

Surgical treatment of trigeminal neuralgia in adults

Tratamiento quirúrgico de la neuralgia del trigémino en adultos

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Abstract

Trigeminal neuralgia is a painful disorder of the face that negatively affects the functionality of those who suffer from it. Microvascular decompression remains the top choice for its short and long-term outcomes. In those who are not candidates for open surgery, ablative options become valuable, including radiosurgery, and radiofrequency, balloon, and glycerol rhizotomies. Radiosurgery can be useful in cases of trigeminal neuralgia associated with multiple sclerosis. A scheme is proposed to facilitate decision-making considering outcomes, predictors of response and complication rates.

Keywords: Neuralgia. Facial pain. Microvascular decompression. Radiofrequency. Rhizotomy.

Resumen

La neuralgia del trigémino es un desorden doloroso de la cara que afecta de forma negativa la funcionalidad de quienes lo padecen. La descompresión microvascular sigue siendo la mejor opción por sus desenlaces a corto y largo plazo. En aquellos no candidatos a cirugía abierta cobran valor las opciones ablativas, entre ellas la radiocirugía, y las rizotomías por radiofrecuencia, balón y glicerol. La radiocirugía puede ser útil en casos de neuralgia del trigémino asociada a esclerosis múltiple. Se propone un esquema para facilitar la toma de decisiones, considerando predictores de respuesta y tasas de complicaciones.

Palabras clave: Neuralgia. Dolor facial. Descompresión microvascular. Radiofrecuencia. Rizotomía.

Introduction

According to the International Classification of Headache Disorders (ICHD-3)¹, trigeminal neuralgia (TN) is characterized by recurrent, brief, unilateral, electric shock-like pain with abrupt onset and end, limited to the distribution of one or more divisions of the trigeminal nerve, and can be triggered by an innocuous stimulus (Table 1). Burchiel's classification² considers two forms of facial pain: typical and atypical. In the typical form there are type 1 TN (> 50% of the pain is

episodic and typical) and type 2 TN (pain > 50% constant and typical). Atypical forms include trigeminal neuropathic pain (secondary to dental or sinus injury, or trauma), trigeminal deafferentation pain or painful anesthesia, symptomatic TN, postherpetic neuralgia, and atypical facial pain as a somatoform disorder. Drug treatment is the first-line therapy for TN, but patients with resistant pain or intolerance to drugs are candidates for surgical management. Surgery can be divided into two groups: non-destructive procedures, such as microvascular nerve decompression (MVD),

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Table 1. Diagnostic criteria for trigeminal neuralgia

- Paroxysmal and recurrent unilateral facial pain in the distribution of one or more divisions of the trigeminal nerve, without radiation to other nerve distributions and meeting criteria B and C.
- The pain must have all of the following characteristics:
 - Lasts from a fraction of a second to 2 minutes.
 - Be of serious intensity.
 - Be of the electric shock, shot, piercing or lancing type.
- Be precipitated by an innocuous stimulus within the affected trigeminal distribution.
- Not be explained by another ICHD-3 diagnosis.

Adapted from Vincent M. et al.¹**Table 2. Barrow neurological institute pain intensity classification tool**

Clasificación	Definición
I	No pain, no medication required
II	Occasional pain, does not require medication
IIIa	No pain, completely controlled with medication
IIIb	Some pain, can be adequately controlled with medication
IV	Some pain, cannot be adequately controlled with medication
V	Severe pain, no pain relief

Adapted from Rogers CL et al.³

and destructive procedures, in which an injury is generated either by radiation, thermal, chemical or physical. In measuring outcomes, one of the key variables is pain control, being the pain intensity classification tool of the Barrow Neurological Institute (BNI) (Table 2)³ the most used.

In this review, the outcomes of the different surgical treatment modalities are discussed to determine the rate of pain control and recurrence, as well as complications, in order to establish an individualized surgical therapeutic proposal according to the characteristics of pain and surgical risk.

Non-destructive surgical treatment: microvascular decompression

In patients refractory to pharmacological management with conflict between the trigeminal nerve and cerebral vessels, DMV is the first line surgical treatment. It is a non-ablative⁴ microsurgical procedure in which, through a retrosigmoid approach, the trigeminal nerve is identified and its relationships in the cerebellopontine cistern (Fig. 1) are explored in search of

compressions, very frequently by the superior cerebellar artery, although they can also be of venous origin, such as the superior petrosal vein complex. Initial pain control is variable in VMD, from 80% to 96%⁵⁻⁷. In a meta-analysis with 3897 patients, the rates and predictors of pain freedom were investigated. It was found that 76% remain free of pain in an average follow-up of 1.7 years, and as predictors the duration of the condition ≤ 5 years, compression by the superior cerebellar artery and having a Burchiel type 1 classification were identified⁸. The outcomes of immediate and long-term pain control in patients with atypical TN treated with VMD show that 91.8% of patients experienced complete pain relief, compared with 93% in those with classic TN, but with 60.3% recurrence in atypical cases in an average of 20.6 months⁹. Much later outcomes (8 to 15 years) report freedom from pain in 70%^{10,11}. Patients with episodic pain have higher pain freedom rates than their persistent pain counterparts; the latter, in the short term reaches 77% control¹². In cases of bilateral pain, a less frequent subgroup, the option is to perform DMV on the more symptomatic side and in a second stage proceed with the opposite side. Zhao et al.¹³ have reported their experience in the management of 13 patients with bilateral TN, of whom 11 achieved an excellent outcome, 3 experienced improvement on the opposite side, and 9 underwent a second stage of surgery. Age is a relevant factor, since TN in children under 30 years of age is infrequent and there is very little evidence on surgical treatment in this age group; however, in this context the DMV is a useful option¹⁴, as well as for older adult patients, who compared to younger ones have significantly better long-term outcomes¹⁵. It is known that in TN the nerve suffers atrophy, with potential repercussions on the outcomes; in patients with proximal nerve atrophy it is associated with vascular compression and is correlated with better outcomes after MVD, but in cases of distal atrophy it is associated with significantly worse outcomes¹⁶.

After MVD, a decrease in the burden of disease in patients has been shown by reducing productivity losses related to pain, and less use of health resources. 68%, at 4.27 years of follow-up, had a BNI ≤ 2 and 62% do not report limitations in their work activities¹⁷. In cases of symptomatic TN, inferior outcomes have been observed, particularly in cases of multiple sclerosis¹⁸ in other much less frequent circumstances, such as Chiari malformation type I¹⁹ or Charcot-Marie-Tooth²⁰, disease, DMV has been the option that has best resulted in pain control. Even in case of persistence or recurrence of TN after MVD, repeat MVD can offer a good outcome;

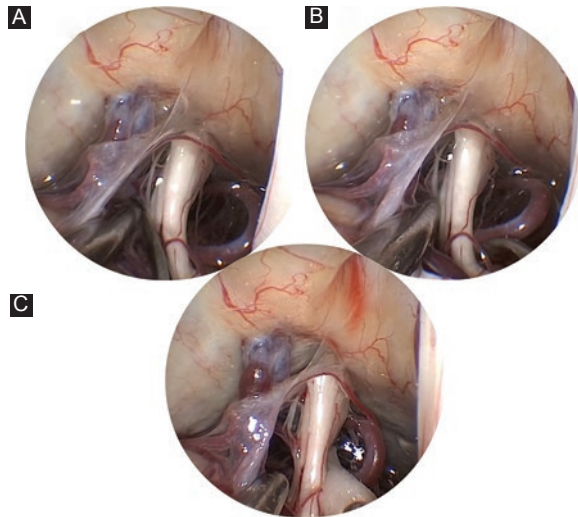


Figure 1. Endoscopic view of the cerebellopontine angle during a retrosigmoid approach to perform microvascular decompression of the fifth nerve. **A:** the angle is explored once the arachnoid dissection has been completed, identifying a loop of the superior cerebellar artery contacting the medial and proximal aspect of the cisternal portion of the nerve. With microdissectors the loop is mobilized. **B:** teflon is placed between the vascular loop and the nerve. **C:** removing the contact.

a negative intraoperative finding at reintervention and no improvement after the initial surgery are prognostic factors for an unfavorable outcome in this circumstance²¹. Some authors recommend that intraoperative neurolysis be performed during reintervention, especially in cases in which the persistence of compression or distortion of the nerve is not documented²².

Despite the invasiveness of MVD, with trained surgeons complications can be < 4%²³. Probably the most reported complication is facial numbness (5.5-14%), followed by facial dysesthesia (5.3-5.7)^{24,25} and mild hearing problems (around 2.7%)²⁶. Fortunately, the more serious complications are less frequent (< 3%), such as cranial nerve injuries, hearing loss, cerebrospinal fluid fistula and infections^{24,27,28}; intraoperative or postoperative bleeding has also been reported²⁹. Mortality is very low (0-0.4%)^{9,28,30}.

Destructive surgical treatment

Radiation injury (radiosurgery)

This option is of interest in patients with refractoriness, but in whom it is not considered that there is a neurovascular conflict, or who is not a candidate for an open procedure, or because the patient prefers it. Stereotactic radiosurgery has a destructive

effect on ion channels, blocking conduction in the irradiated structure, particularly in low caliber unmyelinated nociceptive fibers³¹. The radiation dose is 60 to 90 Gy; higher doses do not increase efficacy, but rather the probability of adverse events. The currently selected target site is the intracisternal portion of the nerve, which maintains efficacy with fewer complications. Radiosurgery can be performed by linear accelerator (LINAC), by Gamma Knife (GK) or by Cyber Knife (CK).

In the practical guide of the International Society for Stereotactic Radiosurgery published in 2018³² pain freedom with or without medication is reported for GK, LINAC and CK of 84.8%, 87.3% and 79.3%, respectively. There are no significant differences between the modalities. The time to achieve pain relief is 15 to 78 days with GK and 28 to 81 days with LINAC; for methodological reasons, in the CK studies it was not possible to establish the average time. Facial hypoesthesia was reported in an average of 21.7% for GK, 27.6% for LINAC, and 29.1% for CK. Other less frequent complications include paresthesias, deafferentation pain, dry eye, and keratitis. The recurrence frequency for GK was 24.6%, for LINAC 32.2%, and for CK 25.8%, with mean times to recurrence of 6-48 months for GK and 7.5-20.4 months for LINAC; Only one study reported the time to recurrence in those treated with CK, being 9 months.

Patra et al.³³ evaluated the management of recurrence cases in patients initially treated with GK, comparing repeat GK versus MVD. Adequate pain control was achieved in 83% with repeat GK and 88% with VMD, and complete pain control in 46% in the repeat GK group and 72% in VMD, without significant differences between the groups, so it is not possible to identify superiority of one modality over another; however, after a failed GK the DMV option could be considered. The effect of a third GK session has also been evaluated, finding a reduction in pain with a low additive risk of complications, so it may be an option for the elderly who are not candidates for a microsurgical or percutaneous procedure³⁴. It should be taken into account that accumulating doses > 115 Gy are associated with the appearance of effects derived from radiation, in addition to hypoesthesia and facial numbness³².

Thermal injury (radiofrequency rhizolysis)

Radio frequency can be generated continuously (RFC), in pulses (RFP) or combined (RFCC). In the case of RFC, friction and vibration produce heat, leading to

Table 3. Success rates and complications for surgical treatment options for trigeminal neuralgia

Option	Initial response rate (%)	Long-term response rate (%)	Response predictors	Complications (%)
MVD	80-96	1 a: 84 5 a: 72-85 10 a: 74	Positive: Type I, arterial compression, trigger points, short evolution Negative: Bilateral pain, associated with MS, type II	NC V: 1.6-22 NC VII: 0.6-10.6 NC VIII: 1.2-6.8 Painful anesthesia: 0-4 CSF fistula: 1.5-4 Mortality: < 0.8
RRF	97.6-99	1 a: 61.8 5 a: 57.7 10 a: 52.3 20 a: 41	Positive Type I Negative: Bilateral symptoms	NC V: 3.3 ↓ corneal sensitivity: 5.7-17.3 Keratitis: 0.6-1.9 Painful anesthesia: 0.6 - 0.8
RG	71-97.9	1 a: 53-63 5 a: 43.5	Positive: High BNI score, POP hypoesthesia, pain-free intervals Negative: ≥ 3 previous PGR	CN V: 23.3-72 ↓ corneal sensitivity: 6.3-15 NC VIII: 1.9 Aseptic meningitis: 0.12-3 Bacterial meningitis: 1.5-1.7
RB	82-93.8	1 a: 74.6 5 a: 69-80 10 a: 68.1	ND	NC V: 4.6-40 ↓ corneal sensitivity: 0-3.1 NC VIII: 2.4-6.3 Aseptic meningitis: 0.7 Bacterial meningitis: 0.7-1
ROSC	79-91.8 (late 10 d a 3.4 m)	1 a: 75-90 5 a: 44-65 10 a: 30-51.5	Positive: Early response, no prior treatment, response to medication, facial numbness	NC V: 6-42 Painful anesthesia: 0.2

a: years; BNI: Barrow Neurological Institute Pain Intensity Classification Tool; d: days; MVD: microvascular decompression; MS: multiple sclerosis; CSF: cerebrospinal fluid; m: months; NC: cranial nerve; ND: no data; PGR: percutaneous glycerol rhizotomy; POP: postoperative; RB: balloon rhizolysis; ROSC: stereotactic radiosurgery; RG: rhizolysis by glycerol; RRF: radiofrequency rhizolysis.

Adapted from Bick SKB et al.⁴⁵

thermocoagulation, protein denaturation, and necrosis in the target tissue. In the RFP a lower temperature is used and the energy is transmitted in the form of pulses. Wu et al.³⁵ evaluated 34 studies with a total of 3558 patients to determine the effectiveness and safety of radiofrequency modalities in typical TN, and found that the cure rates with RFP and RFC were not significantly different, but RFC It is more effective than the RFCC. There are no significant differences between RFP and RFC in terms of complications. Reported complications were painful anesthesia (0.6-0.8%), masseter muscle weakness (4%), and facial numbness³⁴. Up to 17% of patients experience decreased corneal sensation, reaching a rate of 2% progression to keratitis³⁶.

Chemical injury (rhizolysis with glycerol)

There is no clarity on how glycerol rhizolysis works. It is known that absolute ethanol has destructive effects on myelinated or non-myelinated fibers, and for this reason it is hypothesized that since ephaptic conduction

can cause episodes of pain, nerve injury with glycerol could cause the aberrant stimulation to disappear³⁷. Glycerol rhizolysis can be performed percutaneously or openly under microscopic vision. A duration of effect of 11 months has been reported²³. Unfortunately, to date there are no randomized studies that make it possible to establish recommendations with high-quality evidence. A success rate of 92.1% has been reported in 179 patients³⁸; the mean reinjection time was 23 months, mostly multiple sclerosis cases. The frequency of injections was not found to be associated with an increased likelihood of complications. The authors recommend considering this technique in older adults. In measuring long-term outcomes (average 13.1 years) in 3,370 patients treated between 1983 and 2003, it was reported that 99.5% experienced complete resolution of pain after the first procedure³⁶. The frequency of recurrence varied by year of follow-up: 0.3% at the first, 21% between 1 and 5 years, 7% between 5 and 10 years, 4% between 10 and 15 years, and 3% between 15 and 23 years. The main reported complication was facial numbness; there

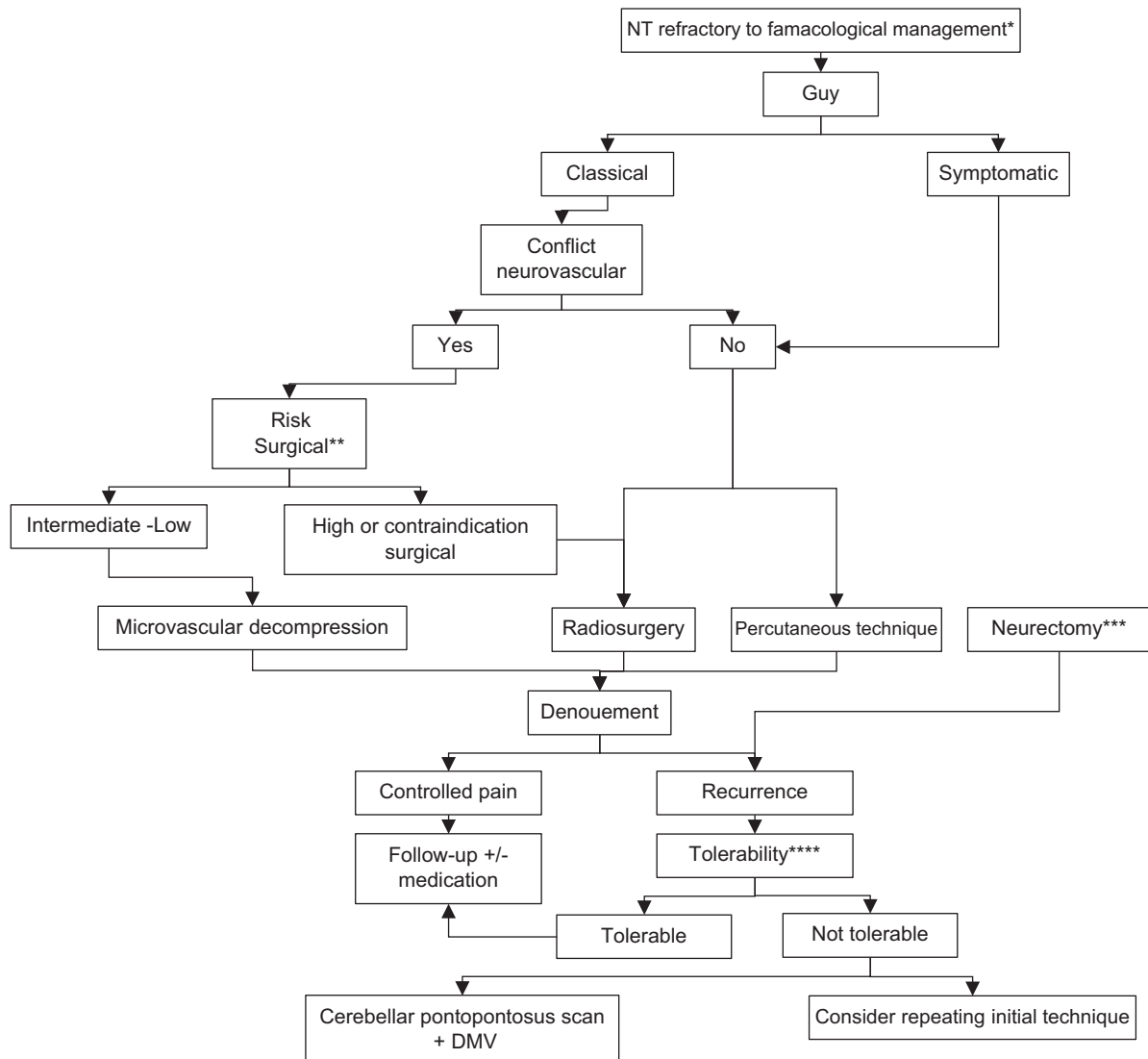


Figure 2. Diagram of the surgical management of adult patients with trigeminal neuralgia.

*And/or the patient does not tolerate the pharmacological treatment due to adverse effects.

**If the patient is at high surgical risk or is contraindicated for a major surgical procedure (eg, anticoagulation or antiplatelet therapy), it is preferable to offer radiosurgery or a percutaneous modality.

***It should not be considered first or second line treatment.

****Assess the degree of pain control in the patient (whether or not it allows them to continue with their usual activities).

were no cases of painful anesthesia or mortality. Short-term complications include transient facial hypoesthesia (97%), followed by nausea/vomiting (9.6%) and less frequently (< 1%) corectasia, paresis of the trigeminal-innervated muscles, infections, hemorrhages, and optic nerve injury. Patients with involvement of the third branch of the nerve have worse outcomes than those with involvement of the others (pain control in 40% and 90%, respectively)³⁹. When comparing the effectiveness of rhizolysis by glycerol and thermofrequency in patients with TN and multiple sclerosis and in those

with typical TN, in 822 patients, between 1998 and 2010, it was found that after 15 sessions with glycerol, 68% and 67% of the patients with multiple sclerosis and with typical TN, respectively, were free of pain and without medication⁴⁰.

Physical injury (balloon rhizolysis, neurectomy)

In balloon rhizolysis, an initial response rate of up to 94% is reported, but with recurrence at one year of

25% and in the long term of 69%⁴¹. When rhizolysis by balloon is repeated, or as a second-line modality after a previous different treatment, 93% of patients can experience immediate pain relief, with recurrence of 16% at 2 years and 40% at 5 years⁴². When used as a second line after VMD, 96% of patients have immediate pain relief without medication and 13.5% resort to an average of 38 months⁴³. Complications include facial numbness (98%, the highest frequency among all modalities), masseter muscle weakness (59%), paresthesias (9%), and diplopia due to sixth nerve injury (< 2%)⁴³.

Neurectomy involves partial avulsion of distal branches of the trigeminal nerve, often the inferior alveolar nerve, and has been used less as an option. The vast majority of studies on this modality have small samples and are followed for very short periods of time. In a review of 7,913 patients from a conglomerate of 43 research articles, it was evidenced that neurectomy is associated with low-quality pain relief, offering control in the short and medium term⁴⁴. Neurectomy should not be considered as a first-line therapeutic option.

Surgical decision-making in patients with trigeminal neuralgia: final considerations

Table 3 summarizes the initial and long-term response rates, the predictors, and the complications of the exposed therapeutic modalities⁴⁵. Figure 2 shows the exposed management scheme. After establishing the refractoriness and the type of TN, the BNI and the impact on the quality of life are determined. If a neurovascular conflict is demonstrated, the best entry option is MVD, unless the patient is at high surgical risk or has explicit contraindications for the procedure. If MVD cannot be performed, the next option is destructive procedures, considering stereotactic radiosurgery in the first instance and using the best available technique (GK or LINAC). Among the percutaneous modalities, the first option is radiofrequency rhizolysis. As has been shown, the outcomes with TN peripheral neurectomy are not favorable, so it is not considered as a first or second line surgical option. If refractoriness is demonstrated, it is recommended to evaluate its impact; if the pain is tolerable or manageable with medication, the option proposed is follow-up (conservative management), and in the case of severe pain or pain that limits the patient in his daily life, it is recommended to try to repeat the technique used or perform an exploration of the angle pontocerebellar and determine if MVD is feasible (of course, if the patient has no surgical contraindications).

Conclusions

Refractory TN remains a condition whose management is a considerable challenge; many elements remain to be understood about its pathophysiology and, consequently, about the way to treat it. MVD continues to be the reference surgical option for both first and second line (in cases of recurrence). Destructive modalities can be considered in those patients who are at high risk of operative complications due to comorbidity or pharmacological conditions such as anticoagulation. It is necessary to go deeper into neurosurgical outcomes, which is why studies of high statistical value are required.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were carried out on humans or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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