Evaluation of Surgical Procedures for Trigeminal Neuralgia

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Trigeminal neuralgia is a type of facial pain that is difficult to treat. The pain can be excruciating and debilitating. The wide range of treatments currently used for trigeminal neuralgia is ample evidence that there is no simple answer to how it should be managed. This review will evaluate the current surgical procedures used for the treatment of trigeminal neuralgia. A critical analysis of the evidence-based studies to date was done to evaluate and compare the efficacy of the different surgical procedures. Arguments for and against the use of surgery for trigeminal neuralgia are presented. In addition, the surgical procedures were compared with other treatments for trigeminal neuralgia.

Key Words: Pain; Neurectomy; Radiofrequency thermocoagulation; Microvascular decompression; Rhizotomy.

Trigeminal neuralgia is characterized by episodic, paroxysmal, triggered pain in a distribution of 1 or more divisions of the trigeminal nerve. The pain is usually unilateral at any one time, although 5–10% of patients may at some time in their lives have contralateral paroxysmal triggered pain.[1] The paroxysms of pain are usually severe and debilitating. It can be difficult to treat, and patients have committed suicide when the pain could not be controlled. Fortunately, effective medical and surgical therapies for the disorder exist. The wide ranges of treatments currently used for trigeminal neuralgia are ample evidence that there is no simple answer to how it should be managed. Opinions can differ greatly regarding the best treatment for this condition. Even when the patient is referred, quality medical care requires that the physician be acquainted with current evidence-based practice. Such practice may be radically different from the traditional view. We will confine this review to a critical analysis of the literature regarding the efficacy and adverse effects of surgical procedures used for trigeminal neuralgia. The surgical procedures will also be compared with the medical treatment of trigeminal neuralgia.

A literature review was done for evidence-based studies on the management of trigeminal neuralgia. Studies were identified by computer search with MEDLINE, Pubmed, Embase, Cinahl, and the Cochrane Library from 1966 to 2002. A broad free text search with restriction to publications in English was undertaken using all variants of terms "trigeminal neuralgia," "facial pain," and "surgical." A hand search of relevant books or journals not indexed by the above indexes was also done, as well as a search through the references of relevant papers for useful citations. Only studies that included valid measures of pain relief from the surgical procedures were included. Both clinical, basic sciences evidence and review papers were included as appropriate. Although prospective randomized control trials are considered the scientific standard in clinical research for establishing a cause-and-effect relationship, other study designs, including retrospective case-control studies, were also included. This was the result of the lack of randomized control trials in this area.

OUTLINE OF REVIEW

The following surgical procedures used in the treatment of trigeminal neuralgia will be evaluated: (a) peripheral

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surgery (neurectomy, cryotherapy, and alcohol injection); (b) surgery at the gasserian ganglion level (radiofrequency thermocoagulation, percutaneous retrogasserian glycerol injection, and percutaneous microcompression); and (c) posterior fossa surgery (microvascular decompression, rhizotomy, and gamma-knife radiosurgery). The surgical procedures will also be compared with the medical treatment of trigeminal neuralgia.

PERIPHERAL SURGERY

Most of these procedures can be carried out under local anesthesia and do not require the patients to be medically fit. All of these procedures depend on accurate assessment of which nerve branch is acting as the trigger area; surgery is then carried out on that branch. To date, there are no long-term longitudinal studies for these peripheral procedures. All studies were retrospective case series reports. It is difficult to compare results for peripheral surgeries from the current literature, especially in terms of pain relief, as variable techniques of analysis were used and end points were not clearly defined. There was also often little or no statistical analysis used. Findings on neurectomy, cryotherapy, and alcohol injections will be discussed.

Neurectomy

Neurectomy is probably the oldest recorded surgical procedure for trigeminal neuralgia. Most of the studies done for neurectomy were published 20–50 years ago,[2–7] with only one recent paper by Murali and Rovit[8] found in the literature. All of these studies were retrospective case series reports.

Quinn[3] reported a retrospective case series of 63 patients with 112 neurectomies. A follow-up period of 0–9 years was noted, and a pain relief period of 24–32 months was reported. Grantham[2] also reported a case series of 55 patients with 55 neurectomies. A follow-up of 6 months to 8 years was noted, and an average pain relief period of 33.2 months was achieved. A recent study by Murali and Rovit[8] reported on a case series of 40 patients, 12 with neurectomies performed as the primary procedure, and 28 as a second procedure to treat pain recurrence after radiofrequency thermocoagulation. The follow-up period was 2–10 years. It was reported that 79% had excellent pain relief (defined as total loss of pain without need of medication) lasting 5 years or more, and some had excellent pain relief until their deaths. The mean age of their patients was 72 with an age range of 50–94. Dysesthesia or sensory loss in the area supplied by the avulsed nerve was reported as a significant morbidity of the surgery. However, the corneal reflex was kept intact in neurectomies. They concluded that neurectomy is an effective and safe procedure for elderly patients, particularly those who have a limited life span. Unfortunately, life-table analysis of data was not used in these studies. This would have enabled the researchers to include those patients who had died or been lost to follow-up. Instead, these patients were "censored," but their inclusion prevented distortion of the data. In addition, none of the above neurectomy studies had been subjected to good statistical analysis.

Cryotherapy

Cryotherapy is the therapeutic use of cold to obtain pain relief. Under local anesthesia, the affected nerve is exposed surgically and a cryoprobe placed directly on the nerve for three 2-minute freeze-thaw cycles. Few complications have been reported; sensation, although initially lost, returns before pain recurs.[9,10] The procedure can be repeated, and the results have been similar.[9,10] Recent cryotherapy studies appear to be of better quality than those for neurectomy; many researchers had used Kaplan-Meier analysis, which allows for comparison of the results.[9–11]

After follow-up of 1 month to 6 years, Zakrzewska and Nally[9] observed in 145 patients who had undergone cryotherapy a median time to recurrence of pain of 14 months for the infraorbital nerve and 9 months for the mental nerve. Zakrzewska[10] reported again in a 10-year follow-up series of 145 patients and found a median pain relief period of 6 months and a mean time to recurrence of 10 months, as compared with the median pain relief period of 24 months in 265 patients treated with radiofrequency thermocoagulation. However, many patients continued to take carbamazepine after cryotherapy, although the doses were lower. The above authors probably used the same patient sample in both publications, as the patients were recruited from the same department and hospital.

Alcohol Injection

Although alcohol injection is essentially a simple technique, the alcohol must be injected very precisely as it is highly toxic. Most of the studies done for alcohol injection were published 30–50 years ago,[2,12–15] with only one recent paper by Fardy[16] found in the literature search.

Stookey and Ransohoff[12] combined several reports totalling 1500 patients and found the length of pain relief to be 12 months or less. Repeated injections were more difficult due to fibrosis. Fardy and Patton[16] reported on a series of 413 alcohol blocks administered

over a 20-year period. The mean period of pain relief was 13 months, and only 3 (0.73%) significant complications were noted. These included local tissue necrosis, diplopia, and sensory loss. All of the studies on alcohol injections were retrospective case series, and none had been subjected to statistical analysis.

SURGERY AT THE GASSERIAN GANGLION LEVEL

Surgery at the gasserian ganglion level is achieved by a specially designed device inserted into the cheek. Under radiographic control, the device is directed through the foramen ovale into the gasserian ganglion or retrogasserian rootlets. Partial destruction of the trigeminal nerve is achieved with radiofrequency-induced heat, glycerol injection, or balloon compression. The varying degree of damage that results from any of these modalities depends on a number of factors, especially the duration and intensity of denervation.

Currently, radiofrequency-induced heat, glycerol injection, or balloon compression destruction of the gasserian ganglion are the procedures that have been subjected to rigorous statistical analysis and long-term longitudinal follow-up of a large series of patients in order to evaluate the long-term efficacy. The strength of many of these studies lies in their proper cohort study design. The same groups of patients were followed over time and the data were collected and followed prospectively. This is the best type of study for understanding the causes of a disease and the risk factors.

Radiofrequency Thermocoagulation

Currently, radiofrequency thermocoagulation (RT) is the most common surgical treatment for trigeminal neuralgia.[17] The value of this technique has been confirmed in many large-series patients.[18–21] Although 37 studies with a total of more than 14,000 patients have been identified by Zakrzewska,[22] many were small series of less than 500 patients each, and the details of the outcome end points and follow-up periods were not mentioned. The recurrence rate quoted ranges from 4–65%.[22] This wide variation in part depends on what constitutes recurrence. Some studies classified recurrence as pain severe enough to require surgery, and some classified any pain as recurrence. The most important factors influencing recurrence are the duration of follow-up and the degree of denervation.[22] Two isolated cases of deaths have been reported. Other major complications include moderate dysesthesia in 5–25% of patients, anesthesia dolorosa occurring in 1–5%, and keratitis in 1–3%.[23] However, more recent controlled studies using improved techniques of proper lesion control seem to be associated with fewer complications and few recurrences.[19] Two excellent longitudinal large-series studies of patients have been reported by Broggi et al[18] and Taha and Tew.[19]

Broggi et al[18] have reported in a 10-year follow-up of 1000 consecutive patients treated with RT. The authors reported that impressive pain relief was obtained in 95% of the treated patients. There was a recurrence rate of only 18.1% after a 3-year follow-up (pain recurrence was defined as pain that required further surgical treatment). The mortality rate in these series was zero. Weakening of corneal reflex without corneal damage was seen in 19.7% of patients, and corneal reflex impairment with keratitis was seen in 0.6%. Of the 181 patients with recurrence, 160 patients had the procedure repeated, and their neuralgia resolved. This is a good study with the largest series of patients and the longest follow-up period. In addition, all of the essential details on the range of follow-up, temperature and duration of thermocoagulation, and recurrence rate were properly reported. The study was also conducted with a good homogenous sample selection; only patients with essential trigeminal neuralgia who failed medical therapy were selected, as selection of patients who had previous surgery such as alcohol injections may have a higher recurrence rate. However, this study may be a little biased in that the authors did not report any patients who were lost during the follow-up. It is doubtful that none of the 1000 patients with trigeminal neuralgia—who were likely to be elderly—had been lost or died during the 14-year follow-up. In addition, no Kaplan-Meier analysis was done for this study, which is the proper statistical analysis that allows comparison of the results between different series.

Taha and Tew[19] compared the results of RT in 500 patients that were followed for 2–12 years with patients that had undergone other surgical treatments for trigeminal neuralgia. The authors found a 100% technical success rate for completion of the RT procedure, the highest rates for initial pain relief, and one of the lowest pain recurrence rates for RT when compared with other surgical procedures. An impressive recurrence rate of only 20% in 9 years was reported. Glycerol injection was incomplete in 6% of patients because of failure to locate the needle site. Balloon compression was incomplete in 1% of patients because of failure to cannulate the foramen ovale. Fifteen percent of patients for microvascular decompression underwent a partial trigeminal rhizotomy, because significant vascular compression was not found or adequate decompression could not be safely performed. However, it should be noted that this study might be a little biased, as the authors clearly selectively chose and analyzed the literature, using only

selected studies with larger series of patients. The authors used these selected results to bolster personal opinions relative to the outcomes after RT. This type of report is not a comprehensive meta-analysis.

Glycerol Injection

Glycerol injection involves the injection of sterile glycerol into the gasserian ganglion and retrogasserian rootlets. As initially described, there was a low incidence of complications, dysesthesia, or keratitis, and little loss of sensation.[24] However, many recent larger series have shown that complications do occur frequently, and the recurrence rate is relatively high, up to 50%.[25–27] Although 24 studies with a total of more than 1000 patients have been identified by Zakrzewska,[22] many are small series with less than 100 patients each, and with only very short follow-up periods of less than 3 years.

Fujimaki et al[27] reported a series of 80 patients that had been followed for 54 months, which is one of the longest for glycerol studies. Using Kaplan-Meier analysis, they found that the recurrence rate at 54 months was exceedingly high at 74%. Complications were significantly high at 63% with definite hypoesthesia and dysesthesia. One drawback of this study was the inclusion of a mixture of patients with previous surgical procedures performed. Recurrence tends to be more common in patients who have had previous surgery.[22]

Balloon Microcompression

Balloon microcompression of the trigeminal ganglion is done with a Forgarty balloon catheter that can be inserted under fluoroscopy. Fewer studies have been done for this technique compared with RT and glycerol injection. No large-series studies with long-term follow-up have been done for balloon microcompression.

Lichtor et al[28] reported a 10-year follow-up in a series of 100 patients. At 5 years, the recurrence rate was 20%, and at 10 years, it is estimated that 70% of patients will still be pain-free. One of the main advantages of this procedure is that the corneal reflex is maintained in most cases. However, dysesthesia does occur in 7–19% of the cases[28] and may be related to the compression time. The drawback of this study is the variable compression time between 0.5 to 15 minutes, which was not standardized. In addition, patients included were a mixture having previous surgical procedures.

POSTERIOR FOSSA SURGERY

Microvascular decompression (MVD), partial rhizotomy, and gamma-knife radiosurgery will be discussed in this section.

Microvascular Decompression

MVD is based on the concept that compression of the trigeminal nerve causes trigeminal neuralgia.[29] This procedure purports to address the etiological basis of trigeminal neuralgia due to compression of the trigeminal nerve from blood vessels or tumors, which have resulted in demyelination of the nerve. There is evidence from clinical and anatomical studies that support the neurovascular compression theory of trigeminal neuralgia.[30,31] MVD has been highly recommended by many neurosurgeons, as they think that it is the only technique that removes the cause of the pain and does not damage the trigeminal nerve.[29–31] However, the fact that there are still patients who do not experience pain relief following MVD suggests that there may be other etiologies other than the compression of the nerve that could cause trigeminal neuralgia.

To date, many long-term series of patients who have undergone MVD have been reported.[32–35] However, many series also include the evaluation of patients with other types of pain (eg, atypical neuralgia and tumors). This makes the comparison of results difficult. Barker et al[32] have reported an excellent long-term (20 years) prospective longitudinal study on the outcome of MVD for trigeminal neuralgia in 1185 patients. Ten years after surgery, 70% of the patients had excellent final results; they were free of pain without need of medication. Major complications included deaths (0.2%), brain-stem infarction (0.1%), and ipsilateral hearing loss (1%). Initial relief of neuralgia pain was present in 98%. This is one of the best studies for MVD to date for trigeminal neuralgia. The authors were skillful in the selection of patients, including only patients with primary trigeminal neuralgia. In addition, it was a blind study employing an independent observer to collect and analyze the results. Extensive appropriate statistical analysis was also used in this study. Fisher's exact test, Mann-Whitney test, *t* test, and Kaplan-Meier analysis were used.

Partial Rhizotomy

The technique for rhizotomy using the posterior fossa approach is the same as that for MVD. The whole or part of the sensory division is sectioned, taking care to avoid the motor root. The results of partial rhizotomy are comparable with those of MVD.[36] However, there is a trend for a higher recurrence rate following partial rhizotomy compared with MVD.[37] Mortality and morbidity rates are similar as the surgery is approached through the similar posterior fossa. The major complication is sensory loss. Painful dysesthesia and anesthesia dolorosa are more likely after complete section and occur in about 8% of patients.[37]

Gamma-knife Radiosurgery

Gamma-knife radiosurgery is a new technique for the treatment of trigeminal neuralgia for which no long-term follow-up exists. A stereotactic head frame is screwed onto the skull, and stereotactic imaging is performed. The trigeminal system is irradiated. A maximum radiosurgical dose of 70 Gy or greater was associated with a greater chance of complete pain relief.[38] Most patient series reported comprised of less than 100 patients with follow-up of less than 1 year.[38–41] Kondziolka et al[39] reported 80% initial pain relief in 106 patients who were followed for 18 months. Ten percent of the patients developed dysesthesia as a complication.

A recent gamma-knife radiosurgery study provides a longer-term follow-up period of up to 6.5 years.[42] This study evaluated a large series of 220 patients with idiopathic trigeminal neuralgia who had been treated with gamma-knife radiosurgery and were followed for a median period of 2 years. This is an excellent study that selected a homogenous sample of patients with idiopathic trigeminal neuralgia and has the longest follow-up to date for radiosurgery. In addition, good statistical analysis and independent observers were used to collect the data. The median radiosurgery dose used was 80 Gy, with a range of 60–90 Gy. Complete or partial pain relief was obtained in 85.6% of patients at 1 year. At 5 years, 55.8% of patients still had complete or partial pain relief. Complete pain relief was achieved at a median time of 2 months, with most patients achieving this level of pain relief within 6 months. Interestingly, a further 10% of patients obtained complete pain relief at 6–33 months after the radiosurgery. The most important factor for poor response was the presence of atypical pain features in addition to the typical neuralgic pain. Only 10% of patients developed new or increased subjective facial paraesthesia or facial numbness.

It is important to note that it may take a long time to achieve pain relief following radiosurgery. The median time to pain relief was 1 month, with a range of 1 day to 6.7 months.[38] A wait for pain relief for 6.7 months is clinically impractical because trigeminal neuralgia patients need speedier pain relief. Although radiosurgery appears relatively benign and noninvasive, complications like cataract formation, tumor formation, or brain necrosis may occur after long-term follow-up. The low incidence of morbidity, particularly dysesthesia complications, is the greatest advantage of gamma-knife radiosurgery compared with all other surgeries used for the treatment of trigeminal neuralgia. The results for radiosurgery are not as good as those observed after MVD for typical trigeminal neuralgia, as noted in the Barker et al[32] series of 1185 patients: complete pain relief was reported in 70% of patients at 10 years. However, radiosurgery may be a good choice for patients with recurrent pain after MVD or percutaneous surgery has failed.

The Table compares the different surgical techniques used for the management of trigeminal neuralgia. All surgeries at the 3 levels could relieve the pain of trigeminal neuralgia. However, peripheral surgery can be done in the office with little equipment and is suitable for medically compromised patients with low morbidity. The main disadvantage for peripheral surgeries is that the pain relief is relatively short (particularly for cryotherapy and alcohol injection), with recurrence within months. Surgery at the gasserian ganglion is associated with a lower recurrence rate of pain, but the morbidity is higher and the risk of dysesthesia is high, particularly for RT. MVD is associated with the lowest pain recurrence rate but has the highest morbidity and mortality rate.

ARGUMENTS FOR THE USE OF SURGICAL PROCEDURES VERSUS MEDICAL THERAPY

It has been stated that the results of surgical treatments for trigeminal neuralgia is so good that patients are often better served by surgery rather than persevering for prolonged periods with either pain or bothersome adverse effects from medications.[43] As trigeminal neuralgia is a protracted disorder, any medication may need to be given for extended periods of time, thereby multiplying the potential for toxicity of the drug. In addition to the considerable side effects, the pain may become more intractable as the disease progresses. In 30% of the cases, medical treatment fails through inadequate pain control, or because of intolerable side effects.[44,45] In these cases, surgical management is the only viable option.

If surgery is to be done, the timing is controversial. Some neurosurgeons argue that early surgical treatment arrests the progression of the condition and ensures that surgery is carried out on a medically fit younger patient, which theoretically carries less risk of mortality and significant morbidity.[37] This is especially true for MVD, as the evidence from longitudinal studies shows that there is significant morbidity and mortality.

Not a single randomized controlled trial has been done comparing the different surgical procedures for trigeminal neuralgia, in spite of thousands of patients having been operated on for this condition. To date, there is only one recent report (Zakrzewska and Patsalos[46]) that compares the medical and surgical management of intractable trigeminal neuralgia. This is a long-term prospective longitudinal study comparing 15 patients who were followed for a mean duration of 15 years on the effectiveness of medical (oxcarbazepine) versus surgical therapy. Kaplan-Meier analysis 3 years after oxcarba-

Comparison of the Different Surgical Techniques

Procedure	*Peripheral Surgery*	*Radiofrequency Thermocoagulation*	*Glycerol Injection*	*Microcompression*	*Microvascular Decompression*	*Radiosurgery*
Age of patients	Any age	Any age	Any age	Any age	Preferably under 65 years	Any age
Medical fitness of patients	Suitable for medically unfit patients	Care needed if bleeding problems	Care needed if bleeding problems	Care needed with cardiac patients	Medically fit only	Suitable for medically unfit patients
Ease of technique	100% complete	100% complete	94% complete	99% complete	85% complete	100% complete
Initial pain relief (%)	97	98	91	93	98	80
Recurrence rate	Mean 8–33 mo	Mean 3–5 y	Mean 2–3 y	Mean 4.5–6.5 mo	Low; 10 years, 70% pain free	33% recurrence at 18 months
Anaesthesia dolorosa (%)	Not reported	0.3–4	1.8	0.1	None reported	None reported
Keratitis (%)	None reported	0.5–3	None reported	Very rare	None reported	None reported
Mortality	None reported	Very low	None reported	None reported	Up to 1%	None reported

zepine use and then 3 years after surgery showed that the mean time for recurrence of pain after oxcarbazepine was 10 months, whereas for surgery it was 28 months ($P < .0001$). Furthermore, both clinical and patient global analysis of the outcome measures suggested that patients could benefit substantially from having surgery earlier, rather than later, in the disease process to improve the quality of life, freedom from medication, and the need for regular follow-up. This is the first study that has compared outcome in a group of patients who have had both medical and surgical treatments. The authors were also skillful in the selection of patients and in using proper outcome measures. In addition, an independent observer was used to evaluate the records allowing a more objective evaluation. The only weakness in this study is the relatively small numbers of patients studied.

ARGUMENTS AGAINST THE USE OF SURGICAL PROCEDURES VERSUS MEDICAL THERAPY

The only other effective nonsurgical management of trigeminal neuralgia is medical treatment. All new patients are initially treated medically as response to treatment is, in part, diagnostic.[22] If the patient responds to medical treatment, the clinician can be fairly confident that the correct diagnosis has been made. A recent meta-analysis has shown that anticonvulsants are effective for the treatment of trigeminal neuralgia.[47] Thirty-seven randomized control trials were systematically reviewed.

Carbamazepine was found to be the drug of choice in the management of trigeminal neuralgia. Dosing according to efficacy and side effects is clinically feasible. After dose titration, the patients should preferably be given slow-release formulations so that diurnal variations in serum drug levels do not influence efficacy. When carbamazepine cannot be used, the alternative evidence-based medical treatments are lamotrigine and baclofen.[48] In the case of a lack of effect of a single drug, a combination of 2 or more drugs may be used. Only the lamotrigine-carbamazepine combination is evidence-based treatment.[48] Phenytoin, clonazepam, valproic acid, and gabapentin could also be used, but they do not constitute evidence-based treatments for trigeminal neuralgia. Considering the evidence-based benefits of gabapentin in other neuropathic pain conditions, such as painful diabetic neuropathy and postherpetic neuralgia, this relatively new drug may represent an advance in treatment.[48] A good understanding of the mechanism of action of these drugs will ensure good pain control with minimal side effects. Severe hematological and biochemical reactions do occur, but are relatively rare.[22]

Surgical management of trigeminal neuralgia is associated with increased morbidity and mortality. Isolated deaths have occurred in patients undergoing surgery at the level of gasserian ganglion, but there is a 1% mortality rate associated with MVD.[22] It has been argued that a 1% mortality risk is too high a price to pay for the relief of pain from a condition that is, itself, not fatal.[49] Hearing loss is common after MVD and partial rhizotomy. Dysesthesia and anesthesia dolorosa can be extremely unpleasant for many patients. The incidence of dysesthesia is especially troubling for all of the surgical procedures, with an incidence as high as 20–70% after percutaneous procedures.[50] MVD and gamma-knife radiosurgery seems to be the surgical technique that produces the lowest incidence of dysesthesia. All of these factors together with the patient's age and medical status should be considered to decide the choice of surgical procedure or whether to proceed with surgery at all and instead rely on medical therapy.

CONCLUSION

Currently, there is no strong evidence to support either a surgical or medical approach as the best therapy for trigeminal neuralgia. Both surgical and medical therapies are effective for trigeminal neuralgia. However, factors such as pain relief, recurrence rates, and morbidity and mortality rates should be taken into account when considering which techniques to use. For surgery, peripheral procedures seem to be associated with the highest and earliest recurrence rates. But they can be extremely useful in elderly patients with a limited life span. All procedures performed at the gasserian ganglion level appear to have similar recurrence rates, although it is generally considered highest for glycerol injections. Recurrences do occur after MVD, although from data to date the time interval appears to be much longer. It seems justified from the current evidence to start a patient with trigeminal neuralgia with medical therapy and proceed early with surgical treatment once pain control is poor or side effects of medications are intolerable. It is usually a composite of many parameters that must be individualized in each patient before deciding which surgical procedure to use.

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