Trigeminal Neuralgia

Abstract
Trigeminal neuralgia (TN) is a sudden, severe, brief, stabbing, and recurrent pain within one or more branches of the trigeminal nerve. Type 1 as intermittent and Type 2 as constant pain represent distinct clinical, pathological, and prognostic entities. Although multiple mechanism involving peripheral pathologies at root (compression or traction), and dysfunctions of brain stem, basal ganglion, and cortical pain modulatory mechanisms could have role, neurovascular conflict is the most accepted theory. Diagnosis is essentially clinically; magnetic resonance imaging is useful to rule out secondary causes, detect pathological changes in affected root and neurovascular compression (NVC). Carbamazepine is the drug of choice; oxcarbazepine, baclofen, lamotrigine, phenytoin, and topiramate are also useful. Multidrug regimens and multidisciplinary approaches are useful in selected patients. Microvascular decompression is surgical treatment of choice in TN resistant to medical management. Patients with significant medical comorbidities, without NVC and multiple sclerosis are generally recommended to undergo gamma knife radiosurgery, percutaneous balloon compression, glycerol rhizotomy, and radiofrequency thermocoagulation procedures. Partial sensory root sectioning is indicated in negative vessel explorations during surgery and large intraneural vein. Endoscopic technique can be used alone for vascular decompression or as an adjuvant to microscope. It allows better visualization of vascular conflict and entire root from pons to ganglion including ventral aspect. The effectiveness and completeness of decompression can be assessed and new vascular conflicts that may be missed by microscope can be identified. It requires less brain retraction.

Keywords: Cranial nerve, microvascular decompression, neurosurgical procedures/methods, route entry zone, trigeminal nerve diseases, trigeminal neuralgia, trigeminal neuralgia/surgery

Introduction
Trigeminal neuralgia (TN) is defined as sudden, severe, brief, stabbing, and recurrent pain within the distribution of one or more branches of the trigeminal nerve (TR N). Several destructive and nondestructive techniques are available for properly selected cases.[1] Microvascular decompression (MVD) may be considered over other techniques to provide the longest duration of pain freedom.[2] Younger patients benefit from MVD whereas the elderly patients with poor risk are more suitable for percutaneous procedures[3] and gamma knife radiosurgery (GKRS).[4]

This review is based on 17 years search on PubMed and Google including 27 years personal experience of over 600-microvascular decompression surgeries for TN.

Etiology
Although multiple mechanism involving peripheral pathologies at root (compression or traction), and dysfunctions of brain stem, basal ganglion, and cortical pain modulatory mechanisms could have role, neurovascular conflict is the most accepted theory. Artery or vein[5] is usually compressing the TR N near the pons injuring myelin sheath and causing erratic hyperactive functioning of the nerve. Focal arachnoid thickening, angulation, adhesion, traction, tethering or torsion, fibrous ring around the root, cerebello-pontine angle (CPA) tumors, brain stem infarction, aneurism, and arteriovenous malformation (AVM) can also cause TN.[6,7]

Central causes of the disease have also been proposed for TN; reduced basal ganglia μ-opioid receptor,[8] altered gray matter (GM) in sensory, and motor cortex has been implicated.[9] The dysfunction of multiple modulatory mechanisms probably plays a key role in the pathophysiology.[10]

Demyelination, dysmyelination giving increases to electrical hyper excitability, spontaneous and triggered ectopic impulse and cross excitation among neighboring afferents have been proposed in ignition hypothesis.[11] According to the bio
Vascular theory

Although it has been generally assumed that vascular contact at the root entry zone (REZ) cause TN, conflict anywhere on the root at central or peripheral myelin, in the region of REZ, or at transition zone between central and peripheral myelin can cause TN.[40] REZ and transition zone between central and peripheral myelin are distinct sites and that these should never be used interchangeably.[13] Peripheral myelin is more resistant to compression as compared to central myelin or transition zone.[14] The normal pulsation of artery may not be traumatic enough to produce TN, strokes due to unbinding of artery loop usually causes pathological changes in root.[15] Although displacement or grooving of the nerves has been observed in normal individuals,[16] more severe root indentation or distortion in proximal root is likely to produce TN.[17] Arterial compression is commonly seen, venous conflict alone or in combination to arterial compression has been observed in some patients as a cause of TN.[19]

Persistent primitive trigeminal artery,[20] its aneurysm,[21] and vertebrobasilar dolichoectasia[22] may cause TN. Sharper trigeminal-pontine angle,[23] smaller CPA cisterns and short cisternal TR Ns[24,25] can facilitate the neurovascular compression (NVC). Narrow foramen may be etiologically important in a small percentage of TN patients, especially in recurrent or residual cases in the absence of vascular compression during surgery.[26]

Pathophysiology

Exact pathophysiology of TN remains controversial. Chronic nerve compression results in demyelination, with progressive axonal degeneration in small unmyelinated and thinly myelinated fibers. Demyelination can leads to ephaptic transmission; reentry mechanism causes an amplification of sensory inputs. Ultra-structural and biochemical changes in axon and myelin are not only seen in root but also in Gasserian ganglion or in both the structures.[27] Atrophy of the TR N is also seen.[28,29] The GM volume reduction in the primary and secondary somatosensory cortex, orbitofrontal areas, thalamus, insula, anterior cingulate cortex, cerebellum, and dorsolateral prefrontal cortex has been observed.[30,31] Lower axial kurtosis and higher axial diffusivity in corticospinal tract, superior longitudinal fasciculus, anterior thalamic radiation, inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, cingulated gyrus, forceps major, and uncinate fasciculus was observed. There was complex functional connectivity density reorganization of hippocampus, striatum, thalamus, precentral gyrus, precuneus, prefrontal cortex, and inferior parietal lobule.[32] It is difficult to say whether the changes in cortical and subcortical area are cause or effect in TN.

Clinical Features

TN is characterized by episodes of spontaneous pain or a triggered intense facial pain that last for short duration. Pain may be like stabbing, electric shocks, burning, pressing, crushing, exploding, shooting, boring, shock-like sensations, migraine like, piercing, prickling, or a combination. TN is usually of two varieties with Type 1 as intermittent pain and Type 2 is constant. Although a subset of patients can progress from Type 1 to Type 2 TN over time, their pathological and prognostic profiles nevertheless resembled those of Type 1. Proponents of progressive change in character of pain theory think that the TN, atypical neuralgia, and trigeminal neuropathic pain may represent a continuous spectrum rather than discrete pathology,[33] whereas others believe that Type 1 and Type 2 TN represent distinct entities.[34]

Usually, pain resolves completely between the attacks. It usually does not occur when the person is asleep. It is estimated that 1 in 15,000 or 20,000 people suffer from TN, actual figure may be higher due to frequent misdiagnosis.[35] Higher incidence of TN as compared to other cranial nerves neuralgias could be due to longer lengths and more volumes of the central myelin.[36] Disease usually involve single division, it may slowly spread to other division. TN may be associated with ipsilateral hemifacial spasm (painful tic convulsive).[37] Multiple cranial nerve neuralgias, although rare, can occur.[38] It is usually unilateral, bilateral presentation is rare.[39] Rapid spreading to other division, bilateral involvement, or simultaneous involvement of other nerve suggests a secondary disease such as multiple sclerosis (MS) or expanding cranial tumor.

It is common after 50 years of age. TN is uncommon in young adults. Presentation in children is rare.[40] It is more common in females than males. Co-morbid depression is observed. It can be associated with Dandy walker syndrome, small posterior fossa, brain stem infarct, hydrocephalus, MS, lesions in relations to TR N, and opposite side tumor, etc.

Diagnosis

The diagnosis of TN is essentially clinical. Although such patients do not have any neurodeficit with normal blink reflex,[41] quantitative sensory testing have shown subtle sensory abnormalities which may not be detected in routine clinical examination.[42] Magnetic resonance imaging (MRI) imaging is aimed to detect changes in trigeminal root, any NVC and to rule out secondary pathology. MRI can diagnose entire course of nerve,[43] root atrophy, and CPA cistern.[20] Single finding (changes in nerve or the presence
of vascular conflict) in MRI scan may not be helpful in deciding symptomatic side, combination of vascular conflict, and anatomical changes in nerve, are highly likely to be associated with symptomatic TN.[44]

Detection of changes in trigeminal root

Diffusion tensor imaging (DTI) can detect increase in apparent diffusion coefficient and decrease in fraction of anisotropy (FA) in TR N.[45,46] Atrophic changes are also associated in TN. Coregistration of three-dimensional fast imaging employing steady-state (3D FIESTA) imaging and DTI facilitates excellent delineation of cisternal segments of TR Ns.[47] The deformity of the cranial nerves can be demonstrated using multislice motion-sensitized driven equilibrium technique.[48]

Vascular conflict detection

3D FIESTA,[49,50] and contrast-enhanced 3D time-of-flight (TOF) magnetic resonance angiography (MRA) in combination with unenhanced MRA could help in the identification of vessel.[51] 3D T2 high-resolution MRI in combination with 3D TOF-MRA and 3D T1-gadolinium enhanced imaging is reliable in detecting the root compression.[52,53] Although 3D - magnetic resonance cisternography can determine NVC in most of patients, it does have limitations in identification of venous compression.[54] Such veins can be detected by the 3D multifusion volumetric imaging using multidetector row computed tomography.[55]

3D high resolution MRI and image fusion technology could be useful for diagnosis of NVC in majority of patients.[56,57] Image fusion of 3D constructive interference in steady-state and high-resolution MRA is able to depict the complex anatomical relationships between neural and vascular structures.[58-59] Fusion MRI with multiplanar reconstruction can provide information about severity of the neurovascular contact.[60] Although both 1.5 and 3.0-T MRI can provide preoperative assessment of the compressing vessels,[61] 3-T may be of value when 1.5-T is equivocal.[62]

Medical Treatment

Carbamazepine (CBZ) is drug of choice in TN; baclofen, lamotrigine, clonazepam, oxcarbazepine, topiramate, phenytoin, gabapentin, pregabaline, and sodium valproate can be used.[63-65] Multi drugs are useful when patients are unable to tolerate higher doses of CBZ.[66] With an availability of increasing number of anticonvulsant drugs, it is likely that surgical option may not be offered for many years.[67]

Intravenous infusion of a combination of magnesium and lidocaine can be very effective in some patients.[68] Five percent lidocaine plaster[69] and 8% capsaicin patch[70] can be useful in some TN. The 5-HT R3 antagonists, neurokinin-1 antagonists, or mast cell stabilizers may have role in the treatment of TN. A multidisciplinary approach using antidepressants and anti-anxiety drugs such as amitriptyline[71] and duloxetine is needed for the management of emotional status.[72]

Botulinum toxin Type A injections may be offered before surgery or unwilling to undergo surgery, and in failed drug treatment.[73] Tetracaine nerve block as an additional treatment after CBZ, acupuncture and peripheral nerve stimulation can be used.[74-76] Deep brain stimulation of the posterior hypothalamus may be considered as an adjunctive procedure for refractory TN of first division,[77] especially in MS.[76] Motor cortex stimulation can be used in certain neuropathic or deafferentation pain.[79] Treatment of associated tumor, AVM, epidermoid, aneurism, and hydrocephalus in Chiari malformation can resolve TN.[80]

Gamma Knife Radiosurgery

Radiation may block the conduction of excessive sensory information responsible for triggering pain attacks.[81] Radiosurgery results in about 50% drop in FA values at the target with no significant change in outside the target nerve. Radiosurgery primarily affects myelin sheath.[82]

TN after a failed MVD, significant medical comorbidities, and MS are generally recommended to undergo GKRS.[44] It is indicated in typical or atypical TN,[83] with or without vascular compression,[84] and in recurrence after GKRS, glycerol rhizotomy (GR), radiofrequency thermocoagulation (RFTC), and percutaneous balloon compression (PBC).[85-87] Repeat GKRS provides a similar rate of pain relief as the first procedure. The best responses are observed when there is good pain control after first procedure, with new sensory dysfunction and in single division nerve distribution typical TN.[85-88]

GKRS can be given using one or two isocenters[89] and targeting radiosurgery posteriorly at dorsal REZ,[90] or anteriorly in retrogasserian zone.[91] 80 GY,[90] 85 Gy,[92] and 90 Gy can be used. Lower dose to the root are associated with less side effect, whereas higher doses provide better pain control with less risk of recurrences but more side effect such as facial numbness. The benefits and risks of higher dose must be carefully discussed with patients, since bothersome facial numbness, may be an acceptable for patients with severe pain.[93]

Radiosurgery can be given using single fraction; multiple fractions can deliver comparatively higher doses. Although hypofractionated stereotactic radiotherapy is not associated with any facial numbness, single fraction radiosurgery provides better pain relief and a lower recurrence rate as compared to hypofractionated technique.[94] Radiosurgery can be given with or without frame based method,[95] with MRI or computerized tomography (CT) planning when there is contraindication to MRI.[96]

Initial pain relief is 77%–96%, which takes about 1–3 weeks (sometimes 10 weeks or longer). Results are
Percutaneous Balloon Compression

PBC selectively avoids injury to the small unmyelinated fibers that mediate the corneal reflex. Balloon compression is indicated in patients difficult to communicate, MS, failed MVD, with significant medical comorbidity, multiple divisions including first division, without vascular compression, and in repeat PBC. PBC is reserved for patients in whom the effect of GR has been of short duration or difficult to repeat due to cisternal fibrosis. 3D CT reconstructions can identify an ideal pear shape configuration to improve outcome. Procedure can be performed under local or general anesthesia. There is controversy regarding duration of compression, in one study there were no differences in outcomes between 60 s and longer times, whereas in other study, longer compression time of 70–90 s resulted in better outcome. Pear shape balloon is an indication of proper compression and higher pain-free survival, whereas persistent elliptical shape is a bad sign and an indication for aborting the procedure. There is 2% risk of technical failures.

PBC is a safe, simple, and effective method of about 90% temporary pain relief. Repeat PBC, though associated with some increase in complications, is reasonably safe. Single trigeminal division, primary procedure in the absence of previous operations, and the pear shape balloon are associated to higher pain-free survival. Results in MS patients are comparable to classic TN. About 14%, 18.9%, 29.5% recurrence is observed within 2, 3, and 5 years follow up, respectively. Symptomatic dysesthesia, masseter muscle weakness, cardiovascular stress, cheek hemorrhages, corneal ulceration, infections, and transient diplopia are also observed.

Glycerol Rhizotomy

GR is indicated in patients unresponsive to pharmacotherapy, significant medical comorbidities, MS, unilateral and bilateral pain, and after failed MVD. It is cost-effective than MVD, RFTC and GKRS. GR is a safe and efficacious method as a repeat procedure. The immediate success rate is about 95% with 50%–60% recurrence at 24 months follow up. GR is a simple procedure, and most of the complications are reversible. There is significant positive correlation between the presence of cerebrospinal fluid (CSF) outflow and good success rate. Significant number may experience either mild numbness or dysesthesias. New facial numbness after GR is associated with excellent pain control. Anesthesia dolorosa although rare may be observed.

Radiofrequency Thermocoagulation

RFTC can be used in bilateral pathology, elderly, recurrence after failed MVD, verteobasilar dolichoectasia, and MS. Peripheral nerve block, and general anesthesia could relieve perioperative pain without an increase in complications. Although pulsed radiofrequency (PRF) treatment is associated with less complication than conventional RFTC, it is not as effective as the conventional procedure. Higher intraoperative PRF voltage and electrical field intensity may provide better pain relief. Combined PRF and continuous radiofrequency (CRF) can achieve comparable pain relief with lesser side effects as compared to CRF. Initial pain control rate is about 95% with about 25% recurrent pain, occasional jaw weakness, corneal anesthesia, and troublesome dysesthesia.

Peripheral Nerve Section

Peripheral neurectomy is a safe and effective procedure for elderly patients, in rural and remote centers where neurosurgical facilities are not available. Pterygopalatine fossa segment neurectomy of maxillary nerve can be used in elderly who may not tolerate craniotomy, or when RFTC and GR treatment is not possible. Pain relief can be lasting from 15 to 24 months. Loss of sensation and recurrences are associated with peripheral neurectomy.

Partial Sensory Root Section

Partial sensory root sectioning (PSRS) is indicated in MS associated with negative vessel explorations during MVD and in large intra neural vein that is difficult to mobilize. PSRS is also recommended in re exploration after failed MVD when there is no NVC. Excellent to good outcome is observed in 70% cases with minimal sensory loss.
**Microvascular Decompression**

MVD is indicated in Type 1 or Type 2 TN with NVC. The cure rate is higher in arterial compression compared to venous or no NVC. MVD is also indicated in MS isolated V2 TN, ectatic vessel with neuralgia, and after SRS. MVD is recommended in younger patients with longer life expectancy and healthy elderly [Figure 1]. Although less invasive procedure may be preferable in elderly patients, as complications do tend to increase gradually with an advanced age, MVD in physiologically healthy elderly population remains a reasonable surgical option.

Dissection in MVD is not significantly difficult after GKRS. Presurgical virtual endoscopy and 3D computer graphics models can provide excellent visualization of NVC and allows simulation. The dextroscope system can also create a stereoscopic neurovascular model to shorten the learning curve.

Indocyanine green angiography could be a helpful adjunct in decompressing the TR N and can guide the surgeon to the nerve-vessel conflict. All vessels, including the transverse pontine vein near meckel’s cave, in relation to the nerve should be decompressed. There may be multiple vessels related to the root. Sacrifice of a small intraneural vein can be performed while PSRS is preferred over extensive mobilization of large vein. Wrapping techniques can better decompress intraneural artery.

Prominent suprameatal tubercle should be drilled out for better exposure of entire TR N and vascular conflicts. Laterally placed craniotomy helps to visualize the whole nerve root along with REZ. Dissection of the cerebellar horizontal fissure and rostral retraction of the superior semilunar lobule allows easy identification of the REZ with minimal traction. Supracerbellar route permit identification and dissection of the offending supracerebellar artery. Whole surface of the TR N can be observed easily by combining these two approaches. Preservation of the vestibular nerve arachnoid minimizes complications and optimizes surgical outcome.

Autologous muscle graft oxidized regenerated cellulose and fibrin glue alone can be used to transpose vessel away from the nerve. Transposition of the offending vessel with Teflon wool or slings, especially in tortuous NVC, is a useful. Aneurysm clip with or without unabsorbable dural sling can be used.

Adhesion between the trigeminal root and surrounding structures, secondary to fibrin glue or prosthesis, can stretch nerve which can cause recurrence. Prosthesis if used should be lying in subarachnoid space or cistern avoiding contact to dura matter or tentorium. Arachnoid membrane of CPA can be used as a sling to transpose the superior cerebellar artery.

Combining OS or PSRS can be combined with MVD when no vascular conflict is detected. Muscle pieces interposition between the duramater, artificial dura mater, cranioplasty, sealing of mastoid sinuses by bone wax and muscle can be effective technique for the prevention of CSF leak. Re surgery is an effective and safe after failed MVD. The preservation of the petrosal vein and its tributaries, lateral inversion vein of ventricle IV is important in preventing the postoperative vestibular and cerebellar disorders.

Early outcome after MVD in typical TN with associated NVC is 90%–95% which drops to 75% at 1 and 5 years follow up. MVD is significantly superior to GKRS. TR N combing has a much higher pain relief in patients without vascular compression than those with vascular compression. 3D models by fusing CTA and FIESTA can be used to evaluate the translational and rotational shift of the compressive artery, and decompressed distance from the root after failed MVD.

Immediate postoperative pain relief is a good predictor of better long-term outcome. Type 2 TN, presence of autonomic symptoms, MS are associated with poor prognosis. Shorter preoperative duration, older age, and typical features are good predictors of favorable outcome. Subset of patients progressed from Type 1 to Type 2 TN over time also have good outcome resembling Type 1. Low FA values can be reversed after successful MVD. Significant reduction of FA value may predict an optimistic outcome of MVD.

The trigemino-cardiac reflex due to stimulation of the TR N during MVD may result in about 50% fall in heart rate and mean arterial blood pressure, cessation of manipulation lead to normalization of parameters. Facial nerve dysfunction, hearing abnormality, and TR N dysfunction may be observed, especially after more dissection and mobilization.
of respective nerve. Brainstem auditory evoked potential monitoring and neuro-endoscopy during MVD can preserve hearing function.\(^{[201]}\)

Recurrences, ranging from 18% to 34%, may be seen at long-term follow up.\(^{[202,203]}\) It is more common within 2 years of surgery and thereafter at a rate of 2%–3.5% per year.\(^{[202]}\) Significant predictors of recurrence are younger age, and symptoms lasting longer than 10 years.\(^{[203]}\) Recompression due to regrowth of new vein or artery\(^{[204]}\) can cause TN. Hardened Teflon can pierce nerve and produce TN,\(^{[205]}\) therefore the contact of prosthesis, if used, with the nerve should be avoided. Outcome can be improved by establishing center dealing TN.\(^{[206]}\) Late communicating hydrocephalus may be a potential complication of MVD surgery.\(^{[207]}\)

### Endoscopic Vascular Decompression

Endoscopic techniques are increasingly being used in spine,\(^{[208‑210]}\) skull base\(^{[211‑213]}\) and intracranial pathologies.\(^{[214‑216]}\) Endoscopic technique can be used alone in TN\(^{[217,218]}\) or as an adjuvant to microscope\(^{[219‑221]}\) It is a minimally invasive technique,\(^{[222]}\) allows better visualization of entire root from pons to ganglion\(^{[217,222,223]}\) including ventral aspect.\(^{[223]}\) The endoscope is a valuable tool during MVD, especially when a bony ridge hiding the direct microscopic view of vascular conflict.\(^{[224]}\) Effectiveness and completeness of decompression can be better assessed.\(^{[217,223]}\) New nerve-vessel conflicts can be identified which may be missed by microscope in 7.5%–33% of patients.\(^{[225‑228]}\) It is safe,\(^{[218,229‑232]}\) requires less brain retraction\(^{[217,225,233‑235]}\) and associated with improved pain relief with lower complications as compared to MVD.\(^{[236]}\) The vascular conflict is mostly distributed in the medial side on second division while it is in lateral area for third division in TN.\(^{[237]}\)

### Our recommendations

Medical treatment with drugs should be tried in TN. With an availability of increasing number of drugs it is likely that surgical option may not be offered for many years. Microscopic or endoscopic vascular decompression is recommended because of nondestructive nature, especially when NVC is present in young adults or healthy elderly [Figure 1]. GKRS, RFTC, GR, and PBC can be used in elderly patients with medical comorbidity and without NVC.

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### Conflicts of interest

There are no conflicts of interest.

### References

Trigeminal neuralgia due to neurovascular compression: Door-to-door survey of major neurological patients with idiopathic trigeminal neuralgia have a subtle sensory abnormalities detected by quantitative clinical analysis of trigeminal neuralgia caused by vertebrobasilar dolichoectasia. Neurosurg Rev 2013;36:573-7.


DeSouza DD, Hodaie M, Davis KD. Structural magnetic resonance imaging can identify trigeminal system abnormalities in classical trigeminal neuralgia. Front Neurol 2016;10:95.


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study comparing preoperative imaging analysis to surgical findings in 40 consecutive patients who underwent microvascular decompression for trigeminal neuralgia. Neurosurgery 2011;69:15-25.


World Neurosurg 2012;78:149-54.


