight running locked nonabsorbable suture (3–0 Proline) in the skin. Extubation is done with care to avoid excessive Valsalva coughing.

Post-operatively, the patient's ability to swallow must be confirmed before they are allowed to be fed. Temporary dysphagia can occur and patients may need to be tube fed until it resolves. The function of the patient's vocal folds can be assessed at the bedside by listening to their voice. A soft, raspy voice may indication vocal fold dysfunction.

The benefits are typically seen immediately but, like hemifacial spasm, may require some time to resolve. Our small but growing surgical experience with this condition has been published (4). Six patients have had more than five-years follow-up and five remain symptom free. The sixth patient had resolution of their cough but incomplete improvement of their choking. One patient developed dysphagia four years post-operative and had repeat MVD to decompress the Teflon off the lowest rootlet of the vagus nerve. Their dysphagia resolved (see Future Issues below). Two patients had post-operative ipsilateral vocal fold paralysis. These two had complete glottic closure and denied dysphonia, dysphagia or aspiration. One patient had temporary dysphagia with complete resolution by two months and was able to have their pre-operative tracheostomy removed.

VANCOUVER syndrome

Sensory fibers of the vagus nerve innervate the tracheobronchial tree and generate a "tickling" sensation (not pain) when activated. A vascular compression of this component of the vagus nerve can trigger coughing. This is similar to trigeminal neuralgia from compression of the sensory fibers within the trigeminal nerve except the sensation is a tickle not pain and the location is in the lungs not the face. The syndrome was named to reflect its etiology and as an homage to the location of its discovery. Vagus Associated Neurogenic Cough Occurring due to Unilateral Vascular Encroachment of its Root (VANCOUVER syndrome) can be diagnosed by a combination of history, physical examination and special tests (2).

History

Patients present with a medically refractory, chronic, dry cough. They describe an intermittent tickling sensation that triggers an irresistible cough. The sensation (and resultant cough) can be aggravated by prolonged or loud talking, harsh fumes or an upper respiratory infection and sometimes has a positional component (i.e., lying down on one side may worsen or ease the symptoms). The sensation and cough can occur while asleep and will awaken the patient. Patients should be seen by a laryngologist or respirologist to rule out postnasal drip, asthma, gastroesophageal reflux, infection, chronic obstructive lung disease, side effect from angiotensin-converting enzyme inhibitors, aspiration, bronchiectasis, bronchiolitis, cystic fibrosis, lung cancer, sarcoidosis, idiopathic pulmonary fibrosis or CANVAS. The symptoms will slowing worsen over the years but may have months of remission like trigeminal neuralgia. The medications used for trigeminal neuralgia can be effective for this vagal sensory pathology.

Physical

In between episodes, the patient's examination is entirely normal. As with hemi-laryngopharyngeal spasm, the temporal juxtaposition of a patient with a severe, debilitating cough who, moments later, is entirely normal often leads to the misdiagnosis of a psychogenic disorder. Their cough is a normal brainstem response to an abnormal sensory stimulus from their vagus nerve. Their examination is only remarkable for the lack of any findings suggestive of another pathology.

Special tests

MRI must demonstrate a vascular compression of one of the vagus nerves. Imaging sequences are the same as for the other neurovascular compression syndromes (CISS or FIESTA). As with hemi-laryngopharyngeal spasm, care must be taken not to over diagnose the condition because asymptomatic patients can have a vessel on their vagus nerve up to 40% of the time (6). An MRI documented compression of the vagus nerve is therefore required but not sufficient for the diagnosis of VANCOUVER syndrome. If there is no compression, the diagnosis can be excluded. An example of an MRI demonstrating the posterior inferior cerebellar artery (PICA) encroaching the vagus nerve is shown in Figure 4.

We have been using inhaled lidocaine (5 cc of 2% in saline) as a screening test. As with trigeminal neuralgia, anesthetizing the affected area provides a temporary relief. The affected area for VANCOUVER syndrome is somewhere within the vagus-innervated tracheobronchial tree. Nebulized lidocaine is often used by laryngologists to provide a local anesthetic for minor operations in that region and more recently to treat chronic cough (7). If inhaled lidocaine stops the tickling sensation and cough, then we proceed to more definitive tests (see below). If it does not, the diagnosis is excluded.

The definitive diagnostic test for VANCOUVER syndrome is resolution of symptoms followingly a unilateral vagus nerve block. If a vagus nerve block ipsilateral to the vascular compression shown on MRI stops the cough and a vagus nerve block on the contralateral side does not, then the diagnosis of VANCOUVER syndrome is confirmed. We have been completing the contralateral (negative control) test to ensure this is not a generalized problem. If the patient's cough stops when only when one side of their vagus nerve is temporarily blocked then the condition is clearly unilateral. The many conditions that can cause chronic cough (noted above) are unlikely to be resolved with a unilateral treatment. If that side is also the side with an obvious vascular compression of the vagus nerve at the brainstem, then it is likely the cause of their cough and warrants a discussion about the pros and cons of a surgical cure.

The vagus nerve block is performed by our anesthetist who has experience with nerve blocks. The vagus nerve can be seen in the neck with ultrasound guidance (Figure 5) and can be temporarily anesthetized with lidocaine (4 cc of 2%). The vagus nerve travels with the carotid artery (which pulsates) and internal jugular vein (which can be compressed) during ultrasound imaging. When the vagus nerve is anesthetized, there will be a unilateral vocal fold palsy causing a hoarse voice. During the time the voice is hoarse, the patient's tickling sensation and cough should resolve. When the anesthetic wears off, the voice will return to normal and the cough should begin again. This would be a positive test. When the vagus nerve block is performed on the contralateral side, there should be a temporary hoarse voice but no affect on the cough. Any attempted vagus nerve

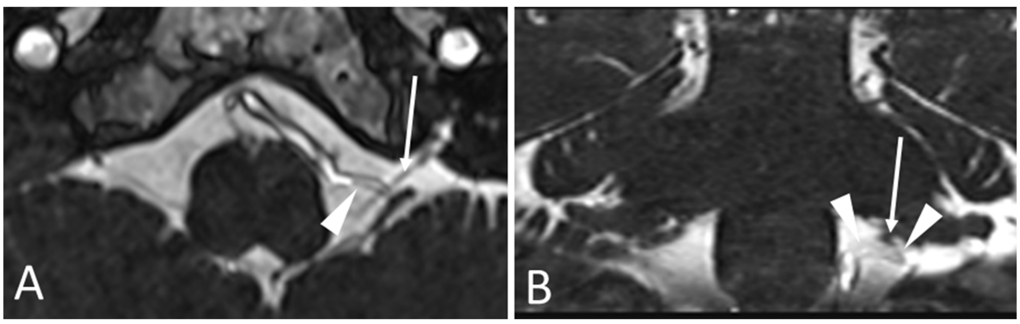

FIGURE 4
Axial **(A)** and coronal **(B)** MRI showing the PICA (arrowhead) encroaching the vagus nerve (arrow).

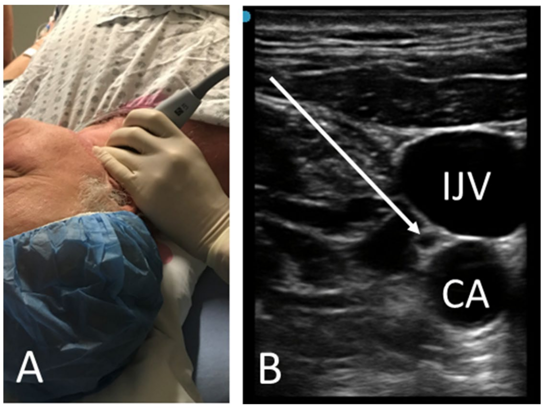

FIGURE 5
Ultrasound technique **(A)** and image **(B)** showing vagus nerve and direction of needle (arrow), carotid artery (CA) and internal jugular vein (IJV).

block that does not cause a hoarse voice was unsuccessful (the vocal fold paralysis and resultant hoarse voice is the positive control for the successful vagus nerve block).

Although vagus nerve block has been described before, it is not a common procedure and should be approached with care (8, 9). Ultrasound guidance has improved the targeting of the nerve and our tests are performed in the operating room by an anesthesiologist with expertise in regional blocks. The much more familiar superior laryngeal block (10) does not sufficiently cover the tracheobronchial tree to be used for this test.

Diagnostic protocol

Patients with neurogenic cough refractory to all medical investigations can be tested for a diagnosis of VANCOUVER syndrome. The diagnostic protocol for patients is shown in Figure 6. Patients may have a response to anti-neuralgia medications but all investigations and other therapies will have failed. The initial screening test is an MRI. If there is no vascular encroachment of the vagus nerve, then the diagnosis of VANCOUVER syndrome can be excluded. If there is a unilateral vascular encroachment of the nerve, then proceed to the secondary screening test – inhaled lidocaine. If anesthetizing the tracheobronchial tree temporarily stops the cough then proceed to the definitive test – vagus nerve block. If the inhaled lidocaine does not stop the cough, the diagnosis can be excluded.

The definitive test is invasive and requires experience in ultrasound-guided nerve block. If unilateral vagus nerve block ipsilateral to the MRI-demonstrated vascular encroachment of the vagus nerve temporarily stops the cough and contralateral vagus nerve block does not stop the cough, the diagnosis of VANCOUVER syndrome is confirmed and warrants discussion of the pros and cons of a potential surgical cure.

Medical therapy

The vagus-mediated tickling sensations can be diminished with anti-neuralgia medications. This is similar to trigeminal neuralgia. The side effects of these medications (e.g., Carbamazepine, Neurontin) are well known and can include rash, sedation and cognitive blunting. For patients who cannot stop their coughing with medications or cannot tolerate the side-effects of the medications required to stop this coughing, surgery may be an option.

Surgical therapy

The definitive therapy for VANCOUVER syndrome is microvascular decompression of the vagus nerve. The surgical approach is identical to that for hemi-laryngopharyngeal spasm describe above. An example of the intraoperative imaging seen before and after decompression of the vagus nerve is shown in Figure 7. The vagus nerve rootlets were displaced posterior toward the microscope by a loop of the PICA. When the loop was rotated 90 degrees, it passed between the vagus and accessory nerves.

The benefits are typically seen immediately. There is a relatively unique potential complication with any residual Teflon left against the lowest rootlet of the vagus nerve – delayed dysphagia. We recommend nothing be left pressing against the vagus nerve; not the vessel nor the Teflon padding.

Concurrent glossopharyngeal neuralgia and HELPS or VANCOUVER syndrome

The anatomical juxaposition of cranial nerves IX and X makes the possibility of concurrent symptoms possible. We have published such a case (5). The presence of unilateral pain characteristic of glossopharyngeal neuralgia makes the diagnostic work-up easier – it is clear what side the pain is on and surgery can be considered if the symptoms are medically refractory. The Rushton et al. case series of patients with glossopharyngeal neuralgia ($n = 217$) reported that the majority of those patients had pain in the characteristic location and pattern without any additional features. Some of those patients, however, reported glosspharyngeal neuralgia with coughing ($n = 18$) and few with stridor or hoarseness ($n = 3$) (11). We postulate that those patients had glossopharyngeal neuralgia and VANCOUVER syndrome (pain with cough) or glossopharyngeal neuralgia with HELPS (pain with hemi-laryngopharyngeal contractions) before the authors knew the conditions existed. The Bohm and Strang series of 18 patients with glossopharyngeal neuralgia treated in Sweden included 2 with the additional symptoms of coughing (12). One of those patients (case 11 from 1947) described her symptoms as, "attacks of severe cramps in the throat, a feeling of suffocation and dyspnoea" in addition to her repeated 15 s bouts of burning pain in the tonsil radiating to her ear. We postulate that she was describing glossopharyngeal neuralgia and HELPS because glossopharyngeal neuralgia alone does not present with throat contractions. These historical reports of patients with additional symptoms (cough or throat contractions) in addition to their glossopharyngeal neuralgia have been found in at least 4 languages and multiple countries (5).

Current issues

The final widespread acceptance of these conditions will require their recognition and treatment by multiple centers. At the present time, all the peer-reviewed publications on these two condition have come from only one group in Vancouver and a single publication from Japan (13). This lack of confirmation from well established

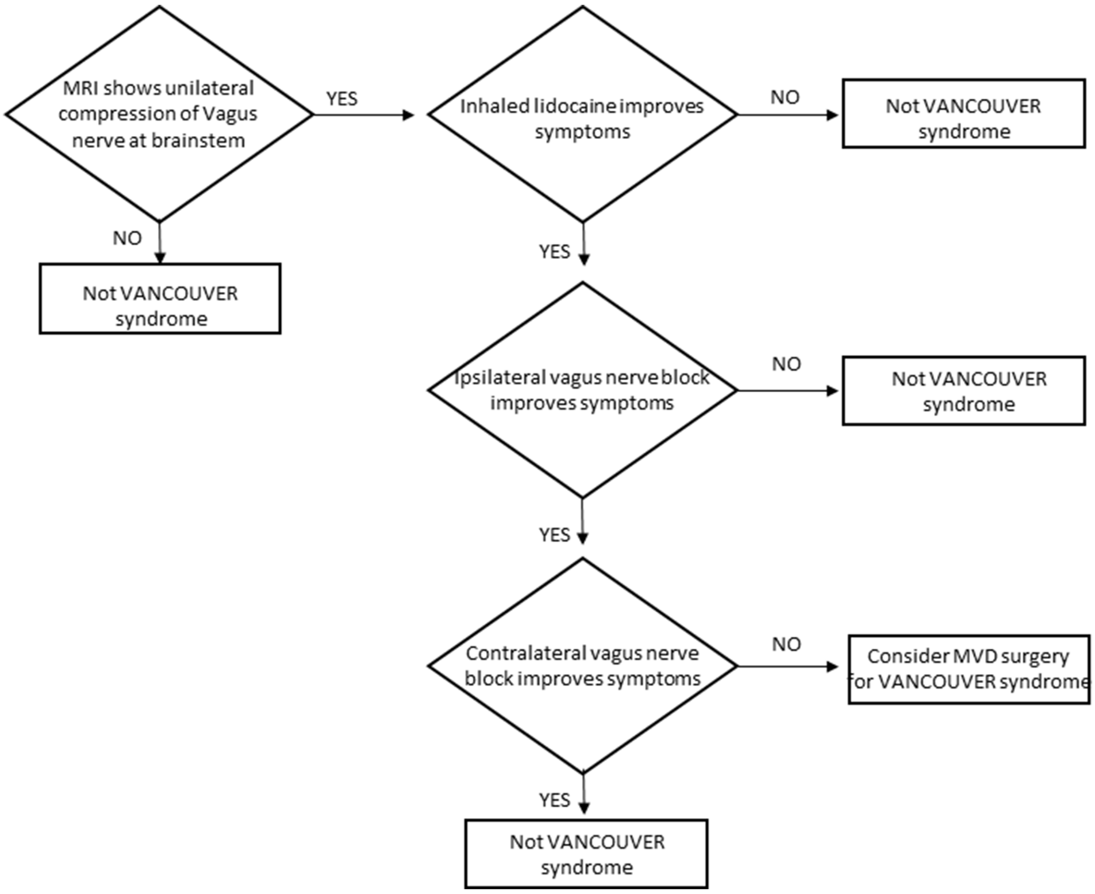

FIGURE 6
Diagnostic protocol for VANCOUVER syndrome.

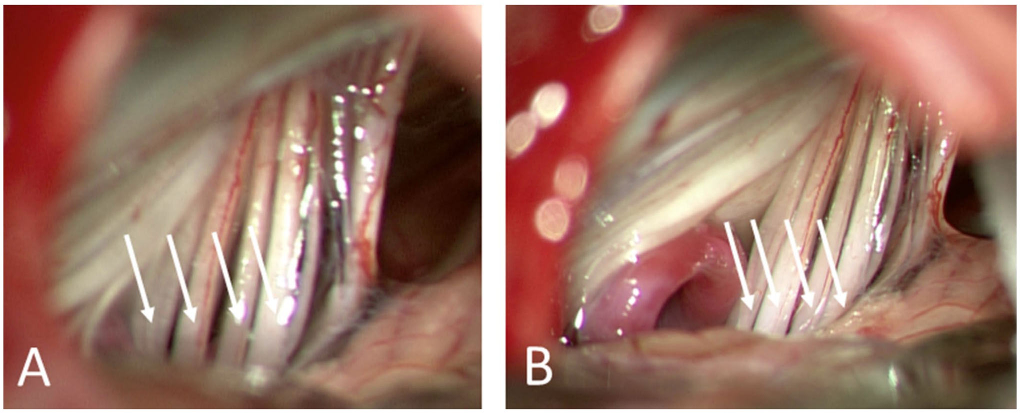

FIGURE 7
Microscopic view of four rootlets of the vagus nerve (arrows) before **(A)** and after **(B)** decompression from a loop of the PICA that was encroaching on the nerve from anterior and displacing them posterior.

neurosurgical centers of excellence around the world continues almost a decade after the initial description of HELPS in the Journal of Neurosurgery. We believe this is partial due to the initial publications being presented in the neurosurgical literature instead of the otolaryngoogy or respirology literature. Neurosurgeons will be needed to cure the condition but will never see a patient until they are referred to them. These patients typically present to our otolaryngology and respirology colleagues (or emergency physicians) and are often misdiagnosed with a psychogenic disorder and referred to psychiatry. Additional work is needed promoting the diagnosis of these conditions within the otolaryngology and respirology communities.

Future issues

The next step may be the recognition of a third vagal rhizopathy. The vagus nerve carries motor, sensory and parasympathetic fibers (14, 15). The clinical ramifications of compression of the motor (hemi-laryngopharyngeal spasm) and sensory (VANCOUVER syndrome) components have been described above. What about the parasympathetic component?

At the present time, we do not have definitive proof of a parasympathetic vagus rhizopathy but have accumulated data that points to the condition. We postulate that compression of the vagus nerve parasympathetic fibers leads to a reduction of parasympathetic function. This would be analogous to compression on the 3rd cranial nerve's parasympathetic fibers causing a pupillary dilation due to imbalance with sympathetic innervation. The vagus nerve innervates the lower esophageal sphincter and facilitates its opening during swallowing. The sphincter's sympathetic innervation facilitates its closure to prevent acid reflux. We postulate that compression of the vagus nerve parasympathetic fibers would reduce the parasympathetic innervation of the lower esophageal sphincter and the resultant imbalance of sympathetic innervation would make it difficult to open this sphincter during a swallow. The clinical result would be dysphagia.

There is a recently described condition, esophagogastric junction outlet obstruction (EGJOO), that has many features in common with what would occur if the lower esophageal sphincter had reduced parasympathetic innervation. One of our patients developed a dyspahia four years post-operatively. Esphagogastric manometry was consistent with dysfunction of the lower eosphagogatric sphincter. Their symptoms resolved following a repeat MVD that decompressed the lowest rootlet of the vagus nerve from the Teflon mass. Future studies will determine if the cause of this currently idiopathic condition is the third vagal rhizopathy. Interestingly, we have not recognized any cardiac issues post-operatively (tachycardia).

Author contributions

CH: Conceptualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Publisher's note

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Monitoring of the lateral spread response combined with brainstem auditory evoked potentials in microvascular decompression for hemifacial spasm

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Objective: Despite high cure rates, symptom persistence and auditory dysfunction occur sometimes after microvascular decompression (MVD) surgery for hemifacial spasm (HFS). This study evaluated whether combined intraoperative monitoring of the lateral spread response (LSR) and brainstem auditory evoked potentials (BAEP) can reduce the incidence of hearing impairment following MVD for HSF.

Methods: A total of 244 HFS patients undergoing MVD were prospectively included and divided into an LSR monitoring group (121 cases) and a combined LRS + BAEP monitoring group (123 cases). Intraoperative recordings of abnormal muscle response (AMR) waves and BAEP were collected and correlated with postoperative HFS and hearing status.

Results: HFS symptoms were similarly improved in the two groups, with no significant differences in the occurrence of AMR or the probability of AMR disappearance postoperatively. For both groups, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of AMR waves were also comparable. However, the incidence of postoperative hearing impairment was significantly lower in the LSR + BAEP group compared to the LSR group. Furthermore, receiver operating characteristic (ROC) analysis of BAEP's performance revealed an area under the ROC curve (AUC) of 0.991 (95% CI: 0.955–1.000), indicating a high diagnostic value of BAEP for predicting postoperative hearing decline.

Conclusion: LSR monitoring is a reliable approach for assessing the effectiveness of MVD surgery for the facial nerve. The combination of LSR monitoring with BAEP does not affect diagnostic accuracy. More importantly, BAEP can sensitively reflect patients' hearing changes during surgery due to its high diagnostic value, guiding surgeons to adjust their intraoperative techniques and effectively reducing the incidence of postoperative hearing impairment.

KEYWORDS

hemifacial spasm, microvascular decompression, brainstem auditory evoked potentials, lateral spread response, hearing impairment

Introduction

Hemifacial spasm (HFS) is characterized by paroxysmal, involuntary contractions of the muscles on one side of the face innervated by the ipsilateral facial nerve. The most common etiology is compression of the facial nerve's root exit zone at the brainstem by the anterior inferior cerebellar artery. Microvascular decompression (MVD) of the facial nerve is an effective treatment for HFS, with a success rate of over 90% (1). However, the incidence of postoperative complications such as tinnitus, hearing impairment, and even complete hearing loss ranges from 1.9% to 20%, significantly affecting patients' prognosis and quality of life (2, 3).

In MVD surgery for the facial nerve, monitoring the lateral spread response (LSR) has become a routine method to predict postoperative facial spasm symptoms (4). In turn, studies have shown that changes in the latency or amplitude of brainstem auditory evoked potentials (BAEP) waves I and V during MVD for HFS can effectively predict postoperative hearing outcomes (3, 5). However, few studies have reported the combined application of intraoperative LSR and BAEP monitoring for timely adjustment of surgical procedures and prediction of auditory outcomes. Can BAEP monitoring detect early involvement of the vestibular nerve during surgery, where auditory damage may still be reversible? If the surgeon adjusts the procedure promptly, can BAEP signals recover? Could this further reduce the incidence of postoperative hearing loss? Based on these questions, this study compares HFS symptom improvement and hearing status after MVD surgery applying either LSR monitoring alone or in combination with BAEP.

Materials and methods

Study design

Based on random digital allocation, patients admitted to the Department of Neurosurgery of the First Affiliated Hospital of

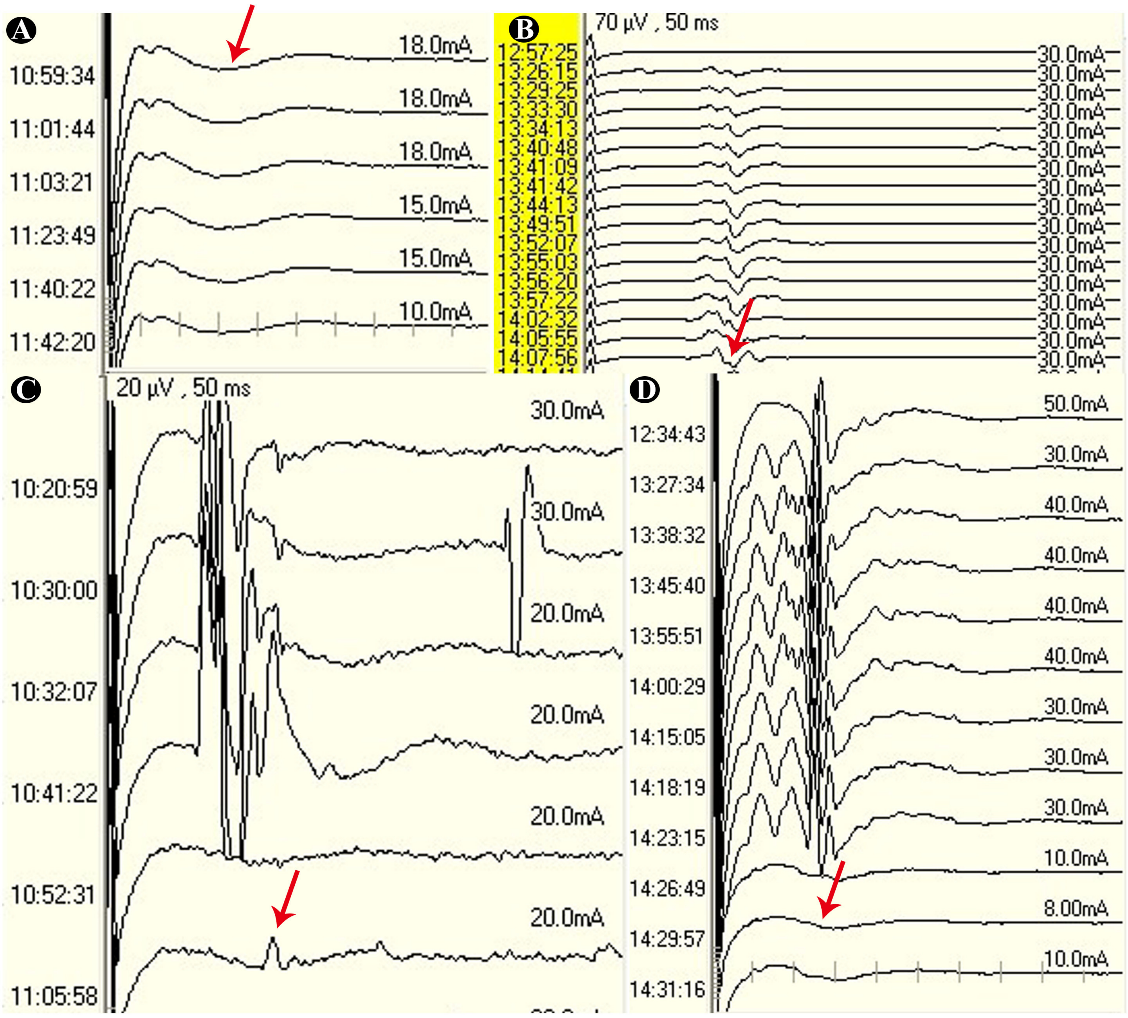

FIGURE 1
(A) The red arrow indicates the absence of the AMR wave; **(B)** the AMR wave is persistently present; **(C)** after the completion of the surgery, the amplitude of the AMR wave decreases by more than 90%; **(D)** after the completion of the surgery, the AMR wave disappears.

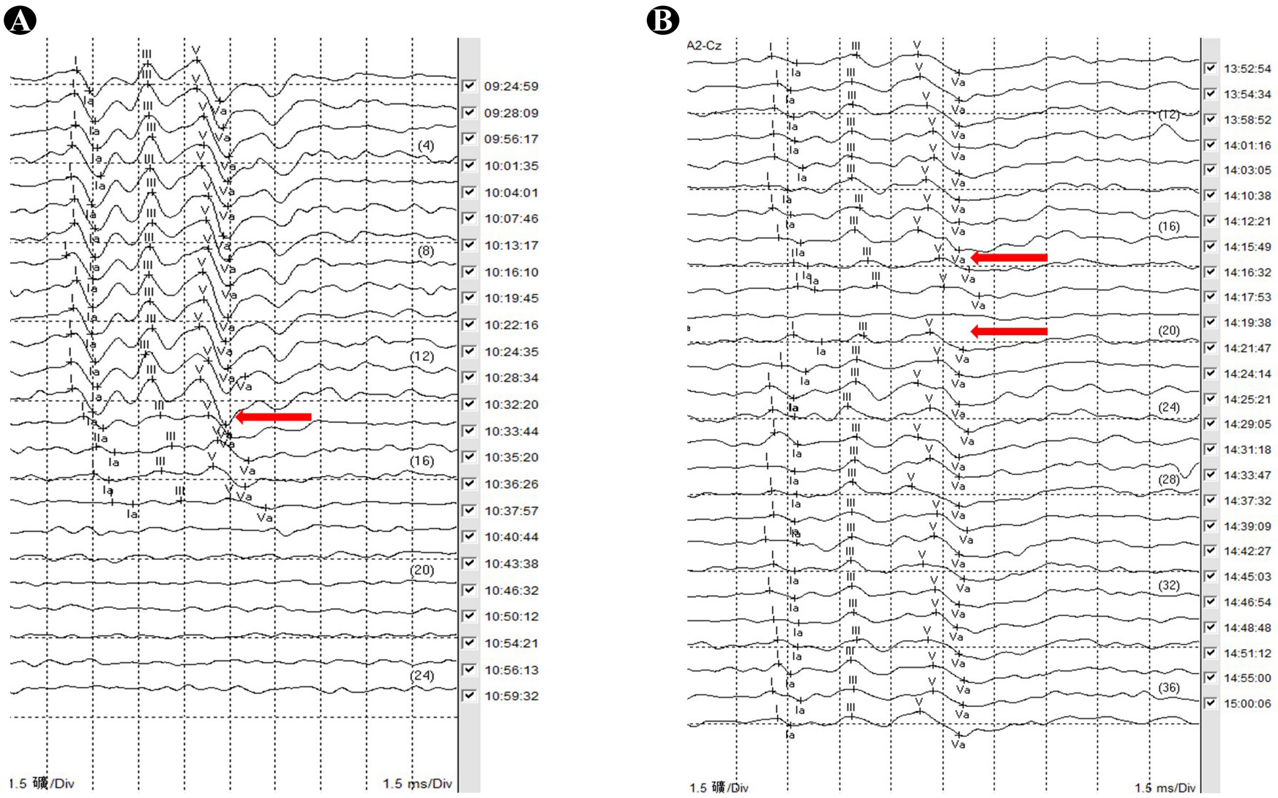

FIGURE 2
(A) At 10:33:44, the amplitudes of waves I and V show a significant decrease, and the latencies are prolonged. At 10:35:20, the amplitudes of waves I and V decreased by more than 50%, with latencies prolonged by more than 0.6 ms. Subsequently, the amplitudes of waves I and V continue to decrease until they disappear; **(B)** at 14:16:32, the amplitudes of waves I and V show a significant decrease, and the latencies are prolonged. At 14:19:38, no distinct waveforms are observed, and by 14:21:47, the waveforms gradually recove.

Soochow University between January 2022 and December 2023 were divided into two groups: lateral spread response (LSR) monitoring group, and combined LSR + brainstem auditory evoked potentials (BAEP) monitoring group. All enrolled patients signed informed consent forms with the approval of their families, and preoperative evaluations and data collection were conducted. A total of 244 patients with HFS were included in this study over a 2-year period, with 121 cases in the LSR monitoring group and 123 cases in the combined LSR + BAEP monitoring group.

The inclusion criteria were: (1) patients diagnosed with HFS based on preoperative symptoms, physical examination, and imaging data; (2) patients undergoing MVD of the facial nerve for the first time, with intraoperative monitoring using either LSR alone or LSR combined with BAEP; and (3) patients with complete clinical records.

Exclusion criteria: (1) patients who did not undergo surgery; (2) patients with recurrent HFS; (3) patients with preoperative hearing impairment.

Lateral spread response monitoring

Intraoperative neurophysiological monitoring was performed using either a Cadwell (Cadwell Industries, USA) or Nicolet Endeavor CR (Nicolet Biomedical Inc., USA) system. As outlined in Figure 1, stimulation was applied to the zygomatic and mandibular branches of the facial nerve, with abnormal muscle responses (AMR) recorded from the mentalis and orbicularis oculi muscles, respectively. Single-pulse electrical stimulation was used, with a pulse width of 200 μs and a stimulation intensity ranging from 5 to 50 mA. The analysis window was set at 50 ms. The surgeon was promptly informed when the lateral spread response waveform appeared, decreased, or disappeared (6).

We assessed the accuracy of LSR monitoring in predicting HFS outcomes after excluding those patients with no intraoperative AMR waves. Persistent AMR waves (decline <90%) were defined as persistent AMR, while AMR waves that declined by more than 90% or completely disappeared were defined as disappeared AMR.

Intraoperative BAEP monitoring

An earplug was inserted into the external auditory canal on the affected side. The recording electrode (A1/A2) was placed anterior to the tragus, with a reference electrode (CZ) positioned at the vertex. The affected side received short-tone stimuli at a frequency of 11.33 Hz and an intensity of 100 dB. The analysis window was set at 15 ms, with 100 to 1,000 responses averaged (Figure 2). The contralateral side received short-tone stimuli at a frequency of 11.33 Hz, an intensity of 100 dB and with 60 dB white

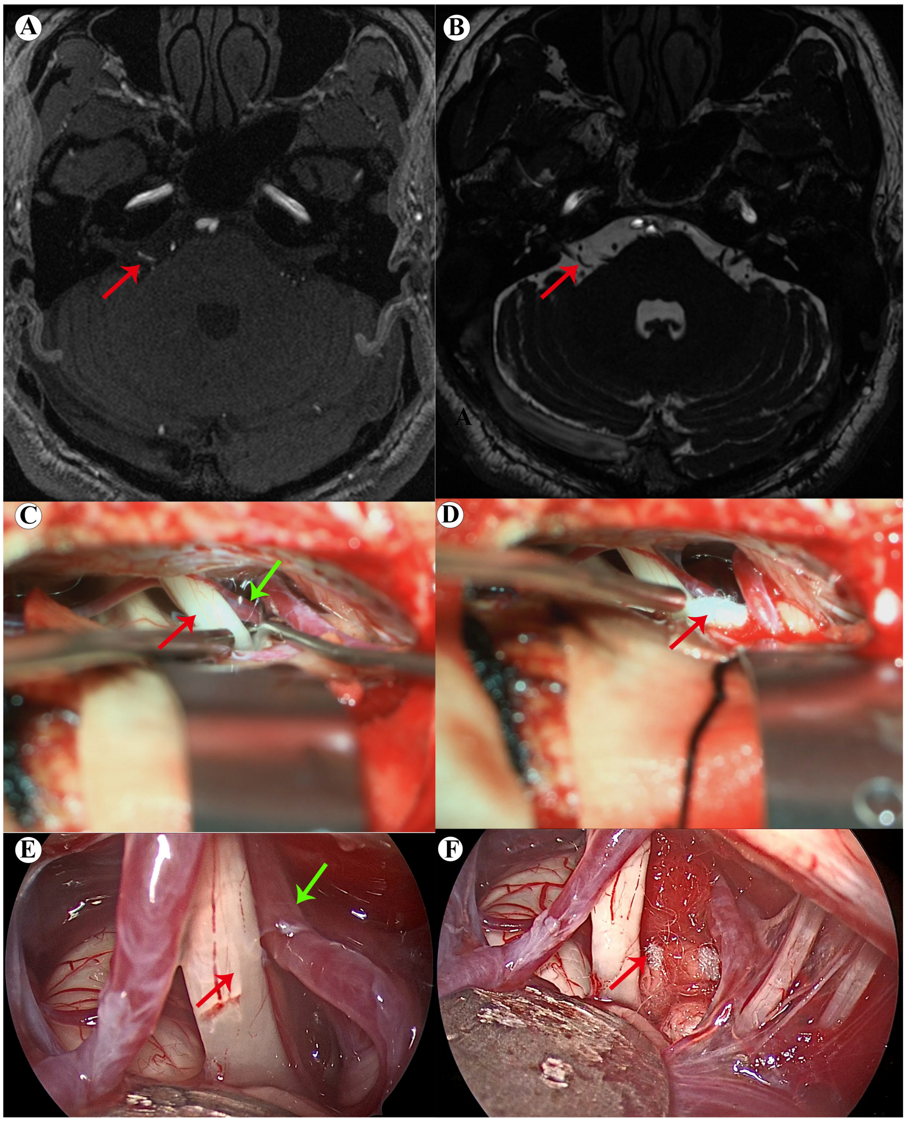

FIGURE 3
(A, B) Preoperative magnetic resonance imaging indicates that the right facial nerve is compressed by the anterior inferior cerebellar artery, with the responsible artery highlighted by the arrow; **(C, D)** microscopic views during surgery; in panel C, the red arrow indicates the facial nerve and the green arrow indicates the responsible artery. In panel D, the red arrow represents the status after the responsible artery has been separated; **(E, F)** endoscopic views during surgery; in panel E, the red arrow indicates the facial nerve and the green arrow indicates the responsible artery. In panel F, the red arrow represents the status after the responsible artery has been separated.

noise masking. The surgeon was alerted when the latency of wave I or V was prolonged by more than 0.6 ms or when the amplitude decreased by more than 50% (7).

We defined no change in BAEP or transient changes in BAEP as unchanged BAEP, while persistent changes in BAEP were classified as changed BAEP. This study aimed to intervene in surgical operations by assessing changes in BAEP during surgery, with the goal of improving hearing outcomes. The transient and permanent changes in BAEP are specific to the surgical procedure. When BAEP changes occur during surgery, electrophysiologists provide timely feedback to the surgical team, allowing them to adjust for neural or vascular manipulation. BAEP amplitudes and/or intervals typically recover within 5 min (possibly extending slightly), which defines a transient change. If BAEP does not recover even after adjustments by the surgical team throughout the procedure, it is considered a permanent change.

Anesthesia and surgical technique

General anesthesia was administered through a combination of intravenous agents and endotracheal intubation. During anesthesia, we used small oral doses of sevoflurane for inhalation, remifentanil and dexmedetomidine for intravenous administration with sufentanil added intermittently. During surgery, the use of muscle relaxants was minimized, except during the induction phase, to avoid interference with neurophysiological monitoring. Fluid administration was carefully controlled to manage the total

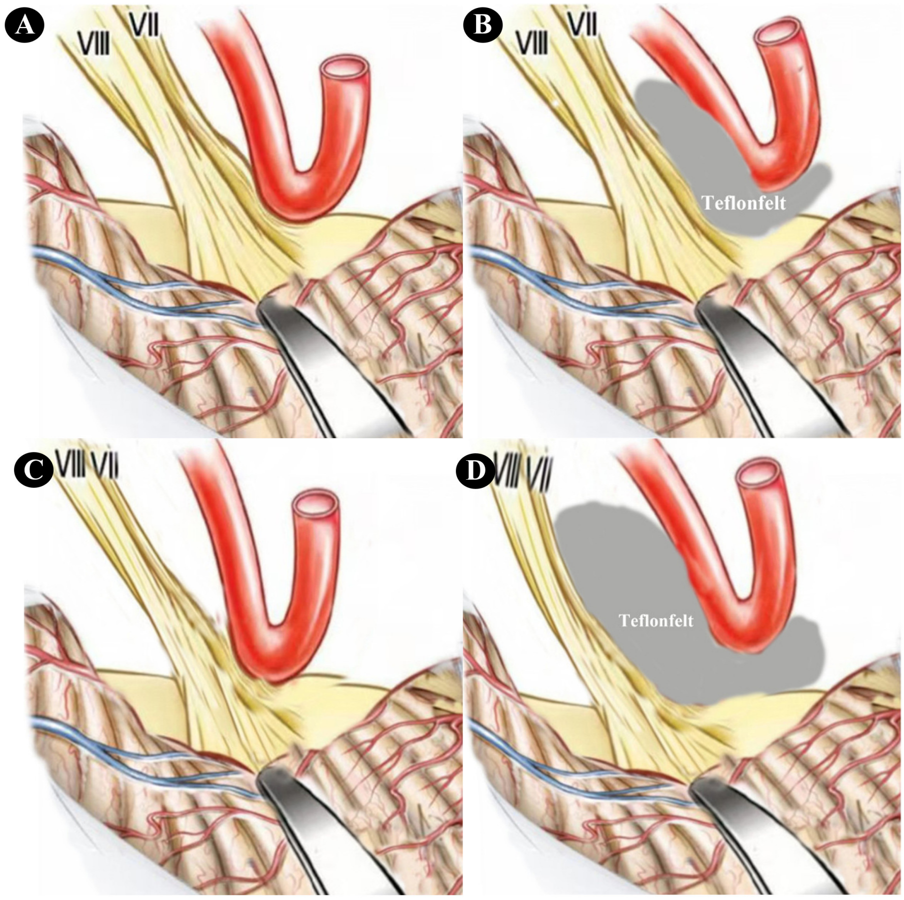

FIGURE 4
(A) Pulling the cerebellar hemisphere posteriorly exposes the VII and VIII cranial nerves and the responsibility artery; **(B)** using Teflonfelt to separate the VII and VIII cranial nerves from the responsibility artery; **(C)** excessive posterior pulling of the cerebellar hemisphere leads to elongation and thinning of the VII and VIII cranial nerves; **(D)** using overly thick or excessive Teflonfelt results in displacement and strain of the VII and VIII cranial nerves.

volume, and the partial pressure of carbon dioxide (PaCO2) was maintained at ∼26 mmHg. β-blockers were used as necessary to facilitate surgical procedures (8).

Whether employing a microscopic or endoscopic approach, MVD of the facial nerve was performed via a retrosigmoid approach. The patient was positioned in the lateral decubitus position with the head securely fixed in a head frame. The head was elevated at an angle of 15°–20°, and the chin was flexed toward the sternum, approximately two fingerbreadths away. The shoulder strap was gently retracted toward the caudal direction to maintain head hyperextension while avoiding excessive traction on the brachial plexus, ensuring that the root of the mastoid process was positioned at the highest point.

Surgical procedure: the subarachnoid space was accessed to release cerebrospinal fluid (CSF), allowing for a decrease in intracranial pressure. Once the pressure was reduced, a sharp dissection of the arachnoid membrane was performed from the caudal end of the cranial nerves to the rostral end, completely separating the cerebellum from the cranial nerves. The intraoperative exploration focused on the intradural segments of the facial nerve, specifically areas I to IV. If exposure was challenging, endoscopy could be utilized for multi-angle exploration. All vessels in contact with the facial nerve were meticulously dissected and retracted, and appropriate decompression techniques (such as Teflon felt, adhesive agents, or suspension) were employed. Careful release of the arachnoid membrane was crucial to prevent traction on the cranial nerves (Figure 3) (9–11).

Surgical technique highlights combined with electrophysiological monitoring: (1) when releasing cerebrospinal fluid, utilize the natural anatomy and gravity of the cerebellum and temporal bone as much as possible while minimizing the use of the brain tractor to avoid excessive traction on the VII and VIII cranial nerves. If changes in BAEP amplitude or latency occur during this process, immediate adjustment of the cranial pressure is necessary. (2) When operating near the blood vessels surrounding the VII and VIII cranial nerves within the brainstem's REZ area, first ensure complete separation of these structures. Perform this step gently to prevent vasospasm or excessive bleeding caused by large operative movements. If BAEP changes during operating blood vessels, the operator must halt the procedure immediately to minimize blood vessel traction or stimulation. Additionally, applying local anesthetics like papaverine on the blood vessel's surface can help relax the vessels and prevent vasospasm if necessary (12).

TABLE 1a The occurrence and non-occurrence rates of AMR wave.

AMR waves during surgery	LSR alone		LSR + BAEP	
	Occurrence rate	Non-occurrence rate	Occurrence rate	Non-occurrence rate
	117 (96.7%)	4 (3.3%)	119 (96.7%)[a]	4 (3.3%)[b]

[a,b]The occurrence and non-occurrence rates of AMR wave showed no statistically significant difference between the LSR monitoring group and the combined LSR and BAEP monitoring group ($p > 0.05$, continuity-corrected Chi-square test). LSR: lateral spread response; BAEP: brainstem auditory evoked potentials.

TABLE 1b The occurrence and non-occurrence rates of the disappearance of AMR wave.

Disappearance of AMR waves after surgery	LSR alone			LSR + BAEP		
	Non-occurrence rate	Occurrence rate		Non-occurrence rate	Occurrence rate	
	10 (8.5%)	107 (91.5%)		9 (7.6%)[c]	110 (92.4%)[d]	
	Persisted	**Decreased by more than 90%**	**Completely disappeared**	**Persisted**	**Decreased by more than 90%**	**Completely disappeared**
	10	2	105	9	3	107

[c,d]Similarly, there was no statistically significant difference in the occurrence and non-occurrence rates of the disappearance of AMR wave between these two groups ($P > 0.05$, Chi-square test). LSR: lateral spread response; BAEP: brainstem auditory evoked potentials.

(3) During Telfonfelt reduction, avoid over-filling. If Telfonfelt between blood vessels and nerves is too thick, it may lead to unnecessary nerve traction; thus, monitor BAEP changes during this process to ensure appropriate use of Telfonfelt for effective decompression (Figure 4).

Operation outcome evaluation: We categorized the surgical results as: excellent (E0); good (E1); fair (E2); and poor (E3) (13). E0: Complete disappearance of spasm; E1: Occasional slight spasm; E2: Moderate spasm, apparently persisting; E3: Not cured. Complete recovery and significant improvement were classified as a good outcome, whereas partial relief and no improvement were classified as a poor outcome.

Statistical analysis

Statistical analyses were conducted using SPSS Statistics version 29.0 and MedCalc version 22.0. Continuous variables were expressed as mean ± standard deviation ($x \pm s$), while categorical variables were presented as counts and percentages [n (%)]. A one-way analysis of variance (ANOVA) was used to compare Karnofsky Performance Scale (KPS) scores among different surgical groups. For comparisons of preoperative and postoperative KPS scores within the same group or between two groups, paired t-tests were applied, with results reported as mean differences and 95% confidence intervals (CI). For categorical data analysis, the choice of statistical tests depended on sample size and expected frequencies: Pearson's chi-square test was used when $N \geq 40$ and expected frequency (T) ≥ 5. Continuity-corrected chi-square test was applied when $N \geq 40$ and $1 \leq T < 5$. Fisher's exact test was used for small samples ($N < 40$ or $T < 1$). A P-value < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was performed using MedCalc version 22.0 to compare the diagnostic performance of different monitoring methods. The area under the ROC curve (AUC) was calculated to quantify classification performance: AUC $= 0.5$ suggests no diagnostic ability. AUC < 0.5 indicates performance worse than random guessing. $0.5 \leq$ AUC < 0.7 suggests low diagnostic value. $0.7 \leq$ AUC < 0.9 indicates moderate diagnostic value. AUC ≥ 0.9 represents high diagnostic value. To compare AUC values between groups, DeLong's test was employed. Sensitivity (true positive rate) represents the proportion of actual positive cases correctly identified, while specificity (true negative rate) indicates the proportion of actual negative cases correctly classified. PPV reflects the proportion of predicted positive cases that are truly positive, whereas NPV represents the proportion of predicted negative cases that are truly negative. Accuracy measures the overall proportion of correctly classified cases among all cases. Statistical comparisons of these metrics were performed using Pearson's chi-square test, continuity-corrected chi-square test, or Fisher's exact test, depending on sample size and expected frequencies. If a particular category within a group had zero positive cases (e.g., no "poor outcome positive" patients in the LSR group), this could lead to extreme values in sensitivity or specificity calculations. In such cases, Fisher's exact test or the continuity-corrected chi-square test was used to mitigate the impact of small or sparse data.

Results

General information

A total of 244 patients were included in this study, comprising 93 male and 151 female participants. Among these, 130 patients had left-sided HFS, while 114 had right-sided HFS. The mean age of the patients was 53.7 ± 11.7 years, with a minimum age of 19 years and a maximum age of 83 years. In the LSR monitoring group, 60 patients underwent microscopic surgery, and 61 patients underwent endoscopic surgery. In the LSR + BAEP monitoring group, 64 patients underwent microscopic surgery, and 59 patients underwent endoscopic surgery.

TABLE 2 Outcomes of MVD surgery for HFS symptoms.

		LSR					LSR + BAEP				
		No AMR wave	AMR wave persistence	AMR wave decreased >90%	AMR wave disappearance	Total	No AMR wave	AMR wave persistence	AMR wave decreased >90%	AMR wave disappearance	Total
Number of patients		4	10	2	105	121	4	9	3	107	123
Outcome	Cured (excellent) E0	2	4	2	78	86	1	3	2	79	85
	Significant relief (good) E1	0	2	0	27	29	1	2	0	25	28
	Partial relief (fair) E2	1	2	0	0	3	0	2	1	2	4
	Ineffective (poor) E3	1	2	0	0	3	2	2	0	1	5
Cure rate		50%	40%	100%	74.3%	71.1%	25%	33.4%	66.7%	73.8%	69.1%
Significant relief rate		0%	20%	0%	25.7%	23.9%	25%	22.2%	0%	23.4%	22.8%
Partial relief rate		25%	20%	0%	0%	2.5%	0%	22.2%	33.3%	1.9%	3.3%
Ineffectiveness rate		25%	20%	0%	0%	2.5%	50%	22.2%	0%	0.9%	4.8%

TABLE 3 Comparison of diagnostic value of intraoperative monitoring methods for treatment outcomes.

	Postoperative outcomes		Total
	Good outcome (+)	Poor outcome (−)	
LSR + BAEP group			
Occurrence rate of AMR wave	106	4	110
Non-occurrence rate of AMR wave	5	4	9
Total	111	8	119
LSR group			
Occurrence rate of AMR wave	107	0	107
Non-occurrence rate of AMR wave	6	4	10
Total	113	4	117

AMR assessment

In the LSR monitoring group, AMR waves were observed in 117 cases during surgery. Among these, 10 cases exhibited persistent AMR waves, 2 cases showed a decline of more than 90%, and 105 cases had AMR waves that disappeared postoperatively. Four cases did not present any AMR waves. In the LSR + BAEP monitoring group, AMR waves were recorded in 119 cases intraoperatively. Within this group, 9 cases demonstrated persistent AMR waves, 3 cases experienced a decline of more than 90%, and 107 cases had AMR waves that disappeared postoperatively. Four cases in this group did not exhibit any AMR waves. There were no significant statistical differences between the two groups regarding the occurrence and non-occurrence rates of AMR waves or the probability of AMR waves disappearing or remaining postoperatively (Tables 1a,b).

Postoperative outcomes

We segregated the intraoperative AMR patterns into four groups (Table 2). In the LSR monitoring group, four cases exhibited no AMR waves, with outcomes of E0 in 2 cases, E1 in 0 cases, E2 in 1 case, and E3 in 1 case. Ten cases demonstrated persistent AMR waves, with results classified as E0 in 4 cases, E1 in 2 cases, E2 in 2 cases, and E3 in 2 cases. Two cases showed a decline in AMR waves of more than 90%, both classified as E0. A total of 105 cases exhibited a complete disappearance of AMR waves, with classifications of E0 in 78 cases and E1 in 27 cases. In turn, in the LSR + BAEP monitoring group, four cases exhibited no AMR waves and outcomes were classified as E0 in 1 case, E1 in 1 case, and E3 in 2 cases. Nine cases demonstrated persistent AMR waves, and outcomes were classified as E0 in 3 cases, E1 in 2 cases, E2 in 2 cases, and E3 in 2 cases. Three cases showed a decline in AMR waves of more than 90%, and were classified as E0 in 2 cases and E2 in one case. A total of 107 cases exhibited a complete disappearance

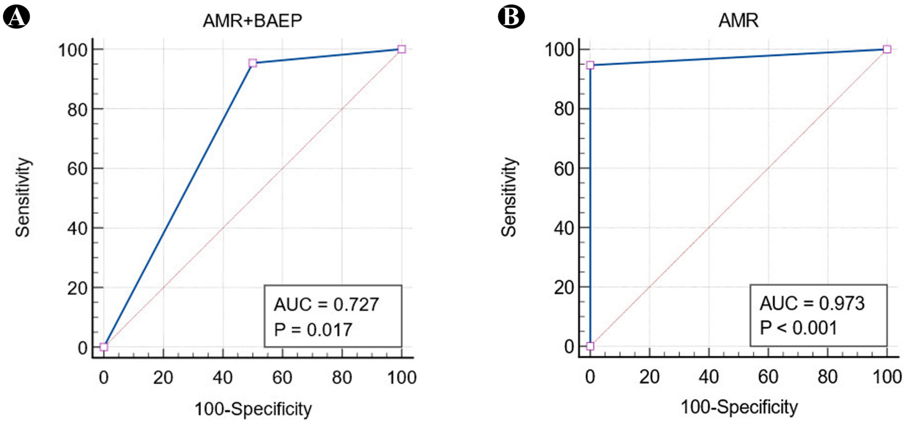

FIGURE 5
Comparison of ROC curves. **(A)** Indicates an AUC value of 0.727 (95% CI: 0.638–0.805), while **(B)** indicates an AUC value of 0.973 (95% CI: 0.926–0.994).

of AMR waves, with classifications of E0 in 79 cases, E1 in 25 cases, E2 in 2 cases, and E3 in 1 case.

For both the LSR and LSR + BAEP monitoring groups, no statistical differences in the cure rate were observed between the respective AMR wave disappearance groups and those showing an AMR decline of more than 90%. In contrast, and compared also with the corresponding AMR wave disappearance groups, cure rates were significantly lower in the groups with no AMR waves and those with persistent intraoperative AMR waves (Table 2).

Diagnostic value of intraoperative monitoring methods for therapeutic effectiveness

Table 3 summarizes the treatment outcomes for the two monitoring methods.

Based on the postoperative outcomes of both groups, ROC curves were constructed. The AUC for the LSR + BAEP group was 0.727 (95% CI: 0.638–0.805), while the AUC for the LSR group was 0.973 (95% CI: 0.926–0.994). The difference in AUC between the two groups (0.246, 95% CI: 0.0586–0.433) was significant (Figure 5).

The LSR + BAEP group demonstrated a sensitivity of 95.50%, specificity of 50.00%, positive predictive value of 96.36%, negative predictive value of 44.44%, and accuracy of 92.44%. In turn, the LSR group had a sensitivity of 94.69%, specificity of 100.00%, positive predictive value of 100.00%, negative predictive value of 40.00%, and accuracy of 94.87%. Chi-square testing indicated no statistically significant differences among the five diagnostic indicators of the two groups (Table 4).

BAEP-based hearing assessment

In the LSR monitoring group, 16 out of the 121 patients experienced postoperative hearing loss, with an incidence rate of 13.2%, including 2 cases of deafness and 14 cases of hearing impairment. In the LSR + BAEP monitoring group, six patients experienced hearing impairment, resulting in an incidence rate of 4.9%, with no cases of complete hearing loss (Table 5).

While comparing the LSR + BAEP group to the LSR group alone, the latter exhibited significantly lower normal hearing rates and a higher incidence of hearing abnormalities. This suggests that during MVD surgery to correct HFS, simultaneous BAEP monitoring can reduce the occurrence of postoperative hearing impairment.

Analysis of the diagnostic value of BAEP

As shown in Table 6, in the BAEP-positive group six patients experienced postoperative hearing loss, while two patients maintained normal hearing. In the unchanged BAEP group, no patients exhibited postoperative hearing loss, with all 115 patients retaining normal hearing.

From these data, analysis of diagnostic test metrics indicated that sensitivity was 100%; specificity was 98.3%, positive predictive value was 75%, negative predictive value was 100%, and overall accuracy was 95.93%. The AUC ROC for BAEP was 0.991 (95% CI: 0.955–1.000), indicating an excellent diagnostic value for determining postoperative hearing decline (Figure 6).

Discussion

LSR monitoring provides valuable information for MVD surgery in HFS, as the observation of AMR wave disappearance can be used to predict the effectiveness of the procedure (14). However, few studies have reported the joint application of LSR and BAEP monitoring during surgery to adjust surgical procedures in real time and predict auditory outcomes. Therefore, we divided the prospective cohort into two groups: one group with only LSR monitoring and another group with combined LSR and BAEP monitoring. To establish whether there were differences in the

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TABLE 4 Comparison of diagnostic value between two monitoring methods.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
LSR + BAEP	95.50%	50.00%	96.36%	44.44%	92.44%
LSR	94.69%	100.00%	100.00%	40.00%	94.87%
χ^2 value	0.078	–	2.209	–	0.588
P value	0.78	0.208	0.137	1.000	0.443

TABLE 5 Postoperative hearing assessment.

Number of patients		LSR	Incidence rate	LSR + BAEP	Incidence rate
No abnormal hearing		105	86.8%	117	95.1%*
Abnormal hearing	Surgical side hearing loss	2	13.2%	0	4.9%#
	Surgical side hearing deterioration	14		6	

*Comparing the LSR + BAEP group to the LSR group, a significantly lower incidence of hearing normalities was observed in the latter group ($P < 0.05$, Chi-square test).
#Comparing the LSR + BAEP group to the LSR group, a significantly higher incidence of hearing abnormalities was observed in the latter group ($P < 0.05$, Chi-square test).

TABLE 6 Postoperative hearing status of patients in the LSR + BAEP monitoring group.

BAEP	Postoperative hearing status		Total
	Hearing loss (+)	Normal hearing (−)	
Changed BAEP	6	2	8
Unchanged BAEP	0	115	115
Total	6	117	123

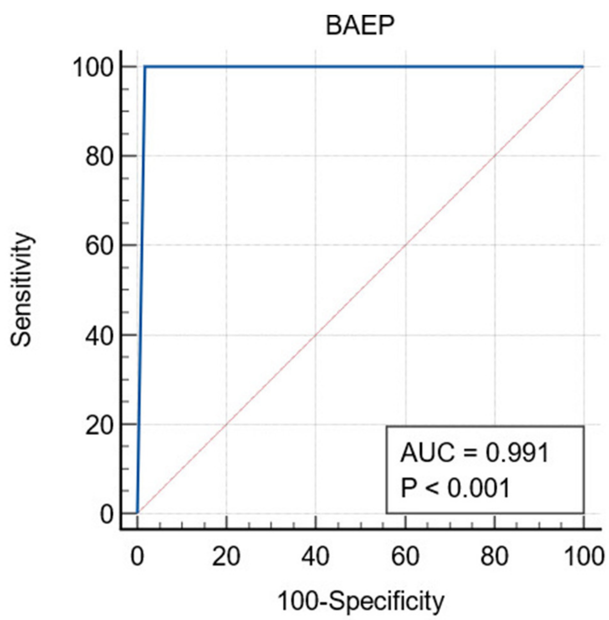

FIGURE 6
Analysis of the ROC curve for BAEP using MedCalc software indicates an AUC value of 0.991 (95% CI: 0.955–1.000).

hearing outcomes between the two groups before comparison, we first compared the LSR results from both groups. Our aim was two-fold: to determine if BAEP interfered with LSR and to assess whether there were differences in HFS conditions across the two groups by using LSR as a baseline measurement. Our findings indicated that there were no statistically significant differences in the occurrence and non-occurrence rates of AMR wave between the two monitoring approaches. Likewise, the probability of AMR waves transitioning from disappeared to persistent during surgery was comparable among the two groups. Postoperatively, the rates of complete recovery, significant relief, partial relief, and inefficacy for both monitoring methods also did not demonstrate any significant differences. We thus conclude that BAEP monitoring does not interfere with the assessment of LSR and there was no substantial difference in hemifacial spasm conditions between the two groups of patients.

Currently, LSR is not considered the gold standard for evaluating postoperative recovery or significant symptom improvement; rather, it serves as an adjunctive assessment tool. Our study found that there were no significant differences in sensitivity, specificity, positive predictive value, negative predictive value, and accuracy between the LSR group and the LSR + BAEP group. Regarding the observed AUC differences, we believe these may be influenced by the sparsity of data (i.e., the absence of patients with poor outcomes) in specific categories.

Zero values in ROC AUC calculations can significantly affect the interpretability of model performance. For instance, the absence of "poor outcome positive" patients in the LSR group may lead to an inflated sensitivity (e.g., 100%) and AUC value (0.973), not necessarily reflecting the model's true classification ability. This data sparsity compromises the smoothness and accuracy of ROC curves and may introduce bias when comparing AUCs between groups. Therefore, the observed difference in AUCs might partly result from data imbalance rather than a genuine difference in classification efficacy. To address this limitation, future studies will aim to expand the sample size for more robust analysis. Despite the absence of poor outcome cases in certain LSR subgroups, no significant differences were found between the LSR+BAEP and AMR groups in terms of sensitivity, specificity, PPV, NPV, and accuracy. This can be interpreted from three perspectives: (1) overall data consistency between groups, as most classification categories remained comparable; (2) the use of statistical methods appropriate for small or sparse datasets, such as Fisher's exact test and continuity-corrected chi-square test; and (3) the interrelationship among diagnostic metrics, where improvements in one parameter (e.g., sensitivity) may not lead to significant differences in overall performance due to compensatory changes in others.

Facial nerve MVD surgery primarily utilizes a posterior approach to the sigmoid sinus. The vestibular nerve is located adjacent to the facial nerve, and during the procedure, traction on the cerebellum can lead to stretching or compression of the vestibular nerve due to vascular manipulation. This often results in the vestibular nerve being affected (12), leading to postoperative hearing impairment in patients (2, 5). The changes in latency and/or amplitude of waves I and V of the BAEP can sensitively predict whether a patient will experience hearing impairment following MVD surgery (3).

In the post-operative follow-up of 26 patients with BAEP transient changes, no single case exhibited hearing loss or hearing deterioration. However, this result alone cannot sufficiently demonstrate that our interventions through BAEP modifications and timely warnings to surgeons led to the subsequent recovery of BAEP, thereby preventing postoperative hearing damage. This underscores a critical gap: whether BAEP can effectively track postoperative auditory trends. Only by monitoring BAEP and accurately predicting post-operative hearing status based on its dynamic changes can we provide evidence-based interventions that influence both surgical procedures and ultimate audiometric outcomes.

We further analyzed the diagnostic value of BAEP. The study revealed that combining LSR with BAEP significantly reduced postoperative hearing loss compared to using only LSR. BAEP's high sensitivity (100%) ensures all cases of hearing impairment are detected, and its specificity minimizes false positives. With a strong negative predictive value, a normal BAEP result reliably confirms preserved hearing. These findings underscore BAEP as an effective intraoperative monitoring tool that enhances surgical decision-making by providing early warnings of potential hearing damage, ultimately improving patient outcome.

The tension of blood vessels and cranial nerves VII and VIII near the REZ area is a key factor contributing to postoperative hearing impairment, and BAEP's sensitivity in reflecting hearing changes makes it possible to detect nerve and vessel issues during surgery. When amplitudes or latencies in BAEP measurements change, surgeons should halt operations and assess potential causes—such as vasospasm, blood accumulation from vascular bleeding, and other hemodynamic factors, excessive nerve traction, or Teflonfelt overused (2, 5, 12, 15). Measures like papaverine application or blood washing or reasonable use of tractor to avoid excessive nerve traction and proper use of Teflonfelt should be considered to prevent complications. This study highlights BAEP's diagnostic effectiveness in MVD surgery and the necessity for adjusting surgical procedures based on BAEP changes.

Conclusions

LSR monitoring is a reliable method for assessing the outcome of MVD surgery for HFS. In combination with BAEP monitoring, the diagnostic accuracy of LSR is unaffected. More importantly, BAEP can sensitively reflect patients' hearing changes during surgery due to its high diagnostic value, guiding surgeons to adjust their intraoperative techniques and effectively reducing the incidence of postoperative hearing impairment.

Of note, this study is a single-center investigation, and due to the limited sample size, the results may be subject to some bias.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics and Review Committee of the First Affiliated Hospital of Soochow University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

DC: Writing – original draft. CL: Writing – original draft. YQ: Writing – review & editing. CJ: Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

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Publisher's note

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