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# EVIDENCE BASED MEDICINE

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## 1. Trigeminal Neuralgia

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■ **Abstract:** Trigeminal neuralgia is a common cause of facial pain. It has a significant impact on the quality of life and the socioeconomic functioning of the patient. The aim of this review is to provide recommendations for medical management of trigeminal neuralgia based on current evidence. Based upon the analyses of the literature combined with experience in pain management, symptoms, assessment, differential diagnosis, and treatment possibilities of trigeminal neuralgia are described and discussed. Recommendations for pain management are given and are displayed in a clinical practice algorithm. Treatment should be multidisciplinary. Various treatment options and their risks should be discussed with the patient. The first treatment of choice is carbamazepine or oxcarbazepine. In younger patients, the first choice of invasive treatment is probably microvascular decompression. For elderly patients,

radiofrequency treatment of Gasserian ganglion is recommended and the technique is described in detail. ■

**Key Words:** trigeminal neuralgia, evidence-based guidelines, radiofrequency treatment, pain management, interventional treatment

### INTRODUCTION

This paper is the first in a series of practical guidelines for pain management to be published in the Evidence Based Practice section of *Pain Practice*. It includes peer-reviewed literature through November 2008.

“Trigeminal Neuralgia is the worst pain in the world,” declared Peter J. Jannetta, MD in “*Striking Back!*”, a layman’s guide for facial pain patients.<sup>1</sup> Trigeminal neuralgia, or “Tic Doloureux”, is a painful condition of the face. This pain has been known since ancient times; there are descriptions of facial pain by Ibn Sina (980–1073) in an Arabic text. An example of early interventional treatment is that by Locke in 1677, who applied sulphuric acid to the face of the Duchess of Northumberland in an attempt to treat her trigeminal neuralgia.

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A survey conducted in 6 European countries indicated that trigeminal neuralgia significantly impacted the quality of life and the socioeconomic functioning of affected patients.<sup>2</sup> Trigeminal neuralgia is the most common form of facial pain in people older than 50 years of age. Various epidemiological studies have shown the annual incidence to be about 4–5 new patients per 100,000. The highest incidence occurs in the ages between 50 and 70 years; in 90% of the cases the symptoms begin after the age of 40 years. Trigeminal neuralgia is more prevalent in women than men with a ratio of 1.5:1.<sup>3</sup>

The pathophysiology is unclear. Based on clinical observations, compression of the trigeminal nerve near the origin of the brain stem, the so-called root entry zone, by blood vessels or tumor, may cause trigeminal neuralgia. Local pressure causes demyelination that leads to abnormal depolarization resulting in ectopic impulses.

### SYMPTOMS

Trigeminal neuralgia is recognized by unilateral short-lived, strong, sharp, shooting pains in 1 or more branches of the fifth cranial nerve. The description of the pain is very important; it must be sharp, shooting, lancinating, and “electric shock”. The pain can be brought on by ordinary stimuli, such as eating, washing, shaving, cold, warmth, and draught. The distribution of the pain in the various branches of the trigeminal nerve is given in Table 1.

In the case history, 6 questions should be asked:

1. Does the pain occur in attacks?
2. Are most of the attacks of short duration (seconds to minutes)?
3. Do you sometimes have extremely short attacks?
4. Are the attacks unilateral?
5. Do the attacks occur in the region of the trigeminal nerve?
6. Are there unilateral autonomic symptoms?

**Table 1. Pain Distribution in the Various Nerve Branches in Trigeminal Neuralgia**

V1 only	4%
V2 only	17%
V3 only	15%
V2 + V3	32%
V1 + V2	14%
V1 + V2 + V3	17%

See Rozen.<sup>3</sup>

In this way, a differential diagnosis can be made relatively quickly and an impression can be formed of whether it is essential trigeminal neuralgia.

### PHYSICAL EXAMINATION

Neurological examination seldom reveals any abnormalities in patients with idiopathic trigeminal neuralgia, but all cranial nerves do need to be tested. Patients who have neurological disorders often have a so-called secondary trigeminal neuralgia whereby the trigeminal neuralgia is a symptom of another disease, eg, tumor of the cerebellopontine angle or multiple sclerosis.

### ADDITIONAL TEST

When the diagnosis of trigeminal neuralgia is made, the patient needs to undergo a magnetic resonance imaging (MRI) scan to exclude specific pathologies such as a tumor or multiple sclerosis, which could cause a secondary trigeminal neuralgia. The MRI scan can also be used if there is a suspected compression of the trigeminal nerve in the posterior cranial fossa. Sometimes the MRI scan is sensitive enough to detect blood vessels that have come in contact with the trigeminal nerve. The role of venous compression in the pathogenesis of trigeminal neuralgia is controversial.<sup>4,5</sup> Notably, on MRI scanning, compressing blood vessels are seen in one-third of asymptomatic patients. A recent evidence-based review concluded that there is insufficient evidence to support or deny the usefulness of MRI to identify neurovascular compression.<sup>6</sup>

### DIFFERENTIAL DIAGNOSIS

Less frequently trigeminal neuralgia is seen in younger patients. It is important that multiple sclerosis always be considered in the differential diagnosis, especially in bilateral cases. The International Headache Society described the following criteria for essential trigeminal neuralgia.<sup>7</sup>

- A. Paroxysmal pain that lasts from a fraction of a second to 2 minutes, occurring in 1 or more branches of the trigeminal nerve, and fulfilling criteria B and C.
  - 1 —intense, sharp, superficial or stabbing.
  - 2 —precipitated from trigger areas or by trigger factors.
- C. The attacks are stereotypically described by the patient.

**Table 2. Trigeminal Neuralgia: Clinical Diagnostic Criteria**

Characteristic	Description
Character	Shooting, like an electric shock, stabbing, superficial
Seriousness	Moderate to very intense
Duration	Each pain attack lasts seconds but a number of different attacks can occur simultaneously after which there is a pain free interval
Periodicity	Periods of weeks to months without pain
Location	Distribution of T. neuralgia, mainly unilateral
Emanation	Within the area of the trigeminal nerve
Trigger factors	Light touching, such as when eating, talking or washing
Alleviating factors	Frequent sleep, anti-epileptics
Accompanying characteristics	Trigger zones, weight loss, poor quality of life, depression

- D. There are no signs of neurological disorders.
- E. The attacks are not caused by other disorders.

The International Headache Society have suggested their own diagnostic criteria for trigeminal neuralgia (Table 2).<sup>8</sup> The differential diagnosis of essential trigeminal neuralgia is extensive and involves all unilateral pain in the pathway of the trigeminal nerve. The most important differential diagnostic considerations are specific facial pain, nonspecific facial pain, temporomandibular arthrosis, dental disorders, and vascular migraine. A detailed overview of the differential diagnosis of facial pain can be found in Table 3.<sup>9</sup>

### TREATMENT OPTIONS

#### Conservative Treatments

The selection of the pharmacological treatment is based on a systematic review of data of relatively older studies<sup>10</sup> or on a more up-to-date Cochrane database.<sup>11</sup> The medication of choice is carbamazepine. From an observational study, it appears that carbamazepine can reduce the pain symptoms in about 70% of the cases. Oxcarbazepine has shown similar efficacy.<sup>6</sup> Other medications that can be tried, although there is no clinical evidence for their efficacy, are gabapentin, pregabalin, and baclofen. Rozen summarized the recommendations for the medical treatment of trigeminal neuralgia in Table 4.<sup>3</sup>

#### Interventional Treatments

If the medical treatment is unsuccessful or has too many side effects, an invasive treatment can be carried out. In this case, there are currently 5 clinically appropriate possibilities:

**Table 3. Differential Diagnosis of Trigeminal Neuralgia**

Indicate answer with a ✓ for the following afflictions	Does the Pain Occur in Attacks?		Are Most of the Attacks of a Short Duration (Seconds to Minutes)?		Do You Sometimes Have Ultra Short attacks?		Are the Attacks Unilateral?		Do the Attacks Occur in the Region of the Trigeminal Nerve?		Are There Unilateral Autonomous Symptoms?	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
• Musculoskeletal	✓											
• Dentoalveolar	✓											
• Ear, Nose and Throat	✓											
• Giant cell arthritis	✓											
• Glaucoma												
• Cluster headaches												
• Atypical migraine												
• Chronic paroxysmal hemicrania												
• Temporomandibular joint syndrome												
• Cracked tooth syndrome												
• Idiopathic stabbing headache												
• Glossopharyngeal neuralgia												
• Nervus Intermedius neuralgia												
• SUNCT												
• Trigeminal neuropathy												
• Atypical trigeminal neuralgia												
• Typical trigeminal neuralgia												

See Nurmikko.<sup>32</sup>

**Table 4. Medical Treatments for Trigeminal Neuralgia**

Medication	Dosage	Time to Pain Relief
Carbamazepine	400–800 mg/day	24–48 h
Phenytoin	300–500 mg/day	24–48 h
Baclofen	40–80 mg/day	?
Clonazepam	1.5–8 mg/day	?
Valproate	500–1500 mg/day	Weeks
Lamotrigine	150–400 mg	24 h
Pimozide	4–12 mg	?
Gabapentin	900–2400 mg/day	1 week
Oxcarbazepine	900–1800 mg/day	24–72 h

See Rozen.<sup>3</sup>

1. Surgical microvascular decompression (MVD).<sup>12</sup>
2. Stereotactic radiation therapy, Gamma knife.<sup>13</sup>
3. Percutaneous balloon microcompression.<sup>14</sup>
4. Percutaneous glycerol rhizolysis.<sup>15</sup>
5. Percutaneous radiofrequency (RF) treatment of the Gasserian ganglion.<sup>16</sup>
6. Gasserian ganglion stimulation/neuromodulation (*experimental*).<sup>17</sup>

**Surgical MVD.** During MVD, the vessels that are in contact with the root entry zone are coagulated and arteries are separated from the nerve using an inert sponge or felt.<sup>18</sup>

**Stereotactic Radiation Therapy, Gamma Knife.** The Gamma knife, a stereotactic radio therapeutic method, entails high dose irradiation of a small section of the trigeminal nerve. This results in nonselective damage to Gasserian ganglion. The advantage is that this is a noninvasive treatment that can be applied under local anesthetic and light sedation. At the moment, while there are an increasing number of efficacy studies being carried out on this treatment, the initial efficacy appears to be limited; between 60% and 70% indicate a reduction in pain. The long-term effects are not yet known.<sup>13</sup>

**Percutaneous Balloon Microcompression.** In microcompression of Gasserian ganglion, the trigeminal nerve is compressed by a small balloon, which is percutaneously introduced into Meckel's cavity using a needle. The effect of this technique relies on ischemic damage of the ganglion cells. Although there are insufficient good qualitative data, this technique, with regard to efficacy, appears to be comparable with percutaneous RF treatment of Gasserian ganglion. The advantage of this

technique is that it is also suitable for treatment of trigeminal neuralgia of the first branch, allowing the corneal reflex to remain intact.<sup>14,19</sup>

**Percutaneous Glycerol Rhizolysis.** During percutaneous glycerol rhizolysis, a needle is introduced into the trigeminal cistern, visualized using fluoroscopy. In a seated patient, with the head flexed, a contrast dye can be injected to determine the size of the cistern. Then, after the contrast dye is aspirated, an equal volume of glycerol is injected.<sup>15</sup>

**Percutaneous RF Treatment of the Gasserian Ganglion.** RF treatment of Gasserian ganglion should be considered in the elderly patient.<sup>14</sup> The outcome of treatment of Gasserian ganglion is reportedly less favorable than with open operation (MVD) but it is less invasive and has lower morbidity and mortality rates.<sup>20</sup>

**Gasserian Ganglion Stimulation/Neuromodulation (Experimental).** Gasserian ganglion electric stimulation was first described by Sheldon et al. in 3 patients with trigeminal neuralgia.<sup>17</sup> Meyerson and Hakansson reported Gasserian ganglion stimulation via a subtemporal craniotomy in 5 patients suffering atypical trigeminal neuralgia.<sup>21</sup> Later, a percutaneous approach was described by Meglio, however, lead migration presented a technical challenge.<sup>22</sup> More recently, Machado et al. reported percutaneous Gasserian ganglion stimulation in 8 patients with trigeminal neuropathic pain. Only 3 patients continued to have >50% pain improvement after 1 year of treatment.<sup>23</sup> They concluded that lead mobility due to difficulty anchoring the lead remains a significant barrier to achievement of optimal results and called for innovative lead designs.

For patients with trigeminal neuralgia refractory to medical therapy Gasserian ganglion percutaneous technique, Gamma knife, and MVD may be considered, although strong evidence on the efficacy of these interventions is lacking.<sup>6</sup> More research is needed to establish the value of these interventions.

Generally, it is accepted that the first choice of treatment in younger patients would be MVD. There are several systematic reviews available that compare the most appropriate techniques in the treatment of trigeminal neuralgia.<sup>20,24–27</sup> Given the most recent studies, MVD treatment remains the best therapeutic option with regard to improvement in the quality of life of the trigeminal neuralgia patient, and also when considering the long-term pain relief experienced after operation.

The other 3 minimally invasive therapies score less well because they have more risk of pain relapse after treatment. However, the differences are very small. Medication therapy scores the least well in the reviews. This is mainly because the pain relief frequently comes at the cost of severe side effects associated with chronic medication use.

For the elderly patient, treatment using RF treatment of Gasserian ganglion is often preferred over MVD. This is due to the increased morbidity and mortality that are associated with the MVD operation. However, one publication stated that in otherwise healthy people over the age of 70, MVD poses no appreciable increase in risk.<sup>28</sup> MVD is more effective than the Gamma knife treatment. About 60% of the treated patients are pain-free for at least 60 months, if the treatment is correctly given. Zakrzewska has indicated that in about 50% of patients, there is sensory loss in the treated branches of the trigeminal nerve.<sup>29</sup> As such, this technique should not be used in secondary trigeminal neuralgia, as seen in postherpetic neuralgia. The only current exception is secondary trigeminal neuralgia due to multiple sclerosis. While pulsed RF treatment would seem to be a reasonable alternative to RF, in the only randomized controlled trial comparing these techniques in the treatment of trigeminal neuralgia, PRF failed to demonstrate efficacy.<sup>30</sup>

### Complications

The percutaneous RF procedure has a very low morbidity and virtually no mortality. The most prevalent complications are sensory loss in the treated branch or paralysis of the Masseter muscle. In the long term, anesthesia dolorosa, corneal hypoesthesia and keratitis, and temporary paralysis of the third and fourth cranial nerves can occur. A more frequent and less serious complication is hematoma of the cheek, which generally disappears after a few days.

Kanpolat et al. reported the results of 25 years experience with 1,600 patients.<sup>31</sup> The above-mentioned complications are: decreased corneal reflex (5.7%), weakness and paralysis of the Masseter muscle (4.1%), dysesthesia (1%), anesthesia dolorosa (0.8%), keratitis (0.6%), and temporary paralysis of the third and fourth cranial nerves (0.8%).

### Evidence for Interventional Pain Treatment

The evidence for interventional pain treatment is summarized in Table 5.

**Table 5. Evidence Interventional Pain Treatment**

Technique	Assessment
Radiofrequency treatment of Gasserian ganglion	2 B +
Pulsed radiofrequency treatment of Gasserian ganglion	2 B -

See van Kleef et al.<sup>33</sup>

## RECOMMENDATIONS

The treatment of a patient with essential trigeminal neuralgia should be multidisciplinary and the various treatment options (MVD, Gamma knife, and RF treatment of Gasserian ganglion) and their risks should be discussed with the patient. These related therapies have never been compared with one another in prospective randomized studies. Recommendations are, therefore, relative. With regard to the elderly patient with comorbidities, RF treatment of Gasserian ganglion can be recommended. In younger patients, a MVD according to Jannetta could be considered.<sup>18</sup>

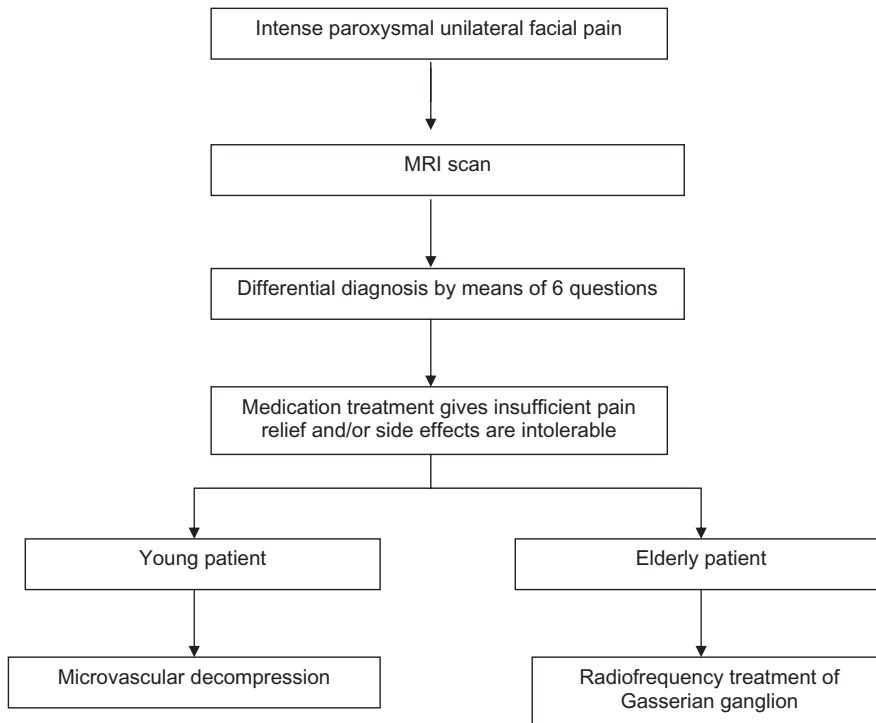
## CLINICAL PRACTICE ALGORITHM

An algorithm for clinical assessment and treatment is illustrated in Figure 1.

### The Technique of RF Treatment of Gasserian Ganglion

The Gasserian ganglion is named after Johann Lorenz Gasser, a Viennese anatomist. The ganglion lies in Meckel's cavity of the cranium close to the petrous bone, a part of the temporal bone. The Gasserian ganglion is surrounded medially by the cavernous sinus, superiorly by the underside of the temporal lobe and posteriorly by the brainstem. From top to bottom the ganglion has 3 branches: the first branch is the ophthalmic nerve, the second branch is the maxillary nerve, and the third branch is the mandibular nerve. The Gasserian ganglion has a somatotopic arrangement, in that the ophthalmic branch is the most craniomedial and the mandibular branch lies the most laterally.

The procedure is performed using fluoroscopy whereby the patient lies supine on the table and the C-arm is rotated to obtain a submental view, then slowly tilted obliquely toward the affected side until the foramen ovale is well visualized medially with respect to the mandibular process, and lateral to the maxilla. The C-arm position is then adjusted such that the foramen is seen as an oval. If one wishes to treat the maxillary branch and the mandibular branch, the entry point of the needle is 2 cm lateral to the corner of the mouth on

**Clinical Practice Algorithm**

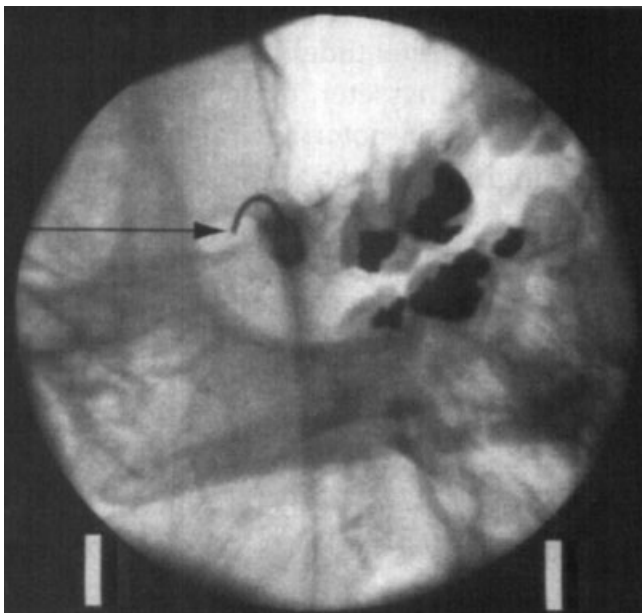
**Figure 1.** Clinical practice algorithm for the treatment of trigeminal neuralgia.

the ipsilateral side of the lesion. The needle is aimed at the middle of the foramen. If one only wants to treat the mandibular branch, the entry point of the needle is 1 cm lateral to the corner of the mouth and one aims the needle at the lateral part of the foramen ovale. If one only wants to treat the ophthalmic branch, the entry point of the needle lies 3 cm lateral to the corner of the mouth and one aims the needle at the medial part of the foramen ovale.

For this treatment, we use an Sluijter-Mehta-Kanula cannula, 10 cm 22 G with a 2 mm active tip. Once the anatomical landmarks have been identified, an intravenous sedative dose of propofol or similar agent is given. The Sluijter-Mehta-Kanula needle is then advanced toward the foramen ovale (tunnel-view) (see Figures 2 and 3). It is important to place a finger in the mouth to be certain that there is no penetration of the oral mucosa. Once the needle is through the foramen ovale into Meckel's cavity, stimulation can take place. The stimulation parameters are as follows: first the motor functions are tested, whereby there should be little or no contraction of the Masseter muscle, preferably above a threshold of 0.6 V. With motor stimulation, the needle needs to be advanced carefully approximately 2 mm.



**Figure 2.** Radiofrequency treatment of Gasserian ganglion: lateral view. Needle is positioned through the base (foramen ovale) of the skull. Note the Sella Turcica and Clivus.



**Figure 3.** Radiofrequency treatment of Gasserian ganglion: oblique submental view. Electrode aimed at the middle of the Foramen Ovale. On the lateral side the Mandibula and on the medial side the Maxillary Sinus.

Then the patient is allowed to awaken, by discontinuing the propofol sedation, and sensory stimulation can be carried out at 50 Hz. Paresthesia should be felt between 0.05 and 0.2 V in the area corresponding to the patient's pain. After appropriate paresthesia, a 60°C RF treatment can be done for 60 seconds. After this, the corneal reflex is tested and the patient is evaluated for hypoesthesia in the treated dermatome. If there is no hypoesthesia, then a second treatment is done at 65°C for 60 seconds, and if there is still no hypoesthesia then a third RF treatment can be done at 70°C for another 60 seconds.

### SUMMARY

As suggested by T. Nurmikko, classical (essential) trigeminal neuralgia can be diagnosed by asking 6 simple questions (Table 3).<sup>9,32</sup>

It is important that an MRI of the brain has been carried out in each patient, in order to exclude a secondary trigeminal neuralgia that requires a more causal treatment, before resorting to invasive therapy. The first treatment of choice is carbamazepine or oxcarbazepine. In younger patients with trigeminal neuralgia, the first choice of invasive treatment is probably MVD. With regard to elderly patients, RF treatment of Gasserian ganglion is recommended even

though there is a lack of prospective comparative data. This treatment should only be carried out in specialized centers.

There is not enough data at this time to support the widespread use of trigeminal neuromodulation and these modalities of treatment should only be reserved for selected patients with intractable trigeminal neuropathic pain who failed to improve with other more conservative options.

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