

Predictive and prognostic factors for outcome of microvascular decompression in trigeminal neuralgia

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Abstract

Background: Trigeminal neuralgia (TN) is a disease characterized by recurring, short-lived, electric shock-like pain experienced on one side of the face. Microvascular decompression (MVD) is one of the most effective surgical interventions for resolving TN caused by neurovascular compression. This study aimed to determine the predictive and prognostic factors of surgical outcomes.

Methods: This retrospective cohort study enrolled patients diagnosed with TN who underwent MVD at our hospital during 2013-2019. The demographic information, pain character, peri-operative Barrow Neurological Institute (BNI) scale, medication, operative finding were recorded. And the outcome was Outcomes were divided into drug-free and drug-dependent group. Predisposing factors for each outcome were analyzed by one-way analysis of variance, followed by a Mann-Whitney *U* test or Kruskal-Wallis test.

Results: A total of 104 consecutive patients received MVD to treat TN, and 88 patients were enrolled in this study. The overall postoperative drug-free outcome was 72.7%. A significant difference in drug-free outcomes was observed for patients with typical TN (80.8%) compared with patients with atypical TN (33.33%, $p = 0.001$). When severe venous compression was encountered during MVD, the drug-free outcome fell to 50% (10/20, $p = 0.009$). The Mann-Whitney *U* test indicated typical TN as a positive predictive factor of a drug-free outcome, whereas severe venous compression was a negative predictive factor. The patients with preoperative BNI score of 4 had better improvement than others ($p = 0.045$). Age, onset duration, and arterial loop had no specific difference in this study.

Conclusion: In our study, atypical TN and severe venous compression were associated with poor outcomes. Regrouping atypical TN into precise diagnosis represents an immediate priority according to our result. The preoperative BNI score could be used as an effective predictive tool for the outcome of MVD surgery.

Keywords: BNI score; Drug-free outcome; Microvascular decompression; Neurovascular complex; Trigeminal neuralgia; Venous compression

1. INTRODUCTION

The International Classification of Headache Disorders (ICHD), established by the International Headache Society,¹ defines

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trigeminal neuralgia (TN) as a recurrent, unilateral, transient, electrical shock-like pain limited to the trigeminal nerve distribution with a sudden onset, resulting in severe pain in response to harmless tactile stimulation.²⁻⁴ Historically, TN is classified as either typical or atypical TN, according to the clinical presentation. TN can also be classified as primary and secondary according to pathological findings. Atypical TN is relatively uncommon and is characterized by constant, dull, aching, or boring pain or the sensation of numbness, in contrast to the transient sharp pain that characterizes typical TN. In the third edition of the ICHD,¹ atypical TN was defined as TN with concomitant and continuous facial pain.

The most popular surgical intervention for TN is microvascular decompression (MVD). The first study to describe MVD was published by Dandy in 1932,⁵ and the theory of neurovascular complex (NVC) was promoted by Jannetta in 1967.⁶ Clinically, the mainstream theory of NVC underlying TN is not as specific

as the theory of NVC underlying hemifacial spasms, which indicate that TN can be associated with unknown causes or multiple etiologies.⁷⁻⁹ In 2019, the American Academy of Neurology (AAN)–European Federation of Neurological Societies (EFNS) released guidelines that reclassified the symptoms previously associated with atypical TN by introducing a new diagnosis of cervical fascia pain.^{3,10,11}

This reclassification reflects the uneven surgical results that have long been reported between typical and atypical TN. Therefore, we conducted a retrospective cohort study to review TN cases over a 7-year period to compare the new classification system with the traditional classification system for TN, including associated clinical processes, to determine whether any factors can be used to predict surgical outcomes.

2. METHODS

2.1. Setting

This study was performed as a single-institution, retrospective study. Our institutional review board approved this research protocol and waived the requirement for patient consent due to the retrospective study design (Institutional Review Board [IRB]: CE21062B). We retrospectively obtained the records of patients diagnosed with TN who underwent standard MVD for the first time. We used the Barrow Neurological Institute (BNI) pain intensity score to classify these patients.¹²

2.2. Patient recruitment

A total of 104 patients matched the inclusion criteria listed below. However, 16 patients (15.3%) were excluded for the following reasons: receiving a second operation ($n = 2$), undergoing previous Gamma Knife treatment ($n = 4$), bilateral TN ($n = 2$), and follow-up less than 6 months ($n = 8$). A flowchart of patient recruitment is shown in Fig. 1.

Patients who met the following inclusion criteria were selected: (1) experienced facial pain with distribution over the trigeminal distribution area; (2) failed to maintain medical pain control; and (3) received MVD surgery for the first time at our institute during 2013-2019, including previous surgeries performed at other hospitals.

Patients were excluded for any of the following criteria: (1) diagnosed with secondary TN, caused by tumor, vascular lesion, multiple sclerosis, or other primary disorders; (2) diagnosed

with bilateral TN; (3) diagnosed with severe and untreated dental problems (4) had a postoperative follow-up period of <6 months; (5) underwent any prior surgical procedure performed at our hospital; or (6) received any prior percutaneous rhizotomy/Gamma Knife radiosurgery.

All patients underwent a preoperative imaging evaluation, involving either a magnetic resonance angiography (MRA) or computed tomography angiography (CTA) to exclude both tumors and vascular lesions.

2.3. BNI scoring¹²

The BNI scoring system rates pain on a 1-5 scale, as follows: (1) no trigeminal pain and no medication use; (2) occasional pain not requiring management with medication; (3) some pain that is adequately controlled using medication; (4) some pain that is not adequately controlled using medication; and (5) severe pain that is not relieved using medication.

2.4. Surgical methods

All patients were placed in the park-bench position and were treated using a suboccipital retrosigmoid approach. The occipital cistern and cerebellomedullary cistern were routinely opened. After identifying the trigeminal nerve, the adhesion band, arterial loop, and venous compression were separated from the entry zone until the whole cistern segment was free. An appropriate amount of Teflon cotton was inserted to separate the NVC from the entry zone. The durotomy was closed using a piece of aponeurosis and a tight suture. The craniotomy was covered with a titanium or absorbable plate. The muscles fascia, cap aponeurosis, and scalp were sutured layer by layer. All operations were performed by our functional neurosurgical team.

2.5. Intraoperative findings

We classified the structures involved in the compression of the trigeminal nerve into arterial loop compression (by the superior cerebellar artery [SCA] from above or by an anterior inferior cerebellar artery [AICA] from below), venous compression (such as the superior petrosal vein or ponto-trigeminal veins), or arachnoid adhesion band compression.

2.6. Grouping and outcome assessment

Based on the preoperative findings, we categorized the patients with preoperative BNI scores of 3, 4, and 5 into Groups A, B, and C, respectively. Postoperative pain outcomes were assessed by the outpatient department, and the value recorded at the last available follow-up >6 months after the operation was used. We categorized a postoperative BNI score of 1-2 as a good outcome (Group I: pain controlled without medication, drug-free outcome) and a postoperative BNI score of 3-5 as a poor outcome (Group II: pain control continues to require medication, drug-dependent outcome).

2.7. Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Science (IBM SPSS version 22.0; International Business Machines Corp, NY, USA). Categorical patient characteristic data were assessed using the Chi-square test. Continuous data were compared using a one-way analysis of variance (ANOVA), followed by a Mann-Whitney *U* test or Kruskal-Wallis test. A value of $p < 0.05$ was considered significant.

3. RESULTS

The patient distribution status was as follows: more women than men (male: 35, female: 53); TN was more commonly

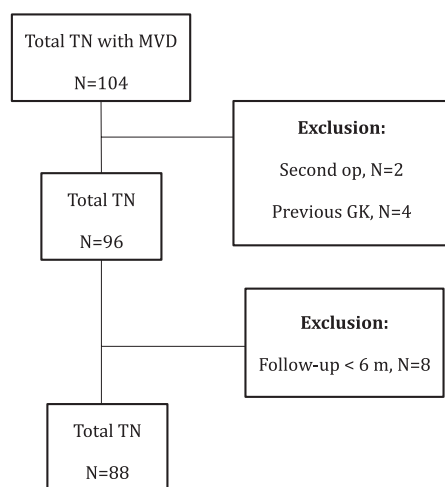


Fig. 1 Flow chart of patient recruitment. GK = gamma knife; MVD = microvascular decompression; op = operation; TN = trigeminal neuralgia.

diagnosed on the right side (right: 50, left: 38); most patients were diagnosed with typical TN (83%, 73/88); distribution segment, V1 (4.5%), V2 (20.5%), V3 (23.9%), V1-2 (14.8%), and V2-3 (38.6%); the average age was 62 (53.0-68.0) years; the average length of hospital stay was 5 days; average time from TN onset to surgery was 33 (12.3-91.5) months; arterial loop (SCA/AICA) were found during surgery in 52.3% (46/88) of cases, a venous component was identified in 22.7% (20/88) of cases, a venous component only was identified in 13.6% (12/88) of cases, and the adhesion band was involved in 37.5% (33/88) of cases. The most common postoperative complication was dizziness (30.7%, 27/88), followed by facial numbness (4.5%, 4/88) and headache (2.5%, 2/88). No infections or otorrhea were reported in any patient. We categorized patients according to their preoperative BNI scores into Groups A ($n = 6$), B ($n = 59$), and C ($n = 23$).

Patients in Group B (preoperative BNI = 4) experienced more significant improvement in BNI than the other groups ($p = 0.045$) and included a relatively high proportion of patients with typical TN (55/59, 93%, $p = 0.001$) and a relatively high proportion of patients with intraoperative findings of arterial involvement (36/59, 61%, $p = 0.004$) (Table 1). No significant differences in age, sex, laterality, V1-3 distribution, or onset time were observed among the three groups. The change in BNI score, diagnosis of typical TN, and intraoperative findings of artery involvement could not be assessed for independence due to an insufficient number of samples.

Our overall postoperative drug-free outcome was 72.7% (64/88), with a clear difference in the response between the typical TN group 80.8% (59/73) and the atypical TN group 33.33%

(5/15, $p = 0.001$). When severe venous compression was encountered, the drug-free outcome fell to 50% (10/20, $p = 0.009$). The Mann-Whitney U test was used to identify a diagnosis of typical TN as a positive predictive factor of a drug-free outcome, whereas the intraoperative identification of venous compression was identified as a negative predictive factor (Table 2). The multivariable analysis also verified that a diagnosis of typical TN ($p = 0.001$) and the presence of venous compression ($p = 0.009$) are independent factors associated with a drug-free outcome (Table 3). In addition, we analyzed the combined involvement of both arterial and venous components, which had no significant effect on the outcome. In this study, factors that have previously been identified as significant in prior studies, such as age, time from onset to surgery, and the presence or absence of NVC, had no significant effects on the outcome.^{2,13-15} Among patients who had received the first time MVD in other hospital underwent an MVD reoperation here, 50% (3/6) achieved a drug-free outcome, but the case number of reoperations was insufficient to determine significant differences in prognosis compared with patients undergoing first MVD operations.

4. DISCUSSION

Patients diagnosed with typical and atypical TN experience significantly different outcomes following MVD surgery. At present, MVD outcomes at our institute are good, with the hope that these findings will provide further improvements. In our study, 72.7% (64/88) of treated patients reported drug-free postoperative outcomes after at least 6 months of follow-up. The probability of drug-free outcomes reached 80.8% (59/73)

Table 1
Pre-op BNI group ($n = 88$)

	BNI score 3 ($n = 6$)		BNI score 4 ($n = 59$)		BNI score 5 ($n = 23$)		p
Sex							0.882
Female	4	(66.7%)	36	(61.0%)	13	(56.5%)	
Male	2	(33.3%)	23	(39.0%)	10	(43.5%)	
Age	54.5	(48.5-64.3) ^a	62.0	(53.0-68.0) ^a	64.0	(54.0-69.0) ^a	0.460
Age group							0.384
<65	5	(83.3%)	35	(59.3%)	12	(52.2%)	
≥65	1	(16.7%)	24	(40.7%)	11	(47.8%)	
Age group							0.937
<70	5	(83.3%)	48	(81.4%)	18	(78.3%)	
≥70	1	(16.7%)	11	(18.6%)	5	(21.7%)	
Second op	0	(0.0%)	5	(8.5%)	1	(4.3%)	0.633
Days in hospital	5.5	(5.0-7.3) ^a	5.0	(4.0-7.0) ^a	5.0	(4.0-6.0) ^a	0.674
Side							0.564
Right	4	(66.7%)	35	(59.3%)	11	(47.8%)	
Left	2	(33.3%)	24	(40.7%)	12	(52.2%)	
BMI	24.0	(22.0-26.9) ^a	24.8	(22.6-28.7) ^a	26.0	(22.7-28.3) ^a	0.788
Duration (mo)	96.0	(31.5-129.0) ^a	36.0	(13.0-96.0) ^a	24.0	(7.0-40.0) ^a	0.057
Diagnosis							0.001*
Atypical TN	3	(50.0%)	4	(6.8%)	8	(34.8%)	
Typical TN	3	(50.0%)	55	(93.2%)	15	(65.2%)	
A-loop	1	(16.7%)	36	(61.0%)	9	(39.1%)	0.040**
Adhesion	2	(33.3%)	23	(39.0%)	8	(34.8%)	0.917
Venous compression	2	(33.3%)	10	(16.9%)	8	(34.8%)	0.182
± A-loop							0.413
without A-loop	2	(100.0%)	5	(50.0%)	5	(62.5%)	
with A-loop	0	(0.0%)	5	(50.0%)	3	(37.5%)	
BNI difference	1.5	(1.0-2.0) ^a	3.0	(2.0-3.0) ^a	2.0	(1.0-4.0) ^a	0.045**

A-loop = arterial loop; BMI = body mass index; BNI = Barrow Neurological Institute scale; IQR = interquartile range; op = operation; TN = trigeminal neuralgia.

^aMedian (IQR).

* $p < 0.01$.

** $p < 0.05$.

Table 2**Outcome grouping (n = 88)**

□	BNI score 1–2 (n = 64)		BNI score 3–5 (n = 24)		Total (n = 88)		p
Sex							0.982
Female	38	(59.4%)	15	(62.5%)	53	(60.2%)	
Male	26	(40.6%)	9	(37.5%)	35	(39.8%)	
Age	62.0	(53.0–68.0) ^a	63.5	(52.5–66.8) ^a	62.0	(53.0–68.0) ^a	0.815
Age group							0.877
<65	37	(57.8%)	15	(62.5%)	52	(59.1%)	
≥65	27	(42.2%)	9	(37.5%)	36	(40.9%)	
Age group							1.000
<70	51	(79.7%)	20	(83.3%)	71	(80.7%)	
≥70	13	(20.3%)	4	(16.7%)	17	(19.3%)	
Second op	3	(4.7%)	3	(12.5%)	6	(6.8%)	0.339
Days in hospital	5.0	(4.0–6.0) ^a	6.0	(4.3–9.8) ^a	5.0	(4.0–7.0) ^a	0.102
Side							0.302
Right	39	(60.9%)	11	(45.8%)	50	(56.8%)	
Left	25	(39.1%)	13	(54.2%)	38	(43.2%)	
BMI	24.8	(22.9–28.7) ^a	25.1	(21.5–28.1) ^a	24.75	(22.6–28.5) ^a	0.518
Duration (mo)	36.0	(14.3–96.0) ^a	24.0	(10.5–73.5) ^a	33.00	(12.3–91.5) ^a	0.567
Diagnosis							0.001*
Atypical TN	5	(7.8%)	10	(41.7%)	15	(17.0%)	
Typical TN	59	(92.2%)	14	(58.3%)	73	(83.0%)	
A-loop	37	(57.8%)	9	(37.5%)	46	(52.3%)	0.144
Adhesion	23	(35.9%)	10	(41.7%)	33	(37.5%)	0.805
Venous compression	10	(15.6%)	10	(41.7%)	20	(22.7%)	0.021**
± A-loop							
without A-loop	5	(50.0%)	7	(70.0%)	12	(60.0%)	
with A-loop	5	(50.0%)	3	(30.0%)	8	(40.0%)	

A-loop = arterial loop; BMI = body mass index; BNI = Barrow Neurological Institute scale; IQR = interquartile range; op = operation; TN = trigeminal neuralgia.

^aMedian (IQR).**p* < 0.01.***p* < 0.05.**Table 3****Logistic regression of drug-dependent outcomes (BNI score 3–5)**

□	Univariate			Multivariable		
	Odds ratio	95% CI	<i>p</i>	Odds ratio	95% CI	<i>p</i>
Sex						
Female						
Male	0.88	(0.33–2.30)	0.790	1.17	(0.35–3.93)	0.802
Age	0.99	(0.95–1.03)	0.504	0.97	(0.93–1.02)	0.236
Age group						
<65						
≥65	0.82	(0.31–2.16)	0.691			
Age group						
<70						
≥70	0.78	(0.23–2.70)	0.700			
Second op	2.90	(0.54–15.51)	0.212			
Days in hospital	1.14	(1.01–1.29)	0.035*	1.16	(1.00–1.36)	0.052
Side						
Right	1.84	(0.72–4.75)	0.205			
BMI	0.96	(0.86–1.06)	0.421			
Duration (mo)	1.00	(0.99–1.01)	0.928			
Diagnosis						
Atypical TN						
Typical TN	0.12	(0.03–0.40)	0.001**	0.09	(0.02–0.37)	0.001**
A-loop	0.44	(0.17–1.15)	0.093			
Adhesion	1.27	(0.49–3.32)	0.621			
Venous compression	3.86	(1.34–11.08)	0.012*	5.13	(1.49–17.66)	0.009**
± A-loop						
without A-loop						
with A-loop	0.43	(0.07–2.68)	0.365			

A-loop = arterial loop, TN = trigeminal neuralgia, BNI = Barrow Neurological Institute scale, op = operation, BMI = body mass index.

p* < 0.05.*p* < 0.01.

among patients who were preoperatively diagnosed with typical TN. However, only 33.33% (5/15) of patients diagnosed with atypical TN achieved postoperative drug-free outcomes. This pronounced difference in outcomes suggested that a diagnosis of atypical TN was insufficient to support confidence in surgical interventions. The precise clinical diagnosis of TN is often difficult to achieve. Several anatomical features found in the pain transduction and processing pathway between the trigeminal nerve and the spinal nerve system can serve as the underlying source of jaw pain, and these often present with partially overlapping symptoms.^{3,11} In those cases in which the patient's symptoms are not specific to the TN region, jaw pain should be reassessed to explore the possible contributions of glossopharyngeal neuralgia, myofascial pain dysfunction syndrome, and other potential pain sources, to determine how the scope of invasion overlaps with TN.^{11,16}

The 2019 AAN-EFNS guidelines have reclassified the symptoms associated with atypical TN as a new diagnosis of cervical fascia pain,^{3,10,11} and in 2019, the European Academy of Neurology (EAN) also released updated guidelines for TN. The largest change in the classification guidelines was a change in the previous classification of primary/secondary to the classification of classic/idiopathic/secondary. Primarily TN presents with NVC associated with morphological change (MC), whereas idiopathic TN presents with NVC without MC. However, this classification cannot be used as a diagnostic tool alone. When imaging results show NVC with MC, indicating a diagnosis of classic TN, the new guidelines recommend MVD; by contrast, MVD is not recommended for NVC without MC, which indicates idiopathic TN. However, MVD has been demonstrated to be effective in some patients without MC. TN patients with no NVC are recommended for ablation.³

The preoperative determination of NVC characteristics can be limited by access to equipment, MRI precision, and judgment, depending on the diagnosing physician's experience. No direct and decisive differences in TN presentation have been associated with NVC characteristics, which was reflected by our analysis. In our opinion, improvements in image quality that have occurred over recent years can be used to identify cases of secondary TN and to determine the presence or absence of NVC. The high spatial resolution 3-dimensional (3D) T2 sequences can be used to identify MCs in the trigeminal nerve.^{17,18} The appearance of NVC with MC can provide evidence to support the performance of MVD in a patient with TN; however, our study results indicate that MVD can benefit patients with typical TN with NVC without MC. Therefore, we have reservations regarding the role that preoperative NVC imaging should play in the determination of TN treatment strategies and suggest that the diagnosis of atypical TN represents a better decision-making factor when determining whether to consider MVD surgery.

Our surgical outcomes were generally successful, but the intraoperative identification of arterial loop involvement did not appear to affect the surgical outcome. By contrast, a significant drop in drug-free outcomes, to only 50% (10/20), was associated with the intraoperative identification of venous compression ($p < 0.001$), with or without arterial loop involvement.^{7,9,19-21} The multivariable analysis also showed that venous compression was an independent risk factor of poor outcomes, which differs from the current theory that the primary NVC associated with TN involves an artery complex, indicating that TN is likely associated with multiple causes. The underlying mechanisms that result in TN remain unclear, and other causes may exist, such as those suggested by the ignition theory and resonance theory, which require additional study in the future.^{14,22,23}

Unlike arteries, veins are relatively difficult to shift, and Teflon should be used to fill the space and disassociate the veins from the nerve. In clinical practice, when encountering serious

sticky venous components, we will attempt to open the petrosal fissure to reduce the use of a retractor.^{7,9,22,24} When we encounter only obvious venous compression, our approach in recent years has been to use an angled endoscope to explore the inside of the trigeminal nerve to avoid the incomplete decompression at the dead corner of the trigeminal nerve. Although this approach increases the scope of exposure, it reduces brain traction.^{19,22}

When evaluating TN severity, current popular pain scales, such as the numerical rating scale and visual analog scales, are unable to truly represent the severity and influence of TN, whereas the BNI scale has been shown to be an effective method for TN evaluation.¹²

We analyzed 3 groups of patients according to their preoperative BNI scores, and patients with a preoperative BNI score of 4 experienced the most improvement following MVD ($p = 0.045$). Patients with a preoperative BNI score of 4 were also more likely to be diagnosed with typical TN (93%, 55/59, $p = 0.001$) and were associated with a high proportion of arterial loop involvement in the NVC (61%, 36/59, $p = 0.004$). This result may also be used to remind us the atypical TN patients clinically presents with BNI scores of 3 and 5. In addition to assessing typical TN before treatment, the BNI score can be used to assess the patient's recovery to a certain extent, in addition to providing better classification and understanding of the patient's progress. Despite intuitive assumptions, serious and mild clinical symptoms do not always correlate with disease severity, which is reflected by patients with BNI scores of 3 and 5 and represents a previously unreported phenomenon.

Age is a factor when determining the appropriateness of MVD in many circumstances²⁵; however, our results indicate that age was not associated with any significant differences in outcomes after MVD, even among individuals older than 65 or 70 years. In the absence of obvious contra-indications or serious comorbidities, MVD should be recommended as a typical TN treatment and remains a reasonable choice, regardless of age. In addition to the same improvements in TN symptoms, older individuals may benefit from reduced drug use.²⁵

The first limitation of this study is that no standard preoperative imaging specifications have been established for the diagnosis of TN, although we excluded tumors, vascular lesions, and other potential causes of secondary TN. However, due to the retrospective nature, this study did not apply any unified imaging standard, such as the use of 3D magnetic resonance imaging (MRI). In the future, we will include imaging standards as preoperative diagnostic tools for subsequent NVC-related research.

The second limitation is that to BNI score is not an isometric difference scale. The BNI differences we have proposed may have small statistical flaws; however, according to the clinical manifestations of TN patients, the BNI appears to reflect the patient's current status better than the visual analog scale or other pain assessment methods.

In conclusion, the BNI scoring system is a representative tool for the severity of TN, and our results indicate that the preoperative BNI score could serve as an effective predictive tool for the response to MVD surgery. The reclassification of atypical TN also represents an immediate priority, according to both the latest guidelines and our results. Although the cause of TN remains unclear, our results suggested that venous compression may play an important role.^{7,20,24,26}

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