Radiosurgery for Trigeminal Neuralgia

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Trigeminal neuralgia (TN), also known as tic douloureux, is a pain syndrome recognizable by patient history alone. The condition is characterized by intermittent unilateral facial pain. The pain follows the unilateral (>95%) sensory distribution of trigeminal nerve (V), typically radiating to the maxillary (V2) or mandibular (V3) area. Ophthalmic division (V1) pain alone occurs in <5% patients. The mechanism of pain production remains controversial. One theory suggests that peripheral injury or disease of the trigeminal nerve increases afferent firing in the nerve, perhaps by ephaptic transmission between afferent unmyelinated axons and partially damaged myelinated axons; failure of central inhibitory mechanisms may also be involved. Pain is perceived when nociceptive neurons in a trigeminal nucleus involve thalamic relay neurons. Blood vessel-nerve cross compression, aneurysms, chronic meningeal inflammation, tumors or other lesions may irritate trigeminal nerve roots along the pons.

Uncommonly, an area of demyelination, such as may occur with multiple sclerosis, may be the precipitant. In some cases no vascular or other lesion is identified, rendering the etiology uncertain. Development of trigeminal neuralgia in a young person (<45 years) raises the possibility of multiple sclerosis, which should be investigated. Lesions of the entry zone of the trigeminal roots within the pons may cause a similar pain syndrome. Thus, although TN typically is caused by a dysfunction in the peripheral nervous system (the roots or trigeminal nerve itself),[8,11,20,25] a lesion within the central nervous system (1–8%) may also cause similar problems.[7]

A variety of medical and surgical treatments exist for trigeminal neuralgia, and long-term results have been reported. A number of factors are considered in making a recommendation. These factors include: Patient's age, Patient's medical condition, Presence or absence of multiple sclerosis, Presence or absence of vascular contact and/or compression on thin section MRI, Presence or absence of prior procedures, type of prior procedure and its response, severity of pain and how long the patient can reasonably wait for pain relief, Patient's concern and risk tolerance for dysesthesias, recurrence or complications from surgery. Gamma Knife® radiosurgery is recommended for older or infirm patients because it is the least invasive option. The lack of mortality and the low risk of facial sensory disturbance, even after a repeat procedure, argue for the use of primary or secondary radiosurgery in this setting. Repeat radiosurgery remains an acceptable treatment option for patients who have failed other therapeutic alternatives.

Pain Relief after Radiosurgery

Several reports have documented the efficacy of Gamma Knifeâ stereotactic radiosurgery for TN.[1,4,13,16,21,22,24,26,28,30-34,37,38,42-44,48,50,54] Because radiosurgery is the least invasive procedure for TN, it is a good treatment option for patients with co-morbidities, high-risk medical illness, or pain refractory to prior surgical procedures. Radiosurgery is a good alternative for most patients with medically refractory trigeminal neuralgia, especially those who do not want to accept the greater risk of an MVD for a greater chance of pain relief.

To date, the largest reported series are still characterized by a wide spectrum of success rates after radiosurgery with Grade I outcome in 21–76. 8% of patients and Grade II outcome in 65–88% of patients.[5,6,23,24,29,40,43,48,53]

Regis et al. reported that 87% of patients were initially free of pain in their series of 57 patients treated with a maximum dose of 75–90 Gy.[43,45] In many patients, they used the higher maximum dose of 90 Gy, and their target was placed at a more anterior site (closer to retrogasserian portion). In a series of 441 patients presented at the 2001 meeting of the International Stereotactic Radiosurgery Society, Young et al. noted that 87% of patients were free of pain after radiosurgery, with or without medication (median follow-up period, 4.8 years, including repeat procedures). Brisman et al. noted vascular contact with trigeminal nerve on thin section MRI in 59% of patients with TN. These authors reported a complete (100%) pain relief without medicines in 22% of patients, 90% or greater relief with or without small doses of medicines in 30% of patients, 75–89% relief in 11% of patients, 50–74% relief in 7% of patients, and less than 50% relief in 8% of patients. Recurrent pain requiring a second procedure occurred in 24% of patients.[6]

In a study, Petit et al. assessed the safety, efficacy and quality of life associated with radiosurgical treatment for TN in 112 patients treated with Gamma Knife® radiosurgery using a standard questionnaire. Ninety-six patients completed questionnaires for a median follow-up of 30 months. Seventy-four patients (77%) reported pain relief at a median of three weeks after the procedure.[36] A decrease in medication usage was noted in 66% of patients.

Seven (7.3%) patients reported new or increased trigeminal dysfunction; however, only 3.1% reported these symptoms as bothersome. Patients with sustained pain relief reported an average of 100% improvement in their quality of life as a direct result of pain relief after radiosurgery, and 100% believed that the procedure was successful. Furthermore, among those patients with temporary pain relief and subsequent recurrence, 65% felt their treatment was a success with an average of 80% improvement in their quality of life.[36]

Smith et al. recently published the results of trigeminal neuralgia radiosurgery using a dedicated linear accelerator.[49] These investigators treated 60 patients with central doses of 70–90 Gy delivered to trigeminal nerve root entry zone using a 5-mm collimator. Pain relief was experienced at a mean of 2.7 months. Significant pain relief was obtained in 87.5% of the patients who had essential TN and in 58.3% of the patients who had secondary facial pain. In a recent article, Longhi et al. reported on the results of Gamma Knife® radiosurgery for treatment of medically and, in some instances, surgically refractory TN.[28] These

authors found 57% Grade I and 33% Grade II pain control after Gamma Knife® radiosurgery. These favorable results are similar to those reported by Pollock et al.[41] and Kondziolka et al.[14] Recurrence of pain occurred in 18% of patients at a mean interval of 14.2 months after radiosurgery. The side effects of trigeminal paresthesia or hypoesthesia were observed in 9.5% of patients; no cases of anesthesia dolorosa were observed. A higher radiosurgical dose and no previous neurosurgical intervention for TN were positive predictors of a pain-free outcome. The growing body of recent literature suggests that low rates of complications of Gamma Knife® radiosurgery, coupled with high success rates and patient satisfaction, allow it to be increasingly used as primary intervention for trigeminal neuralgia for appropiate patients.[2,3,9,10,16,18,21,34]

In a recent long-term study performed at University of Pittsburgh 495 patients with a maximum follow-up of 14 years were included. The median age was 72 years (range 26–95 years). The median target dose was 80 Gy (range, 70 to 90 Gy). Two hundred forty-eight patients (49.5%) had previously undergone at least one microvascular decompression or rhizotomy. Complete or partial relief was achieved in 92.5% of patients at 1 year. Initial complete pain relief was achieved in 78.7% at 6 months, 81.4% at 1 year, and 83.4% at 3 years. The median time to becoming pain free was 30 days. Forty-five percent had some degree of pain recurrence, at a median of 4 years. The median time before recurrence was 48.0 months. Patients with pre-existing trigeminal neuropathy had a lower rate of maintaining pain relief ($p = 0.034$). Sixty-nine (13.9%) patients maintained more than 4 years of pain relief. Only 48 patients (9.7%) developed subjective facial paresthesia or numbness. There was no other morbidity.

Predictive Factors

Several factors have been associated with the positive results achieved by Gamma Knife® radiosurgery in treating TN: the absence of multiple sclerosis, greater radiation dose, no previous surgery, typical pain features, and proximity of the isocenters to the brainstem edge.[5,7] In a population of 54 patients, Rogers et al.[47] found a higher Grade I outcome in patients with idiopathic typical TN in comparison with those with atypical features: 49% (21 of 43) as opposed to 9% (1 of 11). In their series of 179 patients, Brisman et al.[7] reported that 41% of their patients had a Grade I outcome and 17% had a Grade II outcome. Better results were achieved in patients with no previous surgery (60% [35 of 58]). Similar results were reported by Young et al.[53] and Maesawa et al.,[29] who described the presence of atypical pain as the most important factor yielding a poor response to Gamma Knife® radiosurgery (84.4% versus 43.8%). Several authors have reported similar results using linear accelerator based radiosurgery.[15,17,27,35,46,51]

Recurrence After Radiosurgery

Recurrence is still a major concern in the Gamma Knife® treatment of trigeminal neuralgia. The experience suggests that longer follow-up periods are needed before drawing any conclusion.[50] Thirty–one patients underwent repeat radiosurgery at the University of Pittsburgh due to pain recurrence. The time to recurrence after the first radiosurgical procedure varied from 3 to 64 months. The mean time to recurrence was 18.2 months, and the mean interval between

the first and second radiosurgical procedures was 22.3 months (range, 6–73 months).[23] The duration of pain relief after the initial response was analyzed in all patients using the Kaplan-Meier product-limit method. Complete pain relief (excellent or good) was maintained in 63.6 ± 3.3% of patients at one year and in 56.6 ± 3.8% at three years. Greater than 50% pain relief was maintained in 75.8 ± 2.9% of patients at one year and in 67.2 ± 3.9% at three years. A history of no prior surgery was significantly associated with achieving and maintaining complete pain relief ($p = 0.01$). The absence of preradiosurgical paresthesia, which is strongly correlated with no prior surgery, was significantly associated with achieving and maintaining greater than 50% pain relief ($p = 0.02$). According to the other literatures, recurrence rates at the last follow-up after radiosurgery varied from 3.3–21%.23,40 Currently, the etiological basis and physiopathology of TN recurrences after Gamma Knife® radiosurgery still need to be clarified. The recent description of two distinct mechanisms in pain generation, ephaptic transmission and neuronal afterdischarge, will likely explain how glial processes stimulated by radiosurgery might be more efficient in blocking the ephaptic transmission, but not the neuronal afterdischarge, which is a nonsynaptic, nonephaptic transmission that could lead to painful relapses.[12]

Complications after Radiosurgery

The main complication after radiosurgery was new facial sensory symptoms caused by partial trigeminal nerve injury. Seventeen patients (7.7%) in the University of Pittsburgh series developed increased facial paresthesia and/or facial numbness that lasted longer than six months.[29] One patient (0.4%) developed deafferentation pain. No patient developed other neurological morbidities. Other reported risks include new facial sensory symptoms (2.7–10%). Brisman et al.[6,7] reported a 5% complication rate in patients treated with doses ranging between 70 and 80 Gy. Pollock et al.[38,41] reported a significant association between high radiation dose and increased risk of trigeminal neuropathy; 45% of the patients treated with a maximum dose over 90 Gy reported a trigeminal deficit compared with 15% of the lower-dose group. Increased risk of trigeminal nerve dysfunction has been reported with the use of high-dose (90 Gy) radiosurgery for TN.[33,41] Smith et al., using a dedicated linear accelerator for TN radiosurgery, reported a 25% rate of new numbness.[49]

Repeat Radiosurgery

Patients who experience recurrent pain during the long-term follow-up despite initial pain relief after radiosurgery can be treated with a second radiosurgery procedure.[16,19,23,39,52] At the second procedure, the radiosurgical target and dose slightly differ from the first procedure. The target is placed anterior to the first target so that the radiosurgical volumes at the second procedure overlap with the first one by 50%. Dose selection is still controversial. We advocate a lesser radiation dose (50–70 Gy) for the second procedure, because we believe that a higher combined dose would lead to a higher risk of new facial sensory symptoms. On the other hand, Pollock et al.[40] suggested a greater radiation dose to the same target at the second procedure than at the first.

They updated their results in a later study and concluded that repeat trigeminal neuralgia radiosurgery at higher doses had better facial pain outcomes; however, the rate of bothersome numbness was relatively high (16%). Therefore, dose

reduction is recommended to reduce the morbidity of repeat trigeminal neuralgia radiosurgery. Twenty-seven patients who had a second procedure at the University of Pittsburgh were evaluated at a median follow-up of 20 months. The mean time to recurrence was 18 months, and the mean interval between the first and second radiosurgical procedures was 22 months.

After the second radiosurgery, 5 of 27 (18.5%) patients had an excellent outcome, 8 (29.6%) had a good outcome, 10 (37.0%) had a fair outcome and 4 (14.8%) had a poor outcome. The rates of excellent or good outcome (complete relief and complete or partial pain relief) were 48.1% and 85.2%, respectively. We believe that the second radiosurgery procedure is as effective as the first in terms of the initial response.

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