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CLINICAL ARTICLE

Surgical treatment of trigeminal neuralgia. Results from the use of glycerol injection, microvascular decompression, and rhizotomia

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Abstract
Purpose The study aims to assess the efficacy and safety of surgical treatment of trigeminal neuralgia (TN) in our department and to identify prognostic factors.
Methods Seventy patients receiving surgical treatment for TN during the period 2003–2004 were included in this retrospective study. The surgical procedures used were glycerol injection (GI), microvascular decompression (MVD), or rhizotomia (RIZ). All patients were divided into spontaneous onset TN type1 (brief lancinating pain) or TN type 2 (continuous pain component). Two patients had bilateral TN; each side was regarded as a separate case. These 70 patients had a total of 160 interventions (110 GI, 40 MVD, and ten RIZ) performed in the period 1998–2007. Data were obtained by chart review and telephone interview. Patients provided information about pre- and postoperative pain characteristics including subtype, duration, intensity, and the use of antiepileptic drugs. Outcome was evaluated using a pain vector diagram.
Results To quantify self-reported pain, we developed a new vector-based pain diagram. The subtype of TN was shown to be a very important prognostic factor. One year after MVD, 90% of patients with type 1 TN still had positive effect, whereas this was only true in 73% of patients with type 2 TN. After RIZ, the results were 71% and 33% for types 1 and 2, respectively. For comparison, GI had a significant lower effect but if the treatment led to hypoesthesia, 41% continued to have a positive effect 1 year after surgery, compared to only 24% if postoperative sensation was normal. Type 2 TN was found to be dominated by women with left-sided TN outside the V2 dermatome and with a lower probability of a neurovascular conflict. As expected, 1/5 of the cases developed postoperative hypoesthesia in the face following a nerve destructive procedure (RIZ and GI). Using MVD, the risk of serious side effects was about 4%. Complementary and alternative treatment had no general or permanent effect in the investigated population—quite the contrary.
Conclusions Regarding prognosis and outcome, we find that it is very important to classify TN in subgroups (types 1 and 2). Dealing with medically treatment-resistant type 1 TN, MVD and RIZ are reasonably safe and effective interventions. The surgical results dealing with type 2 TN are still very poor. All patients with medically treatment-resistant TN should be offered referral to a neurosurgical unit with experience in treating this painful disease. We recommend using a vector-based pain diagram when evaluating the outcome of multiple interventions.

Keywords Trigeminal neuralgia · Tic douloureux · Microvascular decompression · Glycerol injection · Pain

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Introduction

Trigeminal neuralgia (TN) is a debilitating and progressing pain syndrome characterized by recurrent episodes of brief, intense, stereotyped, sharp, electrical, lancinating facial pain attacks, corresponding to one or more divisions of the trigeminal nerve. Most cases are caused by an arterial compression of the trigeminal nerve in the cerebellopontine angle cistern. Pain is commonly evoked by trigger factors (for example, talking or shaving). Most incidences meet the classic criteria with typical spontaneous onset, lancinating bursts of pain alone (type 1) followed by a refractory period where pain cannot be inflicted. Some patients develop a constant burning, dull background pain (type 2) [6, 7]. The majority of patients initially respond well to medication with antiepileptic drugs (AEDs; for example, carbamazepine), often with complete pain relief [2, 8]. However, in approximately a fifth of the patients, the AED seizes to be effective or the necessary dose increment leads to intolerable adverse effects. At our department, three types of surgical treatment of TN are currently used: (1) percutaneous glycerol injection (GI) in ganglion Gasseri by insertion of a neuronavigated needle through the cheek, (2) retromastoid craniectomy and microvascular decompression (MVD) eliminating the neurovascular compression with Teflon pledgets, and if no clear-cut nerve compression is obvious during the MVD procedure, (3) partial sensory rhizotomy (RIZ) of the trigeminal nerve using thermocoagulation is performed. Previous studies have shown that about 75% (63–86%) become permanent free of pain after MVD while the median time to pain recurrence (using the Barrow Neurologic Institute pain scale) is about 5 months after GI [16]. The goals of this quality assurance study have been to (1) evaluate and compare the results of these three surgical procedures carried out at the Neurosurgical Department, Glostrup Hospital in the period 2003–2004, both in terms of efficacy and possible complications, with reports of previous series; (2) identify prognostic factors more likely to be associated with immediate and long-term pain relief in order to optimize the handling of a patient with medically refractory TN; and (3) develop a vector-based pain diagram (PVD), due to the complicated interpretation of pain variations during treatment.

Methods

This study is a retrospective evaluation of 75 consecutive patients surgically treated for TN at the Neurosurgical Department, Glostrup Hospital, Denmark, in 2003 and 2004. Five patients could not be contacted; of these, three had been treated with GI and had died of other causes. Hence, the investigated population was 70 patients, in total 72 treated sides, since two female patients had bilateral TN (non-MS); each side was treated separately in time. All patients met the classic TN criteria according to the International Classification of Headache Disorders. During the study period (2003–2004), 102 interventions were performed (62 GIs, 32 MVDs, and eight RIZs), and a further 58 interventions were performed before and after this time period (1998–2002 and 2005–2007). Data were gathered from hospital charts and by semi-structured telephone interviews, based on a questionnaire with 130 questions. The subjects were interviewed regarding the diagnosis, demographic information, and comorbidity including the presence of other headache types, pre- and postoperative assessment of pain characteristics, information on referral history, use of medication (AEDs), complication frequency, and the use of other treatment modalities. Self-perceived pain intensity was quantified using the verbal numerical rating scale (VNRS), anchored at 0 = "no pain at all" and 10 = "worst possible pain", which has been demonstrated to correlate well with the visual analog scale [17]. Evaluating pain outcome is complicated especially when several treatment modalities are performed consecutively over many years. The patients were asked about number of hours and number of days with pain to make an approximation of the actual pain load. To assess the pain, we developed a pain vector diagram which enables easy visual evaluation of the treatment effect. By plotting VNRS against number of days with pain per month, the monthly pain load was estimated. Drawing a line between pre- and postoperative status, a vector was created that visualized both the pretreatment state and the effect of the treatment (see Fig. 1). We have defined seven outcome groups according to the termination of the vector in the PVD (Table 3).

The net effect was achieved with or without medication—some patients with positive effect continue to use AEDs for fear that the pain would return. In our opinion, a clinical *significant positive effect* was achieved in group/area A–E—allocating the procedure successful. The cumulative proportion of patients with a significant positive effect after surgery was evaluated using the Kaplan–Meier survival method (Table 1). A multivariate logistic regression analysis (Cox proportional hazard method) was carried out to assess the prognostic significance of the following factors: gender, age, TN subtype, development of postoperative hypoesthesia, the surgeon, use of acupuncture, presence of painless intervals, the prevalence of hypertension, weight loss, affected side, arterial compression, and pain score.

Results

Demographic description of the population

Seventy patients completed the telephone interview (93% of the original study population). During the period 1998–2007 (10 years), 160 interventions were performed in the 70 patients (110 GIs, 40 MVDs, and ten RIZs). Thirty-two patients (46%) only had a single procedure performed. Thirty percent of the patients treated with MVD/RIZ had

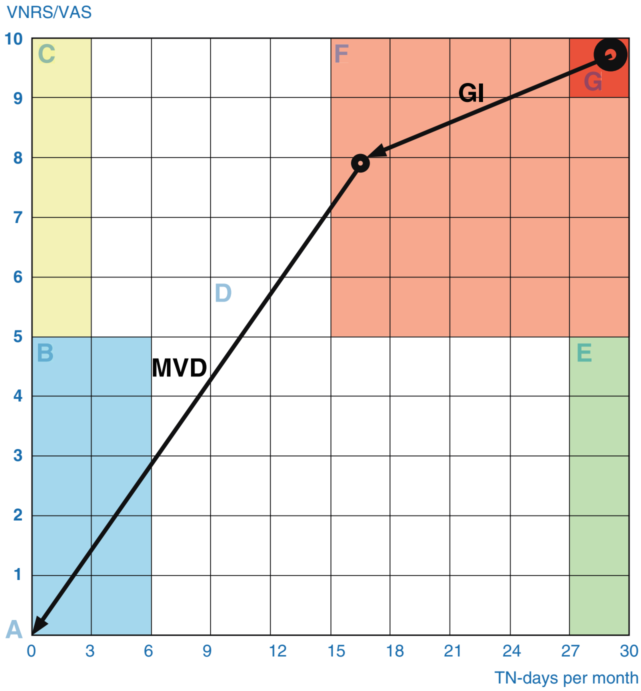

Fig. 1 The pain vector diagram. VNRS plotted against number of days with pain per month. To use the diagram, add one vector for each trigeminal nerve affected. Enlarge start circle in case of many daily attacks. Mark *arrow line* with name of treatment. In the diagram, a case is shown which mainly had reduced frequency of pain attacks after GI but was later cured after MVD. A free copy of the diagram can be downloaded from this website: http://tn.neurokirurgi.info

previously been treated with GI. Gender distribution was equal in all groups except for RIZ (90% women). Patients, who had GI performed, had symptoms for an average of 12 years, MVD and RIZ, respectively, for 9 and 8 years. Most of the patients (69%) were classified as type 1 TN. A comparison of the two TN groups (Table 2) suggested type 2 to be dominated by women with left-sided TN outside the V2 dermatome and with a lower probability of a neuro-vascular conflict.

Outcome

In our opinion, a clinically significant positive effect was achieved in groups/areas A–E (Fig. 1; Table 3)—allocating the procedure as successful. During the interviews, patients in these categories classified themselves as “cured” even though they still experienced rare attacks (C), had a partially pain remnant (B), or a weak dull background pain (E). If there was no change in the pain following the procedure or the pain later recurred (F and G), the incident was registered as a relapse.

Table 2 Comparison of TN type groups

Characteristics	TN 1	TN 2
Female gender** (%)	42	77
Left side affection* (%)	46	71
Age at time of pain debut	57	53
V2 presentation** (%)	38	9
Number of surgical procedures	2.1	2.8
Arterial compression (MVD; %)*	95	50

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

MVD

The Cox analysis revealed that subtype of TN was the most important prognostic factor; patients with TN type 1 had the best outcome ($p=0.03$). Plots of the Kaplan–Meier analysis of outcome over time based on TN type are shown in Fig. 2. In patients with type 1 TN, clinically significant effect of MVD was observed in 90% of patients after 1 year and in 81% after 3 years (see Table 1). In patients with type 2 TN, clinically significant effect of MVD was observed in 73% of patients after 1 year and in 28% after 3 years. The pain alleviating effect of MVD occurred fairly quickly, in most cases momentarily (86%), but for some it could take up to 1 month. Sixty-nine percent discontinued the use of AEDs after MVD.

RIZ

If RIZ was performed, 71% of the patients with type 1 TN still had positive effect 1 year after RIZ, and this effect continued the following years. None of the patients with type 2 TN had a significant positive effect after 2.3 years, and median duration of positive effect ($t_{1/2}$) was about 8 months.

GI

Cox analysis suggests that four factors might predict a better outcome: development of postoperative hypoes-

Table 1 Proportion with significant positive effect depending on TN subtype

Procedure	Type 1 TN				Type 2 TN		
	n	1 year (%)	3 years (%)	$t_{1/2}$	1 years (%)	3 years (%)	$t_{1/2}$
MVD	40	90	81	–	73	28	2 years
RIZ	10	71	71	–	33	0	8 months
GI	110	27	16	3 months	30	14	3 months

Table 3 Outcome groups

A "cured"	Completely free of pain
B "remnant"	Both pain intensity and frequency are reduced to a minimum, pain intensity <VNRS 5 and presentation <7 days/month
C "rare attacks"	Significant reduction in pain frequency with less or no reduction in pain intensity, presentation <3 days/month
D "some effect"	Some pain reduction
E "background pain"	Predominantly reduction in pain intensity with less or no reduction in frequency. This group of patients describes a low-grade chronic ("all month") dull pain most likely representing chronic nerve damage
F "minimal effect"	Limited reduction in both pain intensity and frequency
G "no effect"	No positive effect of treatment at all

Groups A–E correlate with significant clinical positive effect

$PS = VNRS/attack \times number/hour \times TN - hours/day \times TN - days/month$

thesia (p=0.0001), high PS (p=0.02), preoperative loss of weight (p=0.02), and the presence of pain-free intervals (p=0.04). TN type did not influence outcome although presence of pain-free intervals are correlated with type 1 TN. If postoperative hypoesthesia occurred (n=25), 41% still had positive effect 1 year after the injection. Median duration of positive effect ($t_{1/2}$) was 7 months and mean was 11 months (0–3.1 years). Without hypoesthesia (n=85), 24% and 11%, respectively, still had a significant positive effect 1 and 3 years after surgery (median 3 months, mean 7 months), and effect was mainly on pain intensity. The effect was achieved momentarily (71%) or occurred within 1 month of the procedure (98%). In accordance with this, only 30% were able to discontinue the use of AEDs.

Complications

Facial hypoesthesia caused by the treatment was experienced by 89% following RIZ, 20% following GI, and none following MVD. Rare complications after GI were transient facial paresis (3%), pneumonia (3%), corneal anesthesia (2%), stinging tongue sensation (1%), and transient peroperative asystolia (1%). No patients had symptoms of anesthesia dolorosa. Eight patients (16%) had postoperative liquoree after MVD/RIZ which was treated with lumbar drainage; in one patient, mastoid air cells were closed during a new surgical procedure. Regarding significant complications, we included cerebellar infarction or hematoma with permanent disability or death. Three patients had cerebellar complications following MVD: hematoma, infarction, and edema. The patient with a cerebellar hematoma had severe balance and gait problems. The patient with a small cerebellar infarction developed impaired tactile perception in the fingers and balance problems yet in slow recovery. Both cases were regarded as a serious complication (4%). One patient had chemical meningitis following MVD. Six percent had permanent wound problems (for example, chronic irritation, cosmetic scarring, and dysesthesia). The 30-day mortality was 0%.

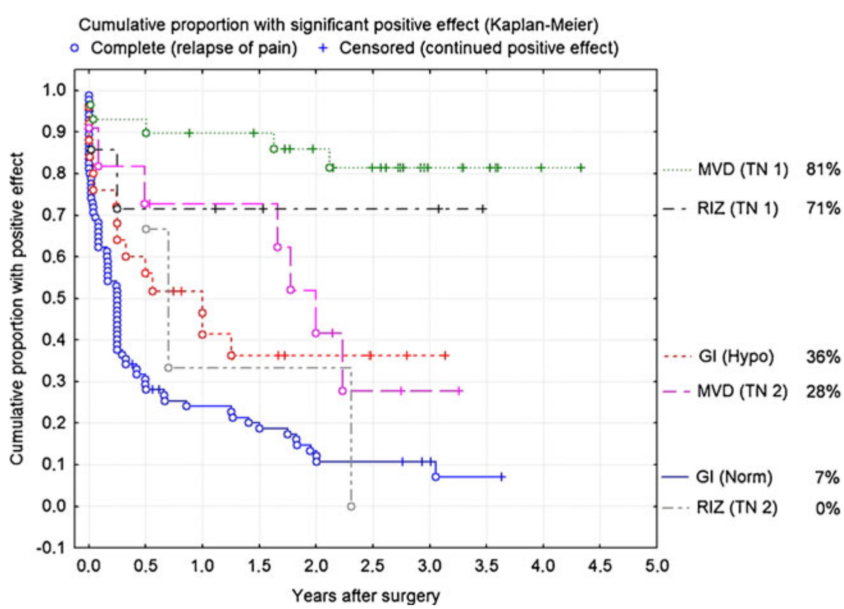

Fig. 2 Plots of the Kaplan–Meier analysis of outcome over time based on TN type. For GI, results are shown both when development of postoperative hypoesthesia occurred (Hypo) and when it did not (Norm)

Complementary and alternative medicine

Most patients had tried other treatments including dental care (43%) and complementary medicine, for example, acupuncture (83%)—but with no permanent effect. Only ten patients (14%) experienced effect for months after acupuncture, while other alternative treatments did not have any effect at all.

Discussion

The concept of a neurovascular conflict as the cause of TN is widely accepted and even extended to other cranial rhizopathies [21]. Even though the pathophysiology is not completely understood, ephaptic conduction caused by segmental demyelination and artificial synapse formation is speculated to be the cause [10, 18]. The superior cerebellar artery is the most frequent offending vessel. Otherwise multiple sclerosis, basilar impression, aneurysm, arteriovenous malformation, atheroscleroses, or natural aging may cause similar demyelination. Even though pain relief through MVD is well documented and is the preferred choice in many cases, there is a renewed interest in percutaneous procedures because of their ease, safety, and low cost [20, 23]. Although these latter procedures contradict modern concepts of non-destructive pain, they might be the preferable choice in cases with high comorbidity. Due to insufficient sustained effect of medical treatment, a substantial number of TN patients are candidates for surgical treatment. Our aim was to study the effect of surgery, in cases refractory to medical therapy. The literature contains several reports on each treatment type; however, direct comparisons between various series are often hindered by different definitions of diagnosis, operative success, different durations of follow-up time, and different observers. For example, exclusion of type 2 TN would inevitably increase the rate of success. Although we cannot exclude the possibility of somatoform pain components, all type 2 patients expressed all classic characteristics of TN according to the internationally accepted criteria. Also uniform outcome measures should be used. Kaplan–Meier actuarial methodology has been recommended as the standard method of reporting pain outcomes for TN [40]. In general, we defined relapse of pain as "return to preoperative pain state", this event corresponds well with areas F and G in the PVD. In our view, the pain perceived by the patient is essential—some patients may not achieve complete pain relief (area A) but might achieve a significant reduction in pain, both in terms of attack frequency and pain intensity. The quality of life for the patients is not only affected by the pain itself but often by the side effects of the medical treatment. Hence, partial pain relief by a surgical procedure often allows reduction or termination of the medical treatment and as a result reduction or complete alleviation of the side effects. In our opinion, such results should be classified as significant positive outcome. Our use of $t_{1/2}$ gives a more stable expression of long-term effect because this parameter is not dependent on the observation time.

MVD

Previous studies have shown that type 1 TN is associated with a better prognosis after MVD [27, 36], while others have claimed that good results can be obtained in surgical treatment of patients with type 2 TN [31]. Other predictors identified include single artery compression and decompression. MVD surgery is known to be especially effective in cases with compression from the superior cerebellar artery [19, 33, 34]. The findings of our study confirm that patients with type 1 TN are more likely to have long-term pain relief after MVD. Greater contribution of type 2 symptoms might be associated with worse outcome because constant rather than lancinating pain may represent more advanced trigeminal nerve damage [7]. Also type 2 pain has been associated with less probability of neurovascular conflict supporting the idea of TN to be a heterogeneous and multifactorial disorder. In accordance with previous publications, we also noticed a marked female representation and left-sidedness in type 2 [26]. These findings might suggest structural gender differences of the posterior fossa (PF) affecting the nearby environment of the trigeminal nerve. Chan et al. [9], using MR volumetric analysis, found both a small PF CSF volume and female gender to be associated with another neurocompressive disease—hemifascial spasm. Other studies have demonstrated females to display greater pain sensitivity partly based on gender-related differences in brain activity [15]. We suggest that a combination of these factors might explain why TN type 2 affect females more than males convergent with many other chronic pain conditions.

MVD does offer certain definitive benefits: The cause is treated and the postoperative pain-relief effect does not depend on the production of a sensory deficit. Our results are comparable with other long-term follow-up studies that found 75% (63–86%) to become permanent free of pain [3, 5, 22, 24, 32, 38, 39, 41]. Prior to surgery, we discussed the possibility of RIZ in case of negative exploration with the patients. The most striking finding in this study is the extremely poor results for type 2 TN; the reason might be an underlying chronic nerve damage which is hardly ever reversible. Consideration of significant prognostic factors is interesting for practical reasons in term of patient selection and surgical management. In our opinion, elderly patients should not be eliminated as candidates for MVD solely on the basis of age [1]. The complication rate in our series is comparable to the reported in the recent literature. In most cases, MVD is a satisfactory, permanent, and non-destructive treatment, but it does carry the potential of serious complications (including death, meningitis, and cerebellar damage). In our study, only 4% had serious complications and none died. Based on more than 3,000 cases in the literature, mortality rate has been found to 0.3% (0–2%). Cranial nerve morbidity has been reported, but generally diplopia, dysphagia, facial weakness, vertigo, and trigeminal hypoesthesia are all reported to be transient. Injury to the acoustic branch of the VIII cranial nerve (loss of hearing) is the only relevant long-term cranial nerve dysfunction reported in several series, ranging from 0.1% to 8%. The risk of cerebellar injury (infarct or hematoma) is estimated to 1%. Cerebrospinal fluid leakage which can be associated with meningitis is seen in 1–12% of cases—commonly treated with lumbar drainage.

GI

Traditionally, GI has been considered as a gentle and inexpensive intervention without significant side effects, but with a shorter duration of effect than MVD [13]. It is thought that glycerol more specifically affects the damaged myelinated axons than normal myelinated axons. The correlation between sensory loss (facial numbness) and duration of pain-free states after percutaneous techniques is well-known [4, 30]. We found the most common side effect (for both GI and RIZ) to be a permanent impaired tactile sensation in the face (deficit CN V) depending on the degree of nerve damage. Fortunately, most patients were rather unaffected by the sensorial deficit—only a very few patients were bothered by the sensory disturbance. In concordance with previous reports, we found the effect of GI to be greater in cases with post operative hypoesthesia, but surprisingly the subtype of TN did not affect outcome. To our knowledge, no investigators have yet evaluated the impact of TN subtype on outcome after RIZ and GI nor have any study defined outcome using a PVD. In our review of factors predictive of pain relief after surgery, we also found "postoperative hypoesthesia", "clinical impression by the surgeon of foraminal perforation during the procedure", and "older age" to be positive predictors of excellent outcome. Before surgery, the patient should be thoroughly informed (in writing) about the possibility of reduced tactile sensation in part of the face and be informed that this is not actually a complication but a side effect which is "desirable" as it provides a good prognosis for the treatment effect. One should also emphasize the possibility of repetition of GIs. Other studies have shown that the effect of GI usually continue at least some months but in some studies up to a year. The calculated half-life of the effect of this procedure based on the Kaplan–Meier method has been reported to be up to 66 months [29]. The literature describes the frequency of hypoesthesia as high as 54% [16]. Another Danish study found a $t_{1/2}$ of 22% [28]. One explanation for the different results includes different selection mechanisms and outcome parameters in the studies.

Comparison with other nerve destructive procedures

Although followed by high initial pain relief, percutaneous radiofrequency thermorhizotomy unfortunately not only has been associated with the greatest number of various complications (especially in inexperienced hands, ranging from death, carotid-cavernous fistula, meningitis, anesthesia dolorosa to transient cranial nerve deficits) but also with high rate of long-term failure [23, 37]. Percutaneous balloon microcompression is considered in the literature to be a safer procedure than other percutaneous surgeries, especially with a low incidence of sensory disturbance (4% with dysesthesia) and is technically easier than radiofrequency thermorhizotomy. But it has the highest rate of postoperative trigeminal motor dysfunction. Skirving and Dan demonstrated clinically significant positive effect in the majority of cases (68%) after 20 years [35]. Stereotactic radiosurgery is associated with the fewest complications compared to those of the other destructive procedures, but it does have a low initial success rate as well as low follow-up pain-free rate [11, 14]. In stereotactic radiosurgery, the initial response is modest, and repeat stereotactic radiosurgery might double the risk of facial numbness [12]. GI offers prompt pain relief but is associated with a shorter duration. Comparing these techniques might render percutaneous balloon microcompression the better choice of procedure in comparison with GI.

Complementary and alternative medicine

Patients in this study all had severe TN (area G in PVD), and unfortunately complementary and alternative medicine did not appear to have any effect in general. Only 14% of the patients experienced some effect for months after acupuncture. Even though a Chinese study [42] found acupoint injection of vitamin B12 to be better that oral administration of carbamazepine proper control groups including sham-needling was absent. A systematic Cochrane review failed to prove any significant effect of acupuncture [25]. Furthermore, if acupuncture had a significant effect, we would expect the treatment to be praised by the patients, and this is not the case according to the national patient association.

Bias

There are two important potential sources of bias in this study: (1) When asked about preoperative pain, patients were asked to recall details of pain they experienced several years previously. Such distant recollection may be inaccurate (recall bias). However, since features of pain are profoundly subjective, we thought that it would be better to obtain information directly from patients rather than from charted material or physician impression and asking all patients the same questions provided uniformity of measurement. A disadvantage of the retrospective study was that many of the patients had multiple interventions, and for some, it was difficult to separate the outcomes of the different interventions. It is possible that recall bias was most pronounced in the patients treated with GI; these patients were about 12 years older than the MVD group. But by comparing the patient's record with the collected information, it was often possible to compensate for this.

(2) The study population consisted only of patients who had undergone surgery, which meant that patients who were not offered the procedures or who refused it were not included. The study thus only deals with medically treatment-resistant cases of TN; hence, the findings should not automatically be used for the more mild cases of TN.

Conclusions

The long-term effects of MVD appear to be superior to any of the ablative therapies. Type of TN pain (type 1 TN versus type 2) is the most significant predictor of good long-term outcome after MVD and RIZ. Application of this information should be helpful in the selection of TN patients likely to benefit from MVD. MVD is a safe and effective method for relieving TN in patients of all ages. It should be proposed as first-choice surgery to all patients affected by severe TN. Preoperative MRI examination in our department is mandatory to exclude nonvascular trigeminal compression but negative MRI could be false—especially when standard MR is performed—and should not deny the patient MVD. Peripheral procedures are usually performed in patients not suitable for or patients, who have been recommended MVD but prefer GI. Some patients want long-term relief of pain at whatever cost, whereas others will accept shorter pain-free periods in return for a lower risk of serious complications. Thus, surgery is not right for everyone, and patients should be informed about their full range of choices.

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Conflicts of interest None.

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