Original Article

Short- and Long-Term Effectiveness of Keyhole Microvascular Decompression for Trigeminal Neuralgia

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Background: Trigeminal neuralgic pain most commonly occurs after neurovascular conflict and can be treated by microvascular decompression [MVD].

Objective: To discuss the effectiveness of keyhole retromastoid retrosigmoid MVD for pain control both in the short- and long-term.

Materials and Methods: Between 2007 and 2016, 444 patients affected by trigeminal neuralgia [TN] underwent keyhole retromastoid retrosigmoid MVD. All patients had already tried conservative treatment using a variety of medications without effective benefit. Clinical presentation, preoperative imaging results, operative findings (causes of compression), pain outcomes, and recurrence rates were reviewed.

Results: In the early phase, the first keyhole MVD provided excellent outcomes in terms of achieving immediate pain control (436 of 444 patients, 98.19%, $p = 0.000$), while the second (re-)MVD of this group achieved favorable outcomes in only 66.66% of cases ($p = 0.059$). In the long-term group, 89.59% (198 of 221 patients) still reported complete pain remission, but the re-MVD for this group resulted in pain relief for only 38.46% of cases ($p = 0.405$). The number of serious complications found in the present series was very low.

Conclusion: Keyhole MVD is an effective and reliable method of pain relief after TN both in the short- and long-term. Re-MVD in both groups attained less favorable outcomes, but the differences were not statistically significant. Thorough intraoperative exploration of the dorsal root entry zone [DREZ], and meticulous dissection by neurosurgeons are both mandatory to achieve pain relief and reduce the incidence of complications after MVD.

Keywords: Trigeminal neuralgia, Microvascular decompression, Keyhole

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Trigeminal neuralgia [TN] or Tic Douloureux is an extremely severe and debilitating condition. It has been described as one of the most severe chronic hemifacial pains. Characteristically, it is a paroxysmal, excruciating hemifacial pain that occupies the trigeminal division. This peculiar disease can sometimes benefit from spontaneous long remissions, and consequently, it is claimed to be idiopathic in origin. Although the etiology of TN remains uncertain, recent persuasive evidence indicates that it could result from compression of the trigeminal nerve root at or near the trigeminal root entry zone [TREZ]. Although limited to the facial distribution of the trigeminal receptive area, recurrent paroxysm of TN can be stimulated on the so-called "trigger zone", where mere light tactile stimuli, as well as sudden temperature changes or light touch, may trigger pain attacks. This leads patients to avoid any stimulation of the face, and subsequently, to develop anxiety or fear that the pain will return. Therefore, during disease progression, patients can experience difficulty in talking, eating, and even maintaining facial hygiene because of the fear of triggering pain of severe intensity and extended duration.

Despite the devastating effects of TN, the disease is not considered of primary importance, probably because of its lack of immediate life-threatening conditions or deformities, as well as its low prevalence and incidence rates. However, while the prevalence and incidence rates may quantify the burden of the disease, the fact should not be overlooked that certain issues could also increase the hardship caused by the disease; for example, when the incidence rate is low and the duration of the disease is long, or when a change in the duration of the disease can be expected, a negative impact on sufferers' quality of life inevitably results. Regarding the duration of pain, once TN develops, it is likely to have both an exacerbating and remitting course. Temporary remission of the pain may

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occur, but over time, the pain also becomes increasingly medically intractable. It is estimated that 50% or more of patients stop responding to medication and may require surgical intervention for pain relief in the course of the disease.

Other than a destructive procedure by using alcohol injection, percutaneous diathermy of semilunar ganglion has also been used to relieve pain after TN[1]. After the neurovascular conflict hypothesis was established by Gardner and Jannetta[2], the goal of the treatment of TN shifted from simple palliative care by medication to permanent/long-term pain control by microvascular decompression [MVD] in which repositioning the neurovascular conflict was found to offer high success rates in achieving pain-free symptoms.

In Thailand, published studies regarding TN, especially in general hospitals, are scarce. The fact that the study of TN is hampered by inadequate data is possibly due to its treatment being a complex sub-specialty that does not lend itself easily to large clinical trials or studies, and because it can only be properly examined in the hands of experienced surgeons. This, however, could pose a substantial dilemma about the efficacy of available treatments and the clinical equipoise of treatment options for patients with TN. One study attempted to report the prevalence of neuropathic pain at four general hospitals in Thailand, Khon Kaen Hospital, Sapasitthiprasong Hospital, Krabi Hospital, and Phranangklao Hospital, between October 2009 and September 2010[3], but the retrieved data only covered the larger group of pain (neuropathic pain), not specifically focusing on TN and its management.

Hence, the present study was designed to address this issue by examining pain management among patients with TN during the inclusion period, whom were operated by one neurosurgeon to assess perceived pain reduction following keyhole MVD for TN in both the short- and long-term.

Materials and Methods

The present retrospective study was approved by the Rajavithi Hospital Ethics Committee. The data were carried out between January 2007 and November 2016.

Diagnostic criteria for TN were based on the guideline of the International Headache Society [IHS] as followed[4]:

A. At least three attacks of unilateral facial pain fulfilling criteria B and C.

B. Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution.

C. Pain has at least three of the following four characteristics:

1. Recurring in paroxysmal attacks lasting from a fraction of a second to two minutes.
2. Severe intensity.
3. Electric shock-like, shooting, stabbing, or sharp in quality.
4. Precipitated by innocuous stimuli to the affected side of the face.

D. No clinically evident neurological deficit.

Demographic details and medicals records of all patients (n = 452) diagnosed with TN during the inclusion period were retrospectively reviewed, including preoperative magnetic resonance imaging [MRI] imaging results, intraoperative findings, pain relief satisfaction, complications of MVD for TN, and pain recurrence rates.

Using the inclusion and exclusion criteria as shown in Table 1, eight patients were ineligible to enroll into the current study. The criteria listed in this table, which were used to screen the patients selected to participate in the study, were also based on the diagnostic criteria of TN of the IHS to exclude other possible neurological deficits/disorders.

Of the 452 patients, 444 fulfilled all the inclusion criteria and were enrolled. To bring long-term prospective outcomes of MVD for TN into consideration, instead of examining the data in a relatively short follow-up period, the data analysis of the present study covered patients' complete remissions following their initial and late MVDs with a minimum of about 10-year period in the whole series, to ensure a period of more

Table 1. Inclusion and exclusion criteria for patient screening

Inclusion criteria	Exclusion criteria
Diagnosis of typical TN at the time of the inclusion period	Secondary TN due to herpes zoster, multiple sclerosis, intracranial tumors, or intracranial space-occupying lesions[5]
History of TN refractory to medical treatment	
Pain lasting from a few seconds to approximately two minutes, affecting one or more divisions of the trigeminal nerve and fulfilling the diagnostic criteria of TN as stated by International Headache Society [IHS]	

TN = trigeminal neuralgia

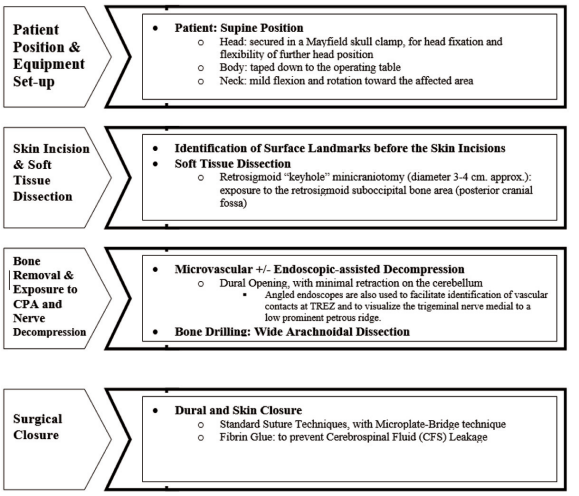


Figure 1. Overview of keyhole MVD.

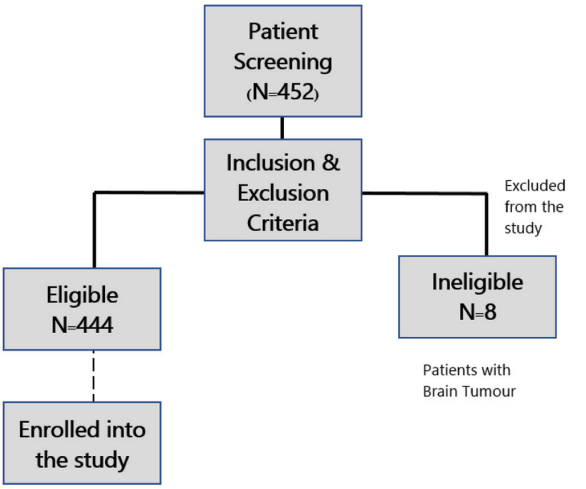


Figure 2. Summary of patient screening (n = 452).

than five years of follow-up among these patients until November 2016.

All MVD for TN in the present study were performed by the same neurosurgeon. Surgical procedures for keyhole retromastoid retrosigmoid MVD are summarized in Figure 1.

It must be noted that MRI of the brain is the cornerstone of preoperative evaluation in all cases and is the most sensitive modality for accurate planning. The identification of brain tumors or neurovascular conflicts not revealed by computer tomographic [CT] may alter the whole preoperative planning. Special techniques and thin-sliced MRI in some cases can reveal the arterial loop that compresses the trigeminal nerve. Extension of the mastoid air cell location of the sigmoid sinus, and low-lying sagittal sinus in some rare cases, will be clearly revealed after MRI. Magnetic resonance angiogram [MRA] can facilitate surgical planning, especially in the large dolichoectatic artery.

Pain relief rating assessment used in the study is outlined in Table 2.

Statistical analysis

Data were analyzed using SPSS software version 11.5. Relationships between the data were analyzed using Chi-square and Fisher's exact test. A difference was considered significant when the *p*-value was less than 0.05.

Results

Data of all patients (n = 452) during the inclusion period, with TN-like presentation were collected. Predominant characteristics were as follows, female gender (female to male ratio of 2:1), age of at least 20 years, with mean age 62 years and 45 years for female and male patients respectively, duration of pain (with longer duration of pain in females), affected side of the face, and distribution of the trigeminal branches (with V1, V2, and V3 to denote the ophthalmic, maxillary, and mandibular divisions of the trigeminal nerve respectively). None of the patients had all 3-branch involvement (V1 + V2 + V3), and all patients had intractable pain because of medical intolerance for TN. Figure 2 presents the overall screening results of eligible patients. Other demographic data of all patients are shown is Table 3.

As previously stated, preoperative MRI of the brain was done in all cases to rule out other abnormalities of the brain resembling TN, comprehensive lesions, or other treatable causes of facial pain, such as brain

Table 2. Description of pain relief rating assessment following MVD for TN

Description	Category: rating
Greater than or equal to 90% pain reduction following MVD for TN during the first week of surgery, without need for medication or further surgical procedure	Excellent
Greater than or equal to 75% pain reduction following MVD for TN during the first week of surgery	Good
Twenty-five percent (or less) pain reduction following MVD for TN during the first week of surgery	Poor/failure

MVD = microvascular decompression; TN = trigeminal neuralgia

Table 3. Demographic data of the patients (n = 452)

Sex, n (%)	
Female	302 (67)
Male	150 (33)
Mean age (years), mean ± SD	
Female	62.00±12.22
Male	45.00±10.34
Preoperative pain duration (months), mean ± SD	
Female	120.50±11.04
Male	46.70±9.72
Affected side (%)	
Female	Right 56%
Male	Right 62%
Pain distribution, n (%)	
Female	
(a) V1 (ophthalmic)	3 (1)
(b) V2 (maxillary)	87 (29)
(c) V3 (mandibular)	59 (20)
(d) V1 + V2	4 (1)
(e) V2 + V3	131 (43)
(f) V1 + V2 + V3	18 (6)
(g) V1 + V3	0 (0)
Male	
(a) V1 (ophthalmic)	1 (1)
(b) V2 (maxillary)	27 (18)
(c) V3 (mandibular)	33 (22)
(d) V1 + V2	3 (2)
(e) V2 + V3	57 (38)
(f) V1 + V2 + V3	29 (19)
(g) V1 + V3	0 (0)

tumors. Though not all eligible patients achieved positive results (vascular compression/contact) in the preoperative MRIs, neurovascular conflicts were confirmed in all operative cases. Neurovascular conflict could be found preoperatively in only 12% (55 of 444 cases).

The results of keyhole MVD in the early phase were very impressive, with nearly all patients getting complete pain relief (n = 436, 98.19%). According to the Table 2, 421 of 436 cases (96.55%) were rated as excellent pain relief, while 15 of 436 cases (3.45%) were rated as good pain relief. After statistical analysis, there was a significant indication (p-value <0.001) that keyhole MVD could alleviate this excruciating pain in most cases. However, eight patients still experienced persistent pain (poor outcome) requiring repeat MVD. In detail, of the eight patients (1.80%) who had persistent hemifacial pain after MVD, seven agreed to undergo repeat surgery. Three of these seven cases resulted from pledgets that were not thick enough to prevent pulsatile pressure of the compressed arteries, and the remaining four were caused by inadequate decompression by the concealed vessels. Of these seven patients that agreed for re-MVD, six (85.71%) attained good outcomes. Four of these six (66.66%) reported complete pain relief without any medication, and the other two cases (33.33%) reported that they had relief from severe pain and were able to cope with it with some painkiller medications (Figure 3). However, after statistical analysis, there was no statistical significance in this re-MVD group (p-value 0.059).

Details of neurovascular conflict were classified as shown in Figure 4.

For ineligible patients (eight cases with brain tumors), there were no treatment delay in removing the tumor, and all patients had complete pain relief immediately after the removal.

Postoperative complications after MVD are shown in Table 4. As with most neurosurgery procedures, most reported complications in the present study consisted of dizziness and nausea, which disappeared a few days after surgery and could have been a result of cerebrospinal fluid [CSF] flow disturbance after posterior fossa exploration. The most serious complication was facial nerve paresis, which could portend further serious neurologic disorders, but in the present study was found to be temporary. The risk of developing rare serious events after MVD for TN in this study was very low, and temporary. Other complications included diminished hearing, complete hearing loss, CSF leakage, CSF

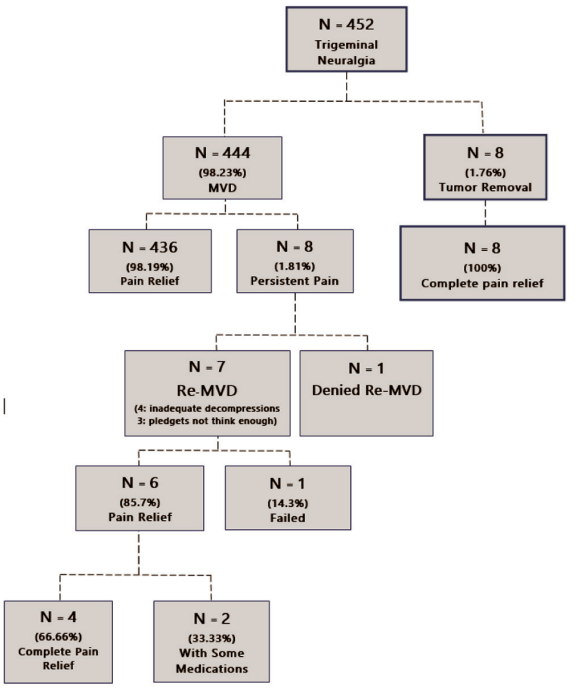
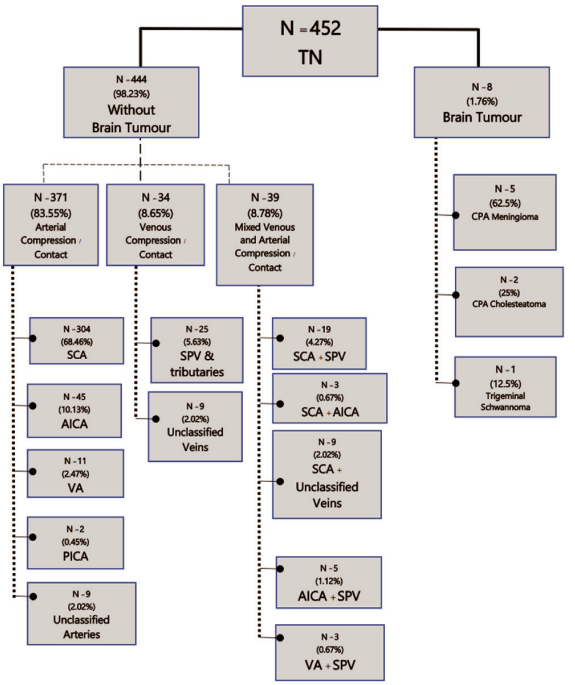


Figure 3. Early post-operative results of MVD (within 3 months after the operation).



AICA, anterior inferior cerebellar artery; CPA, cerebellopontine angle; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; SPV, superior petrosal vein; VA, vertebral artery

Figure 4. Summary of vascular findings and nature of brain tumors.

otorrhea, wound infection, mastoiditis, hemorrhagic cerebellar infarction, aseptic meningitis, and lesser occipital nerve injury. There was no perioperative death. The complications found in this study suggest that keyhole MVD causes the least damage to the patients receiving this surgical treatment, or at least, did not show a deleterious effect.

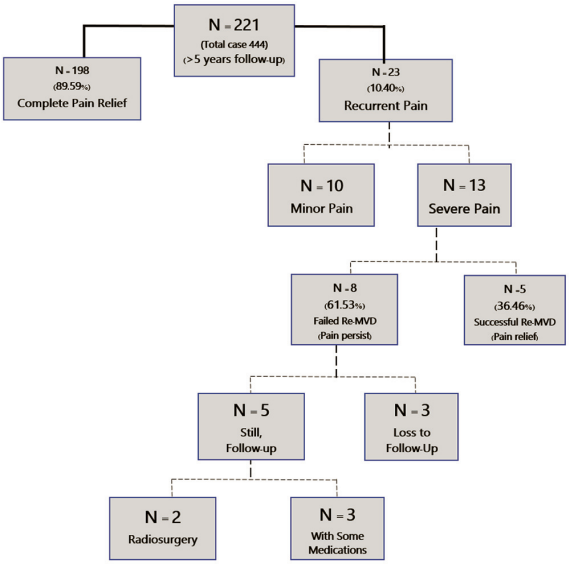


Figure 5. Long-term (>5 years) follow-up (n = 221).

Because long-term follow-up of MVD for TN was an important component of the present study, the patients were monitored for more than five years. Only 221 patients fulfilled long-term follow-up (Figure 5).

As presented in Figure 5, almost all patients in the follow-up period (n = 198, 89.59%) reported prolonged complete pain remission. Twenty-three patients (10.40%) had recurrent pain, and thirteen of these agreed to proceed with repeat MVD because of their severe pain. The outcomes of this late-MVD were less successful

Table 4. Postoperative complications

Complications	Cases, n (%)	Long-term results
Dizziness + nausea + vomiting	325 (71.9)	Improved in all cases within the 14 days after operations
Facial nerve paresis	5 (1.10)	Improved in all cases within 60 days after operations
Diminished hearing	6 (1.32)	Improved in all cases but with partial hearing loss
Complete hearing loss	4 (0.88)	All are permanent
Facial numbness	25 (5.53)	- 15 cases (60%) recover within 90 days after operations - 10 cases (40%) permanent numbness
CSF leakage from wound	4 (0.88)	Improved in all cases after re-operation
CSF otorrhea	1 (0.22)	Improved after re-operation
Wound infection	2 (0.44)	Improved in all cases after medical treatment
Mastoiditis	1 (0.22)	Improved after medical treatment
Hemorrhagic cerebellar infarction	1 (0.22)	Improved after immediate reoperation
Aseptic meningitis	5 (1.10)	Improved in all cases after medical treatment
Lesser occipital nerve injury	12 (2.65)	Permanent numbness

CSF = cerebrospinal fluid

Table 5. Post-operative results: pain relief ratings (n = 444)

Vascular findings: point of contact	Pain relief (%)
Arterial compression/contact (n = 371)	
SCA (n = 304)	98
AICA (n = 45)	100
VA (n = 11)	95
PICA (n = 2)	100
Unclassified arteries (n = 9)	94
Venous compression/contact (n = 34)	
SPV + its tributaries (n = 25)	94
unclassified veins (n = 9)	88
Mixed venous and arterial compression/contact (n = 39)	
SCA + SPV (n = 19)	93
SCA + AICA (n = 3)	96
SCA + unclassified veins (n = 9)	90
AICA + SPV (n = 5)	93
VA + SPV (n = 3)	90

AICA = anterior inferior cerebellar artery; PICA = posterior inferior cerebellar artery; SCA = superior cerebellar artery; SPV = superior petrosal vein; VA = vertebral artery

than those of initial or early intervention, with only five cases (38.46%) improving. The remaining eight cases (61.53%) continued experiencing severe pain and eventually, all of them, decided to seek other treatment modalities such as radiosurgery and painkiller medications. However, there was no statistical significance between the success and failure rates in this long-term re-MVD group (*p*-value 0.405).

Table 5 details the post-operative pain relief ratings of the whole series, with patients rating their pain reduction either as excellent or good.

The effectiveness of each MVD in the early and late groups was compared and is shown in Figure 6.

Discussion

TN (Tic Douloureux) may be the most excruciating pain known to man. Many studies have confirmed that

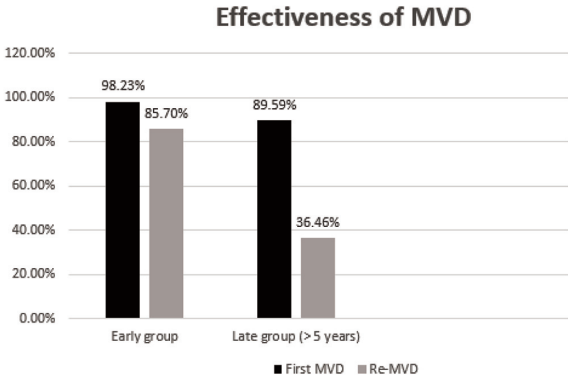


Figure 6. Effectiveness of MVD.

local compression/contact of the trigeminal nerve in the area between the dorsal root entry zone [DREZ] and the Gasserian ganglion leads to hyperactivity of the trigeminal nerve[6,7]. Following the first report of the use of MVD for treatment of TN by Jannetta et al in 1967[2], the role of MVD in the management of TN is now well established and acknowledged to have an effective and long-term effect in pain control for TN. Moreover, MVD is the only surgical means of curing TN without destroying the trigeminal nerve. The goal of the operation is to resolve every neurovascular conflict of the trigeminal nerve. One of the most important factors in the success of MVD is the experience of the surgeon. In the old tradition of MVD, large exposure using long incision (>8 to 10 cm) combined with wide craniectomy (diameter >5 cm) was essential to cure TN with low complication rates. Since the introduction of the keyhole concept, many neurosurgeons have adopted this minimalist concept to their work, and exposure to the neurovascular structures has shifted from large to small exposures. However, MVD is one of the finest and most delicate tasks as neurosurgeons must work in limited space, lateral to the cerebellar hemisphere. The most common obstacle to keyhole exposure for MVD is limited access and scope of maneuverability during dissection and identification of these neurovascular structures, similar to the problems encountered in other keyhole operations. However, once the neurosurgeons gain more experience, they become familiar with working more precisely under limited exposure and can handle the critical neurovascular structures without compromising surgical results. Keyhole retromastoid retrosigmoid approaches can be based on a well-planned small craniectomy as described above. Moreover, this approach can provide access to most of the various posterior fossa explorations including aneurysmal or tumor surgery. However, there are some limitations to this approach. First, in some cases of young patients, the posterior fossa is still tight despite CSF removal. In such cases, the cerebellar hemisphere may be damaged from the pressure exerted by the brain retractor. Second, in cases of accidental tear of the superior petrosal vein or its tributaries, massive bleeding into the posterior fossa may be difficult to control through the limited opening. This problem can be solved by immediate thin-sliced resection of the cerebellar hemisphere. In the author's experience, there have been a few cases of venous injury, but all cases were controlled by the described maneuvers, a small piece of gel foam, and Bioglue®.

In the present study, a large population of trigeminal neuralgic patients (452 cases) were retrospectively reviewed after keyhole retromastoid retrosigmoid MVD. Pain occurred more frequently in the elderly female group with slight right-side predominance. The most commonly affected areas were the maxillary division (V2) and the maxillary-mandibular division (V2 + V3) in the female and male group respectively.

In the present study, all operated (MVD) patients revealed neurovascular conflict despite more than 88% having negative findings from the preoperative MRI. This finding serves as a reminder that preoperative MRI was not helpful in confirming neurovascular conflict of the TN. However, preoperative MRI is still useful for ruling out other causes of TN, especially brain tumors, which require different preoperative planning. It is still mandatory for every trigeminal neuralgic patient to have preoperative MRI before treatment is planned.

Regarding neurovascular conflict, arteries are their most common cause (83.55%), followed by mixed arterial/venous compression (8.78%) and pure venous compression (7.65%). The most common neurovascular conflict is SCA (68.46%).

The overall success rates of the early MVD groups were very high (98.19% and 85.7% for the first and second MVD, respectively) without serious or permanent neurological deficit.

In the long-term study group, keyhole retromastoid retrosigmoid MVD still had good outcomes with 89.59% having complete pain-free periods. However, re-MVD in this long-term group had poor outcomes (38.46%) compared with the early group (85.7%).

The results of the present study correspond with those of many previous studies and showed that MVD is a safe and effective treatment for TN with a high rate of long-term success. The study of Barker second et al confirmed that MVD should be considered for all patients to achieve high rates of long-term success[8]. Oesman and Mooij retrospectively reviewed the long-term results of MVD and concluded that the results of MVD in most patients were good, with no mortalities and no major morbidity[9]. Several other authors have reported similar outcomes of MVD in controlling pain after TN[10-13]. All patients with TN should consider MVD when they are no longer responding to medical treatment or even when they already have had surgery and still have pain.

In the present study, as compared with the others using conventional MVD[14-19], the result of this minimally invasive keyhole technique for MVD were not significantly different. Pain control in both the short- and long-term was excellent, with most patients able to expect pain-free periods without any medication and able to regain their good quality of life immediately after surgery. Moreover, with many great benefits for patients, the keyhole technique without a large incision involves reduced pain, less disruption, speedier healing, excellent cosmetic results, and shorter hospital stay. Furthermore, it is less daunting in the eyes of ordinary people. In terms of complications, results of keyhole MVD are not significantly different from those of conventional means, and surgeon's experience is the most important consideration. Working through a small hole with a narrow corridor requires special training and its success depends on the experience of the surgeon, and the essential specially designed surgical instruments. To achieve similar outcomes in both conventional and keyhole MVDs for newcomer surgeons, matching the complexity of cases with the experience of the surgeon is the key to ensuring the safety of the patients.

Conclusion

Chronic pain can reduce individuals' quality of life due to suffering, failed treatments, medication dependence, limitations of professional, and leisure activities. Keyhole MVD for TN could, to some extent, serve as a guarantee for the patients that TN can be cured or controlled. The present study was clearly in concordance with several previously published studies, reporting similar favorable outcomes of conventional MVD in relieving TN and suggesting MVD as an attractive treatment for eligible patients who expect high rates of long-term pain-free periods and/or a high chance of being permanently off-medication.

The present study represents a significant landmark as it is the first large-scale study to observe keyhole MVD for TN cases in Thailand, and it is one of the very few studies in which long-term favorable outcomes were also evident.

What is already known on this topic?

There have been many previous reports about MVD using a conventional approach (large craniotomy) to evaluate its outcomes and efficacy, but the sampling sizes of most of these studies were usually not large-scale. Furthermore, there have been few studies in MVD for TN that have compared the effectiveness of short- and long-term MVD.

What this study adds?

This was a large-scale study aimed at evaluating

keyhole MVD's effectiveness in both the short- and long-term. The outcomes for pain control were excellent, and although re-MVD had less favorable results, the results were not statistically significant.

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Potential conflicts of interest

The author declare no conflict of interest.

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