European Academy of Neurology guideline on trigeminal neuralgia

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Background and purpose: Trigeminal neuralgia (TN) is an extremely painful condition which can be difficult to diagnose and treat. In Europe, TN patients are managed by many different specialities. Therefore, there is a great need for comprehensive European guidelines for the management of TN. The European Academy of Neurology asked an expert panel to develop recommendations for a series of questions that are essential for daily clinical management of patients with TN.

Methods: A systematic review of the literature was performed and recommendations was developed based on GRADE, where feasible; if not, a good practice statement was given.

Results: The use of the most recent classification system is recommended, which diagnoses TN as primary TN, either classical or idiopathic depending on the degree of neurovascular contact, or as secondary TN caused by pathology other than neurovascular contact. Magnetic resonance imaging (MRI), using a combination of three high-resolution sequences, should be performed as part of the work-up in TN patients, because no clinical characteristics can exclude secondary TN. If MRI is not possible, trigeminal reflexes can be used. Neurovascular contact plays an important role in primary TN, but demonstration of a neurovascular contact should not be used to confirm the diagnosis of TN. Rather, it may help to decide if and when a patient should be referred for microvascular decompression. In acute exacerbations of pain, intravenous infusion of fosphenytoin or lidocaine can be used. For long-term treatment, carbamazepine or oxcarbazepine are recommended as drugs of first choice. Lamotrigine, gabapentin, botulinum toxin type A, pregabalin, baclofen and phenytoin may be used either alone or as add-on therapy. It is recommended that patients should be offered surgery if pain is not sufficiently controlled medically or if medical treatment is poorly tolerated. Microvascular decompression is recommended as first-line surgery in patients with classical TN. No

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recommendation can be given for choice between any neuroablative treatments or between them and microvascular decompression in patients with idiopathic TN. Neuroablative treatments should be the preferred choice if MRI does not demonstrate any neurovascular contact. Treatment for patients with secondary TN should in general follow the same principles as for primary TN. In addition to medical and surgical management, it is recommended that patients are offered psychological and nursing support.

Conclusions: Compared with previous TN guidelines, there are important changes regarding diagnosis and imaging. These allow better characterization of patients and help in decision making regarding the planning of medical and surgical management. Recommendations on pharmacological and surgical management have been updated. There is a great need for future research on all aspects of TN, including pathophysiology and management.

Introduction

Trigeminal neuralgia (TN) is an extremely painful disorder which can be difficult to diagnose and treat. In Europe, TN patients are managed by many different specialities including general practitioners, anaesthesiologists, dentists, neurologists and neurosurgeons and are only rarely concentrated in highly specialized centres. Therefore, there is a great need for comprehensive European guidelines for the management of TN.

The first guideline from the European Federation of Neurological Societies (EFNS) on TN was published in 2008 in cooperation with the American Academy of Neurology (AAN) [1]. Since then, important new knowledge has emerged regarding diagnosis, clinical characteristics and imaging, and new drugs are emerging. Moreover, the recommendations for preparation of guidelines have been updated [2], in particular the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system has been established and endorsed by the European Academy of Neurology (EAN) [2] as the method of choice to establish recommendations. The EAN therefore decided that the guideline for TN management needs revision.

One of the changes that occurred after the publication of the previous AAN-EFNS guideline is with regard to classification and terminology. In an attempt to settle the anarchic terminology and the different settings between the International Association for the Study of Pain and the International Headache Society, a new classification laid out three aetiological categories: idiopathic TN [no neurovascular contact (NVC) or NVC without morphological changes of the trigeminal root], classical TN (due to a neurovascular compression with morphological changes of the trigeminal root) and secondary TN (due to major neurological disease such as cerebellopontine angle tumours or multiple sclerosis). Also two phenotypes were classified: purely paroxysmal TN (with paroxysmal pain only) and TN with concomitant continuous pain [3]. This classification and the terminology have been shared by the latest edition of the International Classification of Headache Disorders [4] and by the World Health Organization International Classification of Disease [5]. Throughout this guideline, the above aetiological and phenotypical classification has been adopted. Previously, classical TN included what is now both idiopathic and classical TN. In this guideline, the term primary TN is used to describe a population consisting of patients with idiopathic TN as well as patients with classical TN.

Methods

The EAN identified an expert panel consisting of 14 members, including members within the fields of neurology, pain, neurosurgery, imaging and dentistry as well as a patient representative. Ten working groups each consisting of four to five members were appointed and were each responsible for one clinical question.

Recommendations were developed for a series of questions that are essential for the daily clinical management of patients with TN. Where possible, the Patients, Intervention, Comparison and Outcome (PICO) [2] method was used.

The first issue facing the clinician caring for a patient with TN is to establish the correct diagnosis. The diagnostic part of this guideline addresses the following questions:

1.1 Which clinical features correctly identify patients with secondary TN?

1.2 Which laboratory tests are required?

1.3 What role does NVC play in TN?
1.4 Which kind of imaging should be performed?

First-line therapy of TN is pharmacological. The pharmacological treatment part of this guideline addresses the following questions:

2.1 How should acute exacerbations be managed?
2.2 Which drugs have shown efficacy in TN in the long term?

Surgery should be considered if medical treatment is not effective or tolerated. The surgery therapy part of this guideline addresses the following questions:

3.1 When should surgery be offered?
3.2 Which surgical technique gives the longest pain-free period with the fewest complications?

Management of secondary TN and management of TN where medical and surgical options are exhausted can be challenging. The final part of this guideline addresses the following questions:

4.1 How should secondary TN be managed?
4.2 What other support can be provided for patients with TN?

The GRADE [2] method was used to develop recommendations. Final quality of evidence was rated as high, moderate, low or very low based on study design, study limitations, inconsistency, indirectness, imprecision, publication bias, effect size, dose response and confounding. Strength (strong or weak) and direction (for or against) of recommendations were determined on the basis of balance between desirable and undesirable effects, quality of evidence, values, and preferences and costs [2].

If GRADE was not applicable, a good practice statement was given, according to the available level of evidence. The Delphi method was used to reach consensus. To keep this guideline within the allowed length and to increase clarity, some of the sections have been condensed. The full background including references and tables is published as Appendix S1 and Tables S1–S12.

Search strategy

Papers published in peer-reviewed journals were identified using PubMed/MEDLINE, Embase and Cochrane Library. Search terms depended on the specific clinical question. A total of 10 working groups were appointed to cover the clinical questions. Each working group identified the relevant search terms and performed the search. The chair for each working group was responsible for the search strategy and selection of papers. Searches were restricted to English language and the time frame was since 2006 (last date of search of prior AAN-EFNS guidelines).

Section 1: Diagnosis

Clinical question 1.1: For patients with TN which clinical features correctly identify patients with secondary TN?

Search strategy and results

Papers studying the diagnostic accuracy of clinical characteristics for distinguishing primary from secondary TN were sought. In addition to the papers included in the previous guideline [6–11], two new papers were identified [12,13]. Involvement of the first trigeminal division and poor response to treatment were not significantly associated with secondary TN (Table 1). Secondary TN patients were significantly younger compared to primary TN patients. However, there was considerable overlap in the age ranges of patients with primary TN and secondary TN. Trigeminal sensory deficits were significantly more common in patients with secondary TN. However, many patients without sensory deficits had secondary TN reflecting low sensitivity. Bilateral secondary TN was in one study very frequent in TN due to multiple sclerosis (MS) but was not seen in studies of TN due to masses. Bilateral pain is thus associated with secondary TN due to MS but most secondary TN patients have unilateral pain reflected in a low pooled sensitivity.

Clinical guide

No clinical features have a high sensitivity for identifying patients with secondary TN. Patients with secondary TN seem to be younger and are more likely to have trigeminal sensory deficits and bilateral pain. However, the absence of these features does not rule out secondary TN and magnetic resonance imaging (MRI) is therefore strongly recommended as a part of early work-up in TN patients.

Final recommendation

Based on low evidence, no clinical characteristics can exclude secondary TN. MRI is strongly recommended as part of the work-up in TN patients.

Clinical question 1.2: For patients with facial pain, which laboratory tests are required to diagnose secondary TN? Which laboratory tests distinguish primary TN from other neuropathic facial pain conditions?

Search strategy and results

Papers reporting on the diagnostic accuracy of trigeminal reflex testing and evoked potentials for distinguishing secondary TN from primary TN were

Table 1 Diagnostic accuracy of clinical features for distinguishing secondary TN (STN) from primary (classical and idiopathic) TN (PTN)

First author	Year	Design	Spectrum	PTN STN	Number	Age of onset ± SD	Current age ± SD	Sensory deficits	First division	Bilateral	Poor treatment response
Liu [12]	2017	CO P	Narrow	PTN	2035	61[a]	63 ± 13	–	–	10/2035	–
				STN	35 (masses)	48[a]	52 ± 13	–	–	0/35	–
Truini [13]	2016	CO P	Broad	PTN	149	60 ± 12	–	0/149	–	–[b]	–
				STN	28 (MS)	50 ± 8	–	14/28	–	–	–
Cruccu [6]	2006	CO P	Broad	PTN	96	62 ± 12	–	0/96	28/96	0/96	–
				STN	24 (mixed)	51 ± 10	–	2/24	9/24	0/24	–
De Simone [7]	2005	CC P	Narrow	PTN	13	60 ± 12		4/13	8/13	0/13	–
				STN	15 (MS)	43 ± 11		10/15	3/15	0/15	–
Sato [8]	2004	CO R	Broad	PTN	43	–	–	–	–	–	3/43
				STN	7 (masses)	–	–	–	–	–	2/7
Goh [9]	2001	CO R	Broad	PTN	36	–	60 ± 13	0/36	–	0/36	–
				STN	6 (masses)	–	53 ± 11	1/6	0/6	0/6	1/6
Hooge [10]	1995	CS R	Narrow	PTN	0	–		–	–	–	–
				STN	35 (MS)	51		3/23	–	5/35	2/22
Nomura [11]	1994	CO R	Broad	PTN	58	47 ± 13		1/26	11/58	–	–
				STN	22 (masses)	48 ± 16		6/16	6/22	–	–
Pooled					*P* assoc	<0.0001	<0.0001	<0.0001	0.971	<0.0001	0.631
					Sen (CI)			32 (24–42)	27 (17–39)	4 (1–10)	14 (5–30)
					Spe (CI)			98 (96–99)	72 (64–79)	100 (99–100)	93 (81–99)
					Pos LR			20.6	1.0	9.5	2.1

CC, case–control; CI, 95% confidence interval; CO, cohort survey; CS, case series; MS, multiple sclerosis; *P* assoc, probability of statistically significant association between the presence of the characteristic and the presence of STN; P, prospective data collection; Pos LR, positive likelihood ratio; PTN, primary (idiopathic and classical) trigeminal neuralgia; R, retrospective or not described data collection; Sen, sensitivity (sensitivities calculated for the presence of the characteristic in STN); Spe, specificity (specificities calculated for the absence of the characteristic in STN); STN, secondary trigeminal neuralgia. [a]Approximate estimates based on symptom duration extracted from current age; [b]bilateral trigeminal neuralgia excluded *a priori*.

sought. Also papers addressing the role of laboratory tests in detecting trigeminal afferent damage in other neuropathic facial pain conditions were sought. Eight studies reported the trigeminal reflex findings in patients with TN [6,14–20] (Table 2). The diagnostic accuracy of trigeminal reflexes for identifying secondary TN patients was relatively high with sensitivity 59%–100% and specificity 93%–100%; pooled sensitivity 94%; pooled specificity 88%. Six studies reported the evoked potential findings in patients with TN [17,19,21–24] (Table 3). In contrast to the trigeminal reflexes, evoked potentials may be altered even in idiopathic or classical TN. A pooled sensitivity of 84% and a pooled specificity of 52% were found.

Two studies reported trigeminal reflex and evoked potential findings in patients with post-herpetic neuralgia [25,26]. The diagnostic accuracy of neurophysiological tests for identifying trigeminal afferent damage in the affected side was high with pooled sensitivity 100%; pooled specificity 100% and 88% respectively. One study reported masseter inhibitory reflex findings in iatrogenic damage to the mandibular nerves [27]. Specificity and sensitivity were 99% and 51% respectively. These findings indicate that masseter inhibitory reflex testing, showing an almost absolute specificity, reliably demonstrates nerve damage, whereas the relatively low sensitivity makes the finding of a normal masseter inhibitory reflex by no means sufficient to exclude nerve damage. Jääskeläinen and colleagues [28] found abnormal mental and lingual nerve blink reflexes in 38% of patients with trigeminal neuropathy due to surgical procedures. Trigeminal reflex recording is particularly helpful in rare cases of trigeminal isolated sensory neuropathy and facial-onset sensory motor neuropathy syndrome [29] that may manifest, in early stages, with unilateral paroxysmal pain.

Clinical guide

Magnetic resonance imaging is the first-choice tool for diagnosing secondary TN. If MRI is contraindicated or unavailable, testing of trigeminal reflexes is useful to distinguish secondary TN from primary TN. Trigeminal reflexes and evoked potentials are also needed to detect trigeminal afferent damage in patients with different neuropathic facial pain conditions.

Table 2 Diagnostic accuracy of trigeminal reflex testing for distinguishing secondary TN (STN) from primary TN (PTN)

First author	Year	STN A/T	PTN A/T	*P* assoc	Spe (CI)	Sen (CI)
Kimura [14]	1970	1/1	1/14	NS	93%	100%
Ongerboer de Visser [15]	1974	16/16	0/11	<0.0001	100%	100%
Kimura [16]	1983	10/17	4/93	<0.0001	96%	59%
Cruccu [17]	1990	4/4	2/30	<0.0003	93%	100%
Cruccu [6]	2006	23/24	7/96	<0.0001	93%	96%
Cruccu [18]	2009	41/46	–	NS	–	89%
Squintani [19]	2015	–	0/11	NS	100%	–
Liao [20]	2010	–	3/49	NS	94%	–
Pooled		95/108	17/304	<0.0001	94% (91–96)	88% (80–93)

A/T, abnormal/total; CI, 95% confidence interval; NS, not significant; *P* assoc, probability of statistically significant association between the presence of the characteristic and the presence of STN; PTN, primary (idiopathic and classical) trigeminal neuralgia; Sen, sensitivity (sensitivities calculated for the presence of abnormal trigeminal reflexes in STN); Spe, specificity (specificities calculated for the absence of abnormal trigeminal reflexes in STN); STN, secondary trigeminal neuralgia.

Table 3 Diagnostic accuracy of evoked potentials for distinguishing secondary TN (STN) from primary TN (PTN)

First author	Year	Method	STN A/T	PTN A/T	*P* assoc	Spe (CI)	Sen (CI)
Leandri [21]	1988	Electrical TEPs	18/23	9/38	<0.0001	76%	78%
Cruccu [17]	1990	Electrical TEPs	4/4	9/30	<0.05	70%	100%
Cruccu [22]	2001	Laser EPs	20/20	24/47	<0.0001	49%	100%
Mursch [23]	2002	Electrical TEPs	6/10	13/37	NS	65%	60%
Squintani [19]	2015	Laser EPs		11/11	NS	0	
Obermann [24]	2007	PREPs		24/24	NS	0	
Pooled			48/57	90/187	<0.0001	52% (45–59)	84% (73–91)

A/T, abnormal/total; CI, 95% confidence interval; EPs, evoked potentials; NS, not significant; *P* assoc, probability of statistically significant association between the presence of the characteristic and the presence of STN; PREPs, pain-related evoked potentials; PTN, primary (idiopathic and classical) trigeminal neuralgia; Sen, sensitivity (sensitivities calculated for the presence of abnormal evoked potentials in STN); Spe, specificity (specificities calculated for the absence of abnormal evoked potentials in STN); STN, secondary trigeminal neuralgia; TEPs, trigeminal evoked potentials.

Final recommendations

In cases where MRI is contraindicated or unavailable, a strong recommendation is given about the use of trigeminal reflexes to distinguish secondary TN from primary TN. For patients with TN, abnormal trigeminal nerve evoked potentials are probably associated with an increased risk of secondary TN. However, there is too much overlap in patients with primary TN and secondary TN for this predictor to be considered clinically useful. A strong recommendation is given against using evoked potentials to identify secondary TN. In patients with different neuropathic facial pain conditions, trigeminal reflexes and evoked potentials are needed to detect trigeminal afferent damage.

Clinical question 1.3: What role does NVC play in primary TN?

Search strategy and results

Reports of prospective studies of broad-spectrum primary TN patients were sought, comparing the blinded symptomatic and asymptomatic side by high resolution MRI and grading the NVC as to whether there are morphological changes of the trigeminal nerve. 'Broad spectrum' was defined to be TN patients from neurological settings. Three studies were identified fulfilling the search criteria [30–32]. All three studies were prospective cohort studies.

Neurovascular contact of any kind was a frequent finding on the asymptomatic side (120/175 asymptomatic nerves) (Table 4), whilst NVC with morphological changes was a rare finding on the asymptomatic side (20/175 asymptomatic nerves). Idiopathic TN was moderately associated with an NVC without morphological changes on the symptomatic side (odds ratio 2.3, $P = 0.008$) (Table 5). Classical TN was highly associated with NVC with morphological changes on the symptomatic side (odds ratio 13.3, $P < 0.001$).

Clinical guide

Trigeminal neuralgia is associated with NVC of any kind on the symptomatic side and highly associated with NVC with morphological changes on the symptomatic side. As NVC without morphological changes is a frequent variation of normal neuroanatomy, NVC should not be used as a diagnostic tool to diagnose or exclude TN in facial pain patients. In a recent prospective study using independent assessors of outcome, it was demonstrated that patients with classical TN have a higher chance of a successful outcome after microvascular decompression (MVD) compared to idiopathic TN patients [33]. However, a significant proportion of patients with idiopathic TN also had good pain relief after MVD [33]. Thus, it seems that an NVC

Table 4 Prevalence, associations, sensitivity and specificity of MRI-verified neurovascular contact of any type and with morphological changes in patients with primary (idiopathic and classical) TN (PTN)

Author	Year	MRI field strength	No.	Symp NVC	Asymp NVC	Odds ratio	*P* value	Sen (CI) %	Spe (CI) %	Symp NVC + MC	Asymp NVC + MC	Odds ratio	*P* value	Sen (CI) %	Spe (CI) %
Masur [30][a]	1995	1.5 T	16	10	6	5.0	0.221	63	62	7	0	15.0	0.023	44	100
Maarbjerg [31][b]	2014	3.0 T	135	120	105	2.0	0.014	89	22	71	18	11.6	<0.001	53	87
Antonini [32][b]	2014	1.5 T	24	21	9	7.0	0.006	88	63	16	2	15.0	0.001	67	92
Pooled confidence interval			175	151	120	3.2 (1.7–6.3)	<0.001	86 (80–91)	31 (25–39)	94	20	13.3 (5.8–30.6)	<0.001	54 (46–61)	89 (83–93)

Asymp NVC, number of neurovascular contacts of any kind on the asymptomatic (pain-free) side; CI, 95% confidence interval; MRI, magnetic resonance imaging; NCV + MC, neurovascular contact with morphological changes; No., number of patients; Sen, sensitivity (sensitivities calculated for the presence of NVC in primary TN); Spe, specificity (specificities calculated for the absence of NVC in primary TN); Symp NVC, number of neurovascular contacts of any kind on the symptomatic (painful) side; T, tesla; TN, trigeminal neuralgia. Morphological changes were defined as compression, distortion, dislocation or atrophy of the trigeminal nerve at the site of a neurovascular contact. [a]The study is based on 18 patients but in two patients NVC status could not be judged due to artefacts; to enable calculation of the odds ratio for NVC + MC 0.5 was added to each cell; [b]for the purpose of this guideline the authors provided the original datasets.

Table 5 Association between neurovascular contact without morphological changes and the symptomatic side in idiopathic TN and association between neurovascular contact with morphological changes and the symptomatic side in classical TN

	Idiopathic TN					Classical TN				
Author	No.	Symp NVC	Asymp NVC	Odds ratio	*P* value	No.	Symp NVC + MC	Asymp NVC + MC	Odds ratio	*P* value
Masur [30][a]	9	3	2	2.0	1.000	7	7	0	15.0	0.034
Maarbjerg [31][b]	64	49	47	2.4	0.021	71	71	18	11.6	<0.001
Antonini [32][b]	8	5	3	2.0	0.344	16	16	2	15.0	0.001
Pooled confidence interval	81	57	52	2.3 (1.2–4.3)	0.008	94	94	20	13.3 (5.8–30.6)	<0.001

Asymp NVC, number of neurovascular contacts of any kind on the asymptomatic (pain free) side; NCV + MC, neurovascular contact with morphological changes; No.: number of patients; Symp NVC, number of neurovascular contacts of any kind on the symptomatic (painful) side; TN, trigeminal neuralgia. Morphological changes were defined as compression, distortion, dislocation or atrophy of the trigeminal nerve due to a neurovascular contact. [a]The study is based on 18 patients but in two patients NVC status could not be judged due to artefacts; for the calculation of odds ratio for NVC + MC 0.5 was added to each cell; [b]for the purpose of this guideline the authors provided the original datasets.

without morphological changes does play a role in some idiopathic TN patients who are therefore not truly 'idiopathic'. In idiopathic TN, and probably also to a lesser degree in classical TN, other currently unknown aetiological factors probably play an important role.

Final recommendations

Based on a high quality of evidence, a strong indication is given that idiopathic TN is moderately associated with NVC without morphological changes and that classical TN is highly associated with NVC with morphological changes. Therefore, demonstration of NVC should not be used to confirm the diagnosis of TN. Rather, it may help to decide if and when a patient should be referred for an MVD.

Clinical question 1.4: For patients with TN, which kind of imaging should be done to demonstrate NVC and rule out other causes of TN?

Search strategy and results

Trigeminal neuralgia studies evaluating NVC using MRI, three-dimensional (3D) imaging, 3D T2-weighted imaging, 3D time-of-flight (TOF) magnetic resonance angiography (MRA) and 3D T1-weighted gadolinium (T1-Gad) were sought. Studies using imaging protocols were investigated to facilitate the diagnosis of TN and to detect the presence of NVC in comparison to intra-operative data. The following criteria for acceptable studies were set: (i) diagnostic criteria stated; (ii) a minimum of 20 patients who had undergone MVD to allow a comparison with preoperative imaging analysis; (iii) MRI characteristics (machinery and sequences) stated; (iv) blinded control studies; and (v) unequivocal data of sensitivity and/or specificity for detection of NVC.

No randomized controlled trials (RCTs) were identified. Fifteen studies were found investigating the accuracy of preoperative imaging examination to predict the presence of NVC [34–48]. All studies compared the preoperative imaging analysis with surgical data. Nine studies were performed using a 1.5-T MR scanner [34,36,38,40–43,45,46], six with a 3-T scanner [35,37,39,44,47,48], five studies applied an imaging protocol with only 3D TOF-MRA [34,37,40,43,45]; five with a combination of 3D T2-weighted and 3D TOF-MRA [36,38,39,42,46]; two with a combination of 3D T2-weighted, 3D TOF-MRA and 3D T1-Gad [41,48]; two with a combination of 3D TOF-MRA and 3D T1-Gad [35,47]; and one study with a combination of 3D T2-weighted and 3D fluid-attenuated inversion recovery (FLAIR) [44]. The sensitivity and the specificity of the imaging protocol in detecting NVC varied, respectively, from 67% to 100% and from 50% to 100%.

Clinical guide

Standard MRI can be used to exclude secondary intracranial pathology such as MS and tumours but has not proved to be sufficient to establish or exclude vessel–nerve contact. High-spatial-resolution 3D T2 sequences (driven equilibrium, DRIVE; constructive interference in steady state, CISS; fast imaging employing steady state, FIESTA) all allow excellent contrast between the cerebrospinal fluid (hypersignal) and neurovascular structures (hyposignal) producing high-performance cisternography [48]. The limitations are the lack of signal differentiation, not only between arteries and veins and between vessels and nerves, but also for the brain parenchyma. 3D TOF-MRA provides good visualization of the arteries in hypersignal, contrasting with the cerebrospinal fluid in hyposignal. Nerves are visible, but they are difficult to distinguish because of their intermediate signal [48]. Veins,

because of their low flow, are not usually visible, especially if a band of presaturation filter is applied. 3D T1-Gad allows the visualization of nerves in intermediate signal in relation to cerebrospinal fluid and shows both arteries and veins in hypersignal [48]. Three tesla is probably preferable over 1.5 T. Thin slices should be used. It should be described whether a vessel contact causes morphological changes of the nerve. It is recommended that the neuroradiologist is blinded to the side of pain in order to avoid bias in evaluation of NVC. If MRI is unavailable or contraindicated a computed tomography scan with contrast should be considered to rule out tumours.

Final recommendations

Magnetic resonance imaging should be performed in all patients to exclude secondary causes of TN. A combination of three high-resolution sequences – 3D T2-weighted, 3D TOF-MRA and 3D T1-Gad – aids the detection of a possible NVC. The neuroradiologist should be blinded to the side of pain. It should be described whether a vessel contact causes morphological changes of the nerve. These recommendations are based on low quality of evidence.

Section 2: Pharmacological treatment

Clinical question 2.1: For patients with primary TN, which interventions are effective in the treatment of acute exacerbations of pain?

Search strategy and results

Reports on the use of intravenous drugs in the emergency management of TN were sought.

One RCT on the use of intravenous lidocaine in acute exacerbation was found [49]. In this trial, a single dose of intravenous lidocaine (5 mg/kg over 60 min) was superior in reducing pain intensity compared to placebo during the first 24 h after the infusion. The most common side effect was somnolence. Three reports were found, totalling five patients with acute exacerbations of TN, responding to intravenous infusion of phenytoin or fosphenytoin, with pain relief lasting 2 days [50–52], but no RCT has been conducted. No reports supporting the use of opioids in acute exacerbations of TN were found.

Clinical guide

In acute exacerbations, in-hospital treatment may be necessary for titration of anti-epileptic drugs and rehydration. Acute pain relief is crucial for affording a window of opportunity to adjust oral drugs and to control pain in consideration of a possible neurosurgical intervention. It is clinical experience that opioids are not effective in acute exacerbations of TN. It is clinical experience that intravenous infusion of fosphenytoin and lidocaine is effective for pain relief of acute exacerbations, but evidence is lacking. The intravenous infusion should be performed only under specialist supervision because hospital admission and cardiac monitoring are required.

Final recommendations

Given the very low quality of evidence there is weak recommendation for the use of intravenous fosphenytoin and lidocaine in acute exacerbations of pain.

Clinical question 2.2: For patients with primary TN, which drugs have been demonstrated to be effective for the treatment of pain in the long term?

PICO

Population: patients with primary TN
Intervention: most used drugs
Comparison: no treatment or most used drugs
Outcome: reduction of pain to an acceptable level with acceptable side effects for the patient (grade of importance: critical).

Search strategy. Criteria for inclusion were published systematic reviews and RCTs, at least single-blinded and containing more than 10 individuals, of whom more than 80% were followed up. For GRADE evaluation see Table 6. Results for each of the relevant drugs are as follows.

Carbamazepine

Results. From the systematic reviews [53] and RCTs [54–58], carbamazepine seems to be more effective at relieving pain compared with placebo but more patients withdrew when using carbamazepine than placebo because of side effects. All the RCTs were small and short term although some converted to open label follow-up, used simple measures for pain outcomes and reported no quality of life outcomes. One RCT showed improved outcome if ropivacaine injections were added [59].

Clinical guide. Carbamazepine is considered the gold standard for the initial medical treatment of TN. Carbamazepine has been shown to increase pain relief compared with placebo, but also causes adverse effects such as drowsiness, dizziness, rash, liver damage and ataxia and has the potential for multiple drug interactions. Consensus expert opinion suggests that carbamazepine may have a 50% failure rate for long-term (5–10 years) pain control [58,60]. Based on the strength of published evidence, carbamazepine remains the best supported standard medical treatment for TN.

Recommendation. Based on a moderate quality of evidence, a strong recommendation is given that carbamazepine is used for long-term treatment of TN.

Table 6 GRADE evaluation of pharmacological treatment studies in primary TN

Studies (participants)	Outcome	Comparison	Design	Quality	Effect size	GRADE quality of evidence	Direction	Strength	Comment
Wiffen (208) [53]	Pain relief	Carbamazepine up to 2400 mg vs. placebo	RCT	−3	+2	Moderate	For	Strong	Quality points deducted for crossover design and short follow-up; directness point deducted for inclusion of different pain severities and uncertainties about diagnostic criteria and outcomes measured; effect size points added for RR = 5 or higher
Liebel (48) [61]	Pain relief	Oxcarbazepine 750 mg vs. carbamazepine	RCT	−3	0	Very low	For	Strong	Quality points deducted for sparse data, incomplete reporting of results, and no direct comparison between groups
Zakrzewska (14) [64]	Pain relief	Lamotrigine 400 mg as add-on vs. placebo	RCT	−3	0	Very low	For	Weak	Quality points deducted for sparse data and crossover design with no pre-crossover results; directness point deducted for concurrent use of other medications
Yuan (1331) [65]	Pain relief	Gabapentin up to 3600 mg vs. carbamazepine	RCT	−3	+1	Low	For	Weak	High risk of bias, wide confidence limits
Morra (178) [66]	Pain relief	Botox vs. placebo, variable doses	RCT	−3	0	Very low	For	Weak	Variable techniques and dosages, varying time periods, quality points deducted for risk of bias, small sample sizes, similar age and duration of symptoms but other drug usage unknown, missing data

RCT, randomized controlled trial; RR, relative risk; TN, trigeminal neuralgia.

Oxcarbazepine

Results. No fully reported RCTs on oxcarbazepine in TN were found. One small RCT was found comparing oxcarbazepine and carbamazepine for relieving pain after 4–6 weeks of treatment [61]. One non-systematic review [62] found that oxcarbazepine and carbamazepine were associated with similar reductions in attacks (pain, global symptoms) of TN; however, oxcarbazepine may possibly be associated with fewer side effects than carbamazepine but both drugs show reduced tolerability in females [63].

Clinical guide. Oxcarbazepine is considered effective for the treatment of TN. It is not known how oxcarbazepine and carbamazepine compare at relieving pain. Clinical experience suggests both the effect and side effects may differ for the individual patient when treated with carbamazepine and oxcarbazepine [63]. Cross-allergy between the drugs is reported.

Recommendation. Based on a very low quality of evidence, but high confidence from clinical experience of the effect of oxcarbazepine in TN, a strong recommendation is given that oxcarbazepine is used for long-term treatment of TN.

Lamotrigine

Results. One small double-blind crossover RCT was found comparing the add-on of lamotrigine versus placebo in patients receiving carbamazepine or phenytoin [64]. Lamotrigine was possibly superior to placebo after 2 weeks of treatment [64].

Clinical guide. Lamotrigine may possibly be associated with fewer side effects than carbamazepine and oxcarbazepine. Lamotrigine can be used in patients who cannot tolerate carbamazepine and oxcarbazepine, or in addition to carbamazepine or oxcarbazepine when the latter become less effective. The dose of lamotrigine must

be escalated slowly in order to avoid rashes, and it is therefore not appropriate for acute management of TN.
Recommendation. Based on a very low quality of evidence, a weak recommendation is given that lamotrigine is used either as monotherapy or as add-on therapy for long-term treatment of TN.

Gabapentin
Results. One systematic review was found [65] which was based on 16 RCTs, all published in Chinese, comparing gabapentin with carbamazepine. However, the diagnostic criteria used were not clarified and the dosages used varied. Gabapentin is probably associated with fewer adverse effects than carbamazepine and oxcarbazepine.
Clinical guide. Clinical experience shows that gabapentin has a lower effect but also fewer adverse events than carbamazepine and oxcarbazepine. Gabapentin can be used in patients who cannot tolerate carbamazepine and oxcarbazepine, or in addition to carbamazepine or oxcarbazepine when the latter become less effective.
Recommendation. Based on low quality of evidence, a weak recommendation is given that gabapentin is used either as monotherapy or as add-on therapy for long-term treatment of TN.

Botulinum toxin type A (Botox)
Results. One systematic review was found [66] which included RCTs. The dosage used varied from 25 to 100 U. There is some evidence that at 12 weeks botulinum toxin type A may result in a 50% decrease in pain severity and frequency with continuation of other systemic drugs. The source, dosage and method of administration are highly variable. An open label study found that 25% of patients remain pain free at 14 months post injection [67].
Clinical guide. There is limited clinical experience, but it is possible that botulinum toxin type A may have an effect as an add-on therapy in some selected cases.
Recommendation. Based on very low quality of evidence, a weak recommendation is given that botulinum toxin type A is used as add-on therapy for medium-term treatment of TN.
Other drugs. It is clinical experience that pregabalin, baclofen and phenytoin may have an effect in TN. The addition of ropivacaine injection to either carbamazepine or gabapentin may have an effect. No good evidence of benefit from any RCTs regarding these drugs was found.

Final recommendations on pharmacological treatment
In acute exacerbations, in-hospital treatment may be necessary for titration of anti-epileptic drugs, rehydration and intravenous infusion of fosphenytoin or lidocaine. For long-term treatment carbamazepine (200–1200 mg/day) or oxcarbazepine (300–1800 mg/day) remain the most effective medications especially in the early stages of TN. Sometimes even higher doses are needed. Retard (slow release) preparations are available but there are no studies to compare them with the conventional forms. However, if these drugs become ineffective or result in poor tolerability, then other drugs need to be considered. Based on low to very low quality of evidence, lamotrigine, gabapentin, botulinum toxin type A, pregabalin, baclofen and phenytoin may be used either as monotherapy or combined with carbamazepine or oxcarbazepine when first-line drugs fail due to either efficacy or tolerability. Patients should be encouraged to alter the dosages depending on pain severity and side effects, as periods of partial or complete remission do occur [68]. However, it is crucial that patients are instructed to increase and decrease dosages slowly over several days. It is not essential to try out all the drugs prior to referral for a neurosurgical opinion. It remains the responsibility of the managing doctor to ensure that the patient is aware of neurosurgical options and can take an informed decision about choice of treatment.

Section 3: Surgical treatment

Clinical question 3.1: For patients with primary TN, how many drugs have to be tested before surgery should be offered?

Search strategy and results
Studies with a minimum of 25 patients evaluating the optimal time for TN patients to be offered surgery, and more specifically how many drugs need to be tried before the option of surgery should be offered, were sought. No studies were identified addressing this topic. Three descriptive studies were identified dealing with the broader question of when surgery should be offered [68–70]. The studies indicated that patients with TN refractory to medical therapy would possibly prefer an early surgical option. In a series of 156 TN patients, most patients (88%) preferred a surgical option to medical management [71]. One prospective study [72] reported that 65% of patients referred to a specialist centre could be satisfactorily managed medically 2 years after referral, whilst 35% were referred to surgery. A retrospective study of 200 patients managed medically for TN revealed that only a minority experienced a worsening of pain over time and/or development of late resistance [73].

Clinical guide

Based on expert opinion, medical management with adequate doses and regular monitoring is recommended before offering surgery for TN. Existing data indicate that not all patients need surgery, but also that some patients may be referred for surgery too late. No data indicate how many drugs must be tested before surgery should be offered.

Final recommendations

Based on a very low quality of evidence, medical management is recommended before offering surgery for TN. Patients should be offered surgery if their pain is not sufficiently controlled medically or if medical treatment is poorly tolerated and should be informed of the possibility at an early stage.

Clinical question 3.2: Which surgical technique gives the longest pain-free period with the fewest complications?

Search strategy and results

Trials involving MVD, other posterior fossa surgery [partial sensory rhizotomy (PSR) and internal neurolysis (IN)], gamma knife surgery (GKS), radiofrequency thermocoagulation (RFTC), balloon compression (BC) and glycerol rhizolysis (GR) were sought up to January 2018. Two different search targets were defined: (i) comparative trials involving any two of the above interventional treatments; (ii) clinical trials of each surgical intervention separately. To be included in the analysis a comparative trial had to involve only patients with classical or idiopathic TN with a minimum of 1-year follow-up and report the outcome as the proportion of patients free of pain [Barrow Neurological Institute (BNI) score of I] or with occasional pain but no need for medication (BNI II). For single intervention studies the following criteria for acceptable studies were set: (i) minimum of 3-year follow-up period; (ii) minimum of 25 patients treated for TN; (iii) study dealing with classic or idiopathic TN; (iv) diagnostic criteria stated; (v) definition of success presented; (vi) definition of recurrence presented; (vii) duration of follow-up period with range and mean presented; (viii) explicit definition of outcome measure used; (ix) mortality rate stated; and (x) report of complications. For GRADE evaluation see Tables 7–9.

Microvascular decompression versus neuroablative treatments. No RCTs were identified. Four non-randomized prospective studies were found comparing the long-term (>1-year) impact of first-time MVD versus first-time GKS totalling 561 patients (MVD, $N = 287$; GKS, $N = 274$) [74–77]. All studies showed

Table 7 Prospective trials comparing microvascular decompression (MVD) and gamma knife surgery (GKS)

Author	MVD (*N*) GKS (*N*)	Outcome[a] 1-year	Outcome[a] 1.5-years	Outcome[a] 2-years	Outcome[a] 4-years	Outcome[a] 5-years	K–M curve log rank,	RR	GRADE
Brisman 2007 [74]	MVD (24) GKS (61)	MVD 68% GKS 58%	MVD 68% GKS 24%				$P = 0.089$		Low
Linskey 2008 [75]	MVD (36) GKS (44)			MVD 88% GKS 50%		MVD 80% GKS 33%	$P = 0.0002$	3.35	Low
Pollock 2010 [76]	MVD (91)[b] GKS (49)	MVD 84% GKS 66%			MVD 77% GKS 56%		$P = 0.003$	2.25 (1.4–4.6)	Low
Wang 2018 [77]	MVD (136) GKS (120)	MVD 83% GKS 71%		Outcome 1–2 years		MVD 61% GKS 47% Outcome 4–5 years	$P = 0.006$		Low
Total	MVD (287) GKS (274)	MVD 68–84% GKS 58–71%		MVD 68–88% GKS 50–71%		MVD 61–80% GKS 33–56%			Low

K–M, Kaplan–Meier; RR, relative risk. [a]Outcome, percentage of patients pain-free on no medication; [b]posterior fossa exploration; 91% had MVD.

Table 8 Retrospective trials comparing microvascular decompression (MVD) and gamma knife surgery (GKS)

Author	MVD (*N*) GKS (*N*)	Outcome time point	Outcome	GRADE
Oh 2008 [81]	MVD (27) GKS (18)	33 months (mean)	MVD 63% GKS 56%	Very low
Dai 2016 [78]	MVD (87) GKS (115)	2 years	MVD 72% GKS 60%	Very low
Nanda 2015 [79]	MVD (20) GKS (49)	5.3 years (median)	MVD 75% GKS 37%	Very low
Inoue 2017 [80]	MVD (179) GKS (52)	3.3 years (median) 5.0 years (median)	MVD 80% GKS 39%	Very low

the superiority of MVD over GKS with a substantial effect size at both medium and long term (Table 7). At 1–2 years postoperatively, 68%–88% of patients who underwent MVD reported being free from pain with no need for medication (BNI I), whilst 24%–71% did so after GKS. At 4–5 years, the percentages were 61%–88% for MVD and 33%–56% for GKS. Four non-randomized retrospective studies involving a total of 957 patients demonstrated a similar superiority of first-time MVD over GKS both at medium and long term (Table 8) [78–81]. Three systematic reviews comparing published results from independent treatment cohorts using various inclusion criteria demonstrated a longer postoperative pain-free status for MVD compared to GKS [82–84]. One non-randomized prospective study evaluated the outcomes at 3 years after MVD versus GR or RFTC [85], showing that MVD provided a greater percentage of pain-free status at 36 months compared to GR and RFTC. A retrospective study with 2–3 years' follow-up showed that significantly more patients were completely pain-free after MVD than BC [86].

Comparison of neuroablative treatments. It was not possible to find any randomized or non-randomized studies fulfilling the above inclusion criteria that compared long-term effectiveness between GKS, GR, BC and RFTC.

Single intervention trials. No RCTs were identified. Forty-five non-randomized cohort studies fulfilling the search criteria (seven, three, five, eight, one and 21 studies for RFTC, GR, BC, GKS, IN and MVD, respectively) were found (Table 9). Accepting some variability in the duration of observation periods across procedures, there appears to be a trend in favour of MVD with a median of 77% (range 62%–89%) of patients being pain free at long-term follow-up. The same percentages for IN, GKS, BC, RFTC and GR are 72%, 58% (30%–66%), 68% (55%–80%), 58% (26%–82%) and 28% (18%–59%) respectively. None of the case series on the effectiveness of PSR fulfilled the inclusion criteria. For more details see Appendix S1 and Tables S1–S12.

Complications. Reported complication rates from cohort studies are summarized in Table 10. For more details see Appendix S1 and Tables S1–S12. Only MVD is associated with reported mortality, although anecdotally it is known that RFTC and BC have in the past very rarely resulted in the patient's death. The distribution of complications reflects the nature of the operation. The small number of complications associated with GKS is noteworthy. Most of the reported complications are transitory and severe permanent adverse effects are rare. It should also be emphasized that facial hypaesthesia following neuroablative

Table 9 Summary of outcomes from single intervention trials

Intervention	No. studies	Total no. patients	Mean/median F/U, years	Pain free at F/U, %	GRADE
MVD	21	5149	3–10.9	62–89	Very low
GKS	8	1168	3.1–5.6	30–66	Very low
RFTC	7	4533	3–9.3	26–82	Very low
BC	5	755	4.2–10.7	55–80	Very low
GR	3	289	4.5–8	19–58	Very low
IN	1	26	3.6	72	Very low

BC, balloon compression; F/U, follow-up; GKS, gamma knife surgery; GR, glycerol rhizolysis; IN, internal neurolysis; MVD, microvascular decompression; RFTC, radiofrequency thermocoagulation.

Table 10 Reported complications from included cohort studies

Intervention	*N*	Mortality	Cerebral	Hearing loss	Facial hypaesth	Corneal hypaesth	V motor weakness	AD	Keratitis	CN palsy	CSF leak	Meningitis	HS
MVD	5149	15	32	95	147	17		1		211	101	20	16
GKS	1168	0			184				3	2			
RFTC	4533	0		6	853	300	280	29	55	36	5	1	
BC	755	0			110	5	34	1	1	12		43	
GR	289	0		1	115	19	5	2					
IN	26	0	0	0	25	0	0	1	0	0	1	0	0

AD, anaesthesia dolorosa; BC, balloon compression; CN, cranial nerve; CSF, cerebrospinal fluid; GKS, gamma knife surgery; GR, glycerol rhizolysis; HS, herpes simplex; Hypaesth, hypaesthesia; IN, internal neurolysis; MVD, microvascular decompression; RFTC, radiofrequency thermocoagulation; V, fifth cranial nerve. Cerebral: oedema, haemorrhage, stroke.

treatments tends to be associated with a better long-term response than any lack thereof. To help a comparison of the diverse complications across all interventions, an attempt has been made to assess their impact on the patient's health-related quality of life [82]. The expected utility scores measuring this effect were reported as similar between MVD and GKS [82].

Clinical guide

Although the quality of published studies reviewed comparing MVD and GKS was low or very low, it is striking that they consistently showed the superiority of MVD over GKS in classical and idiopathic TN, with comparable complication rates. In fully informed patients with classical TN with no previous operations, who have failed pharmacotherapy and who are willing to and can safely undergo neurosurgery, MVD is likely to provide a longer lasting postoperative pain-free state than GKS. Low quality evidence from two comparative studies and indirect data from cohort studies indicate that MVD may be considered more effective in providing relief from pain than RFTC, BC and GR. Due to limited and conflicting results, no preference can be shown for any one percutaneous neuroablative procedure over another. It should be underlined that they all do show considerable effectiveness and should be considered for those patients who cannot or prefer not to undergo MVD.

Final recommendations

Based on low quality evidence but extensive clinical experience, a strong recommendation is given that MVD is preferred over GKS in patients with classical TN who are willing to and can undergo posterior fossa surgery. Based on low quality evidence, a weak recommendation is given that MVD may be considered preferential over other neuroablative treatments (RFTC, BC, IN and GR). No recommendation can be given for choice between any neuroablative treatments or between them and MVD when an MRI scan fails to show significant nerve compression (idiopathic TN). Neuroablative treatments should be the preferred choice if MRI does not demonstrate any NVC.

Section 4: Management of secondary TN and non-pharmacological and non-surgical management of TN

Clinical question 4.1: Should patients with secondary TN be offered the same pharmacological and surgical treatments of pain as patients with primary TN?

Search strategy and results

Reports containing the keywords 'secondary trigeminal neuralgia' or 'symptomatic trigeminal neuralgia' AND treatment or management were sought. One systematic review [87] but no RCTs were found for the medical treatment of secondary TN, but a few small case series reported successful treatment with lamotrigine [88–90], carbamazepine [89], misoprostol [91,92], gabapentin [93], topiramate [94,95] and botulinum toxin type A [96]. Most of these studies investigated TN secondary to MS. Surgical treatment was evaluated in secondary TN with only a small case series reporting treatment outcomes, with a general tendency toward lesser efficacy in this population. Most authors recommend the use of Gasserian ganglion procedures unless a definitive vascular compression of the trigeminal nerve is identified on MRI. Radiofrequency thermocoagulation can be considered in secondary TN following dental procedures [97]. Case reports conveyed a benefit of MVD for patients with MS but suggest less efficacy than in non-MS patients [98,99]. A retrospective cohort study investigating 15 patients with MS over a median observation period of 55 months (range 17–99 months) reported that seven (47%) were completely paroxysm-free and

that an additional four (27%) had significant relief (>50%) of episodic pain. Amongst the eight patients with a constant pain component, all were free of their constant pain and four (50%) were free of their episodic pain [100]. Electrical transcutaneous stimulation was reported to be effective in patients with primary and secondary TN, but the authors did not clearly distinguish between patient types when evaluating outcomes [101].

Clinical guide

Patients with secondary TN generally respond less well to conventional or surgical treatment. As no treatment has sufficient evidence to prove its specific efficacy in secondary TN patients, they should be treated similarly to patients with primary TN. Gasserian ganglion procedures can be considered. In patients with MS, when a definite NVC is present on MRI, an MVD could be considered.

Final recommendation

Based on a very low quality of evidence, medical treatment of patients with secondary TN should be similar to those with primary TN. Surgical interventions should consider Gasserian ganglion procedures and MVD.

Clinical question 4.2: For patients with primary TN, what other non-pharmacological and non-surgical support can be provided?

Search strategy and results

Papers evaluating the overall disability caused by TN and how this can be managed by means other than drugs and surgery were sought. There is increasing evidence that depression, anxiety and poor coping mechanisms are common in patients with TN and result in poor quality of life [68,102–105]. These features are further compounded by the effects of the medications and complications after surgical treatments. There is good evidence that cognitive behavioural therapy is effective for chronic pain [106] and that self-management interventions for migraine and tension-type headache can be better than the usual care provided [107]. An evaluation of three patient-organized national meetings in the UK, USA and Australia showed that these are highly valued by sufferers as an opportunity to improve their knowledge and understanding [108].

Clinical guide

It is important to take into consideration that patients with TN suffer not only from severe pain but also from other factors such as depression and anxiety. A small pilot study using a group cognitive behaviour programme has been run in the UK and has been highly evaluated. This has now been supplemented by a telephone service offered by a clinical nurse specialist who can also prescribe, and patients have found this very helpful. These programmes enable patients to meet fellow sufferers and develop strategies for coping with flare-ups, which may result in fewer visits to emergency services and primary care doctors. Support groups run by TN sufferers were first established in the USA and UK and now also run in Australia, Canada, Denmark, Germany, Spain and France. Sufferers report a great need for the support and advice that they can obtain from support group volunteers who understand the needs of this community. Regular contact with members and others through telephone and e-mail helplines, web-based forums, local groups, national meetings and conferences can be very helpful for these patients.

Final recommendations

Based on very low quality of evidence, it is recommended that patients are offered psychological and nursing support. Patients should be directed to national support groups where these are present.

Conclusions and recommendations for future research

The diagnostic criteria for TN have changed considerably since publication of the previous AAN-EFNS guideline, in order to avoid the differences between the criteria laid out by the International Headache Society and the International Association for the Study of Pain. The recent International Classification of Headache Disorders diagnoses TN as primary TN, either classical or idiopathic depending on the degree of NVC, or as secondary TN caused by other than NVC. It is recommended that MRI is used as part of the work-up in TN patients, because no clinical characteristics can exclude secondary TN. Use of a combination of three high-resolution sequences – 3D T2-weighted, 3D TOF-MRA and 3D T1-Gad – is recommended. The neuroradiologist should be blinded to the side of pain and should describe whether a vessel contact causes morphological changes of the nerve. If MRI is contraindicated or unavailable, trigeminal reflexes can be used to distinguish secondary TN from primary TN. NVC plays an important role in primary TN, but demonstration of an NVC should not be used to confirm the diagnosis of TN. Rather, it may help to decide if and when a patient should be referred for MVD.

In acute exacerbations of pain, in-hospital treatment may be necessary for titration of anti-epileptic drugs, rehydration and intravenous infusion of fosphenytoin or lidocaine. For long-term treatment carbamazepine or oxcarbazepine are recommended as drugs of first choice. Lamotrigine, gabapentin, botulinum toxin type A, pregabalin, baclofen and phenytoin may be used either as monotherapy or combined with carbamazepine or oxcarbazepine. Patients should be encouraged to adjust the dosages depending on pain severity and side effects and should be given specific instructions on titration. It is recommended that patients should be offered surgery if pain is not sufficiently controlled medically or if medical treatment is poorly tolerated. MVD is recommended as first-line surgery in patients where NVC with morphological changes has been demonstrated (classical TN). No recommendation can be given for choice between any neuroablative treatments or between them and MVD when an MRI scan fails to show NVC with morphological changes (idiopathic TN). Neuroablative treatments may be preferred if MRI does not demonstrate any NVC. Treatment for patients with secondary TN should in general follow the same principles as for primary TN. In addition to medical and surgical management, it is recommended that patients are offered psychological and nursing support.

Compared with the previous AAN-EFNS guideline, there are important changes regarding diagnosis and imaging. This allows better characterization of patients and helps in decision making regarding the planning of medical and surgical management. Recommendations on pharmacological and surgical management have been updated. Unfortunately, no substantial progress in management has been made since the previous guideline.

There is a great need for future research in the pathophysiology and prognosis of TN and for development of more standardized outcomes, including quality of life, to allow for a more reliable comparison of results from different studies. Pharmacological management should be evaluated using modern standards and there is a huge need for development of more effective drugs with fewer side effects than current medications. Prospective studies are needed to evaluate outcome after surgery using independent assessors as well as studies comparing the various surgical procedures, and studies comparing these to pharmacological management. Management of secondary TN should be explored, and non-pharmacological and non-surgical treatment options should be evaluated.

Fortunately, there is increased interest and research in TN. It is hoped that this will result in improvements, making an update of this guideline necessary in the not too distant future. It is likely that this guideline will need to be updated in 2025.

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Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Demographic of patients and pain relief data of RFTC series
Table S2. Demographic of patients and pain relief data of GR series
Table S3. Demographic of patients and pain relief data of Percutaneous Balloon Compression (PBC) series
Table S4. Demographic of patients and pain relief data of GKS series
Table S5. Demographic of patients and pain relief data of IN series
Table S6. Demographic of patients and pain relief data of MVD series
Table S7. Reported complications related to RFTC series
Table S8. Reported complications related to GR series
Table S9. Reported complications related to Percutaneous Balloon Compression (PBC) series
Table S10. Reported complications related to GKS series
Table S11. Reported complications related to IN series
Table S12. Reported complications related to MVD series
Appendix S1. Clinical question 3.2: Which surgical technique gives the longest pain-free period with fewest complications?

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