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Trigeminal Neuralgia and Potential Correlations with Anatomical Variations of the Trigeminal Nerve

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Abstract

Objective. Trigeminal neuralgia is a long-term facial pain syndrome. Our aim was to review the anatomy of the trigeminal nerve and its anatomical relationship with the adjacent structures that may contribute to the pathogenesis of trigeminal neuralgia **Methods.** Eligible articles were identified by a search of the Medline Embase, Pubmed Cinahl and Google Scholar bibliographical databases. We checked all the references of the relevant reviews and eligible articles that our search retrieved, in order to identify potentially eligible conference abstracts. Titles of interest were further reviewed by abstract. Case reports were excluded. **Results.** Trigeminal neuralgia syndrome seems to be caused by anatomical variations of the trigeminal nerve and its adjacent anatomical structures, mainly through compression. We depict the causes, the pathogenesis, and the clinical manifestations of the syndrome. The classification, diagnostic approach, differential diagnosis, and treatment modalities are also presented and they may be personalized according to the anatomical variations of the trigeminal nerve present, which may lead to trigeminal neuralgia syndrome. **Conclusion.** It is very important to be very careful in cases of new emerging neuralgia and to avoid the term "idiopathic" until proven otherwise by validating the newer and more appropriate tests and diagnostic criteria. Current data are insufficient and future research is needed in order to discover innovative and more effective treatments of trigeminal neuralgia, considering the anatomy and the anatomical variations of the trigeminal nerve.

Key Words: Trigeminal Neuralgia ▪ Trigeminal Nerve Anatomy ▪ Trigeminal Nerve Surgery.

Introduction

Trigeminal neuralgia is a painful syndrome, which affects 0.07% of the population (1). It occurs mainly in women (60%) and those over the age of 50 (1, 2). The clinical severity of the syndrome is so intense that it may lead some patients to commit suicide (3). The treatment of the disease is pharmacological, while in its complicated forms, surgical treatment can be applied, with varying results and complications. Unexpectedly, effective treatment of the disease has led many scientists and researchers to focus on the pathogenesis of the disease, which still today has not been clearly elucidated.

Our aim was to review the anatomy of the trigeminal nerve and its anatomical relationship with the adjacent structures that may contribute to the pathogenesis of the trigeminal neuralgia. The correlations have been shown in many studies to be positive, and provide the potential for new therapeutics, and invasive or non-invasive treatment modalities.

Anatomy and Functions of the Trigeminal Nerve

The trigeminal nerve is the fifth cranial nerve, and contains motor and sensory fibers (mixed nerve). Its course starts from the brain stem, within which all four nuclei are located (principal sensory, spinal trigeminal, mesencephalic, motor) (4). It emerges from the front surface of the pons, consisting of the thick sensory root and the finer motor root. It passes outward from the posterior cranial fossa, bearing on the upper surface of the apex of the petrous bone in the middle cranial fossa. On the anterior surface of the petrous bone, the sensory root swells and forms the Gasserian ganglion. The Gasserian ganglion occupies the Meckel cavity, which is a dura mater pouch containing cerebrospinal fluid. From the anterior edge of the ganglion the three branches of the trigeminal nerve emerge: the ophthalmic, the maxillary and the mandibular nerve. The ophthalmic nerve (V1) contains only sensory fibers and exits the skull, entering the orbit through the superior orbital fissure. The maxillary nerve (V2) also contains only sensory fibers and exits the skull through the foramen rotundum. The mandibular nerve (V3) contains the sensory and all the motor fibers of the trigeminal nerve and exits the skull through the foramen ovale (4, 5).

The trigeminal nerve and its branches are relatively large, compared to the other cranial nerves, and due to its length and its course towards the face, it is adjacent to various anatomical areas. The most important adjacent anatomical areas are: the superior cerebellar artery (SCA), the posterior vertebral arteries, the facial nerve, the cranial nerve foramina, the teeth, the masticatory muscles, and the brain stem. Anatomical variations, neoplasms or inflammatory processes in these anatomical areas may cause neuralgia (6, 7).

The trigeminal nerve's functions transmit information regarding the sensation of pain, touch, and pressure from the facial skin and mucous membranes. It also serves the movements of the masticatory muscles, the tensor tympani muscle, the tensor veli palatini, the mylohyoid muscle and the anterior belly of the digastric muscle. Moreover, it contains postganglionic parasympathetic fibers derived from four ganglions (otic, pterygopalatine, submandibular and ciliary). Finally, the corneal reflex is mediated by the nasociliary branch of the ophthalmic nerve (V1), only sensing the stimulus on the cornea (8)

Trigeminal Neuralgia Syndrome

The causes of trigeminal neuralgia syndrome are divided into two categories: primary (idiopathic neuralgia) and secondary (9). Secondary causes include all the causes that may compress the trigeminal nerve or induce its activation, some of which are epidermal cysts, neoplasms, aneurysms and post-herpetic infection, that lead to neuralgia (9, 10). It is important to mention that there is probably a familial form of the disease in 2% of people with the disease, in which a structural change in the base of the skull occurs (11).

The mechanism behind the pathogenesis of trigeminal neuralgia is unknown. The main theories refer to the demyelination of the nerve (12), ectopic impulses due to changes in the Ca^{2+} channels, central pain mechanisms, and bioresonance (13, 14, 15)

According to the Headache Classification Committee of the International Headache Society (ICHD-3) (16), trigeminal neuralgia syndrome is classified into 2 categories (classical neuralgia and painful neuropathy). There are specific diagnostic criteria from the same society (Table 1). The

Table 1. Diagnostic Criteria According to ICHD-3

1.	3 seizures of unilateral pain + B, C criteria
2.	Distribution of pain in the course of the branches of the trigeminal nerve, without radiation in another area
3.	≥3 criteria from: 1. Recurrent paroxysmal pain lasting from 1 second to 2 minutes. 2. Very high pain intensity 3. Characteristics of pain compatible with those of the syndrome (abrupt, paroxysmal, like getting hit by lightning, like getting stabbed, etc.) 4. Release of pain after analgesic, innocent activity
4.	No clinically obvious neurological deficit
5.	Not compatible with other ICHD-3 criteria

Table 2. Therapeutic Options in Trigeminal Neuralgia Syndrome

Medication	GRADE 1A: Carbamazepine GRADE 1B: Oxycarbazepine GRADE 2C: Baclofen, Lamotrigine Additional drugs: Opioids, Antidepressants, etc.
Surgical treatment	1. Surgical microvascular decompression 2. Treatment with γ-knife 3. Transdermal microcompression with balloon 4. Transdermal rhizolysis with glycerol 5. Percutaneous radiofrequency neurolysis of the Gasserian ganglion

characteristic of trigeminal neuralgia syndrome is acute, debilitating, sudden and unilateral pain in the face, where the three branches of the nerve pass (17, 18). The pain may also involve more branches and may be bilateral in 3% of cases (18, 19). There is no specific activity that triggers the pain, and the episodes can last for weeks to months, but the seizures last for seconds to two minutes, reaching rapidly their peak, and seizures are sometimes accompanied by muscle spasms (19).

The diagnosis of trigeminal neuralgia syndrome is based on clinical examination (20) and imaging tests - Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography, and High resolution Brain Magnetic Resonance Imaging) (21). The differential diagnosis of the trigeminal neuralgia must be between four diseases: SUNCT syndrome (Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing), cluster headache, jabs and jolts syndrome, and classic migraine. The treatment of trigeminal neuralgia is mainly pharmaceutical, but in its drug-resistant forms the alternative of surgical treatment might be effective (17, 22) (Table 2).

Methods

The protocol of this review has been submitted to the Institutional Review Board of Department of Anatomy, National and Kapodistrian University of Athens, Greece, and is available upon request. Eligible articles were identified by search of the Medline Embase, Pubmed, Cinahl and Google Scholar bibliographical databases for the period from July 2020 to April 2021, due to their detailed articles solely in the field of medicine, and their accessibility, while others such as Scopus, Cochrane, etc were not preferred because they lack this. The study protocol was agreed by all co-authors. The search strategy included the following keywords: trigeminal neuralgia anatomy, causes of trigeminal neuralgia, trigeminal neuralgia surgery and trigeminal nerve anatomical variations.

Study Selection Criteria

Language restrictions were applied (only articles in English, French and German were considered eligible); two investigators (MA and AP), working independently, searched the literature and extracted data from each eligible study. The criteria of this study selection were: Recent year of publication (2011 until now) and/or of previous years, if the study has plentiful cadaveral material; Abundant references and rich bibliography, and Greek, English, French and German language. Articles that did not state the names of the authors and case reports were excluded. In addition, we checked all the references of the relevant reviews and eligible articles that our search retrieved, so as to identify potentially eligible conference abstracts. Titles of interest were further reviewed by abstract.

Study Selection

The search strategy retrieved 348 articles, 43 of which were considered eligible. 15 of these are presented in the results of this study and 28 of them were selected as supplements in this literature review. The other articles were excluded (applying exclusion criteria).

Results

In general, most publications on the relationship between anatomical variations and the occurrence of trigeminal neuralgia focus on the vascular area, and mainly on the superior cerebral artery. There is a limited number of articles available on other anatomical areas and structures, with varying results. These anatomical areas are the foramen ovale, the Meckel's cave, the pterygospinous process etc. Occasionally the results of the studies were used for a more precise therapeutic option and in others, cadaverals were studied to extract data on the pathogenesis of trigeminal neuralgia.

Bowsher et al., 1997 (23) stated that there are insufficient data to show the relationship between anatomical variants of the trigeminal nerve and the occurrence of neuralgia. Krmpotić-Nemanić et al., 1999 (24) presented the results of a study of 100 skulls with anatomical variations in the pterygospinous process. It is suggested that these variations may be the cause of neuralgia. In research conducted by the University of Nepal Ray et al., 2005 (25) 35 cadaveric skulls were studied. Changes in the shape and size of the foramen ovale were found to compress the trigeminal nerve, and cause pain in the facial area. Buch et al., 2012 (26) reported anatomical variations of the inferior alveolar nerve – a branch of the mandibular nerve - in cadavers from India, which may lead to pain in the mandibular region (including the syndrome of trigeminal neuralgia).

In addition, Munyiri Nderitu et al., 2016 (27) presented how a deep understanding of the precise anatomy of the infraorbital nerve is crucial to avoid iatrogenic injury of the nerve. Forty-two nerves in cadavers were fully examined and described. The appearance and course of the nerve varied, most importantly with the complete absence of the nasal branch in 34.53% of cases, and also the existence of other branches. This parameter is of paramount importance, because resistance to therapy in trigeminal neuralgia syndrome may be attributed to infraorbital nerve variations.

Further, a prospective study by Ding et al., 2016 (28) recruited 108 patients with trigeminal neuralgia. The patients were divided into two groups. This paper dealt with Percutaneous Radiofrequency Thermocoagulation (RFT) of the Gasserian ganglion, which is an effective treatment for primary trigeminal neuralgia. The issues that the scientists wanted to resolve were the high recurrence rate and technical difficulties in certain patients with foramen ovale (FO) anatomical variations. In the first group, the Hartel anterior approach was used to puncture the FO. In the second group, a percutaneous puncture through a mandibular angle was used to reach the FO. In both groups, procedures were guided by CT imaging and neuronavigation. The success rates, therapeutic effects, complications, and recurrence rates of the two groups were compared. CT and neuronavigation-guided puncture from a mandibular angle through the foramen ovale into the Gasserian ganglion can be safely and effectively used to deliver radiofrequency thermocoagulation for treatment of neuralgia. This method may represent a viable option to treat this syndrome, in addition to the Hartel approach.

Following these, the study by Zdilla et al., 2016 (29) depicted the results of 139 dry human crania. A total of 223 pairs of foramen ovale and trigeminal nerve variations were assessed in relation to compression. The crania were photographed, and the photographs were examined and measured using ImageJ software. The foramen ovale is a crucial anatomical area, because its anatomical variations may cause trigeminal neuralgia, and surgical therapy is mandated. The average angles from the anteromedial-most aspect of the foramen ovale to the anteromedial- and posterolateral-most aspects of the trigeminal impression were 65° ± 10.2° and 95° ± 8.5°. From the posterolateral aspect of the foramen ovale, the angles at the anteromedial and posterolateral-most aspects of the trigeminal impression were 69° ± 10.3° and 32° ± 11.2°, respectively. The average angles from the centroid of the foramen ovale to the anteromedial- and posterolateral-most aspects of the trigeminal impression were 47° ± 11.2° and 83° ± 9.4°, respectively. Paired t tests did not reveal any significant differences in any angles measured between sides.

In addition, Brinzeu et al., 2018 (30) examined 42 patients with trigeminal neuralgia. Imaging examinations showed that there was a variation of the Meckel cavity with an angle of 86° (by nature 98°, P=0.004) and compression of the branches V2 and V3. Medélez-Borbonio et al., 2018 (31) published a retrospective study of 53 patients with trigeminal neuralgia. They bilaterally measured the cisternal segment of the trigeminal nerve, the trigeminal-pontine angle and the lateral width of the pontine cistern on the Fiesta MRI sequence. These measurements were very important for the surgical procedure that followed, and an understanding of the etiology of the syndrome. The right trigeminal nerve was affected in 36 patients (67.9%), and the left in 17 (32.1%) patients. The average length of the trigeminal nerve was 9.8mm (range: 4.6–16.8mm) on the affected side, and 10.5mm (range: 5.6–18.4mm) on the unaffected side (P=0.02). The average trigeminal-pontine angle was 12.5° (range: 5.4° to 19.5°) on the affected side, and 10.2° (range: 5.0° to 30.5°) on the unaffected side (P=0.01).

Tsutsumi et al., 2018 (32) studied the anatomy of the trigeminal root. Considerable inter- and intra-individual variability was exhibited that may influence the symptoms of trigeminal neurovascular compression. Thin-sliced, axial T2-weighted imaging, and coronal constructive interference in steady-state (CISS) sequence were performed for a total of 167 patients. On axial T2-weighted imaging, 3 divisions of the main trigeminal sensory root were unequivocally delineated in 36% of the 95 patients. 63% of Meckel's caves were bilaterally adjacent to the petrous portion of the internal carotid artery. On CISS sequence, the course of the main trigeminal sensory root was well delineated in all of the 72 patients. The accessory sensory and motor rootlets were identified in 38% and 56% of 144 sides, respectively. Levels of the main trigeminal roots at the original site and entrance into Meckel's cave, as well the morphology of the original segment of the main trigeminal sensory root were variable. Furthermore, in 24% of sides, three divisions of the main trigeminal sensory root were clearly delineated, arranged in variable manners. In 20% of sides, segments of the superior cerebellar artery had contact with the main trigeminal sensory root and motor rootlets.

The next article, by Dupont et al., 2019 (33), dealt with the simultaneous existence of the ossification of the roof of the porus trigeminus with an ipsilateral duplicated abducens nerve behind the entrance to the Dorello's canal. This anatomical variant raises the suspicion of a cause-and-effect relationship for trigeminal neuralgia. Additionally, the publication of Elnashar et al., 2019 (34) refers to percutaneous stereotactic radiofrequency rhizotomy, which is necessary before presenting the precise anatomy of the foramen ovale. The third branch of the trigeminal nerve passes through the foramen ovale, and variability in its shape and size can cause nerve compression, resulting in neuralgia. The researchers analyzed 174 skull bases, and found an area loss of an average of 18.5% ± 5.7%.

Another publication from Clearly et al., 2019 (35) presented three patients with drug-resistant trigeminal neuralgia. Magnetic Resonance Imaging was performed showing the absence or hypoplasia of Meckel's cave as the cause of the neuralgia. The γ-knife treatment was successfully selected.

Hardaway et al., 2019 (36) performed a case control study. Brain MRIs of 232 patients were compared with measurements obtained in 100 age-matched and sex-matched healthy controls (control group). The odd ratio (OR) of females not having NVC compared to males was 2.7 (95% CI 1.3–5.5, P=0.017). In terms of age, patients younger than 30 years were much less likely to have neurovascular compression (NVC) compared to older patients (OR 4.9, 95% CI 1.3–18.4, P=0.017). The posterior fossa volume was significantly smaller in TN patients without NVC compared to those with NVC. Posterior fossa volume in males was larger than posterior fossa volume in females.

Finally, a retrospective analysis published in 2019 by Grigoryan et al., (37) studied 51 patients with trigeminal neuralgia and Cerebellopontine angle (CPA) tumors: 29 meningiomas of the petrous apex, 11 epidermoids, 9 vestibular schwannomas, 1 hemangioma, and 1 cavernoma. After the removal of the tumour and microvascular decompression, all patients were relieved from the pain syndrome.

Discussion

In this paper, we focused on the relationship between the onset of trigeminal neuralgia and anatomical variations of the fifth cranial nerve. We believe that precise knowledge about the variations of the trigeminal nerve is “the key” to developing new and revolutionary therapeutic options, which will relieve a large number of patients with neuralgia around the world. The first paper we perused, Bowsher et al., 1997, states that there are insufficient studies to denote a relationship between the occurrence of trigeminal neuralgia and anatomical variants of this nerve. From 1997 until the present day, the massive development of technology in the field of imaging techniques (especially MRI) (38) has provided enormous possibilities for brain imaging, with the result that subsequent researchers have better data to study. When searching the term “trigeminal neuralgia”, it seems that the publication of papers on this subject has increased rapidly. For instance, in Pubmed the number of publications in 1997 about the term “trigeminal neuralgia” was 146, while in 2020 this number increased to 428.

Regarding papers on cadaveric material, they showed that there are significant variations in the anatomy of the areas adjacent to the trigeminal nerve during its course. These variations mainly concern its shape, but in many cases there is even an absence of the anatomical area itself. The anatomical area that has been studied most frequently is the foramen ovale, which has been described to have a variety of shapes such as: “banana-like”, “triangular”, “oval”, “truly oval”, “elongated oval”, “elongated”, “semicircular”, “almond”, “round”, “rounded”, “slit”, “irregular”, “D- shape” and “pear shaped”. It is essential to describe the anatomical variants of the anatomical structures through which the nerve passes. Most of the skulls belonged to adults, while references to skulls of persons <18 years of age are minimal. It is very likely that these anatomical varieties of the shape of the foramen ovale in adults exert pressure on the nerve, resulting in neuralgia.

In terms of patient data, many cases of trigeminal neuralgia syndrome were initially diagnosed as “idiopathic” and the patient did not receive proper treatment from the beginning. The average time from misdiagnosis to receiving proper treatment was about two years. The majority of patients were > 18 years old and female. Patients continued to suffer from the syndrome, and only when more specialized imaging tests were performed (MRI, MRA) did the neuralgia resolve with surgery. The most common surgical treatment performed on these individuals was microvascular decompression, which has given spectacular results. This is the reason why it is of paramount importance to perform the appropriate imaging examinations early because the diagnostic criteria of trigeminal neuralgia (ICHD-3) (15) do not exclude secondary causes, or the possibility of any anatomical variations of the nerve. According to the European Academy of Neurology, an imaging technique must be performed in order to provide a personalized therapeutic option (39).

As mentioned above, MRI may indicate possible anatomical variations of the trigeminal nerve. In the papers we analyzed, it seems that the anatomical areas through which the trigeminal nerve passes, but also the nerve itself, showed anatomical variations in many cases, with a statistically significant difference in most studies. In fact, Hardaway et al., 2019 (35) examined the anatomical variants of the nerve and the neighboring areas, in relation to age and sex, which produced very interesting results. Women are more likely to develop neuralgia at a younger age compared to men. Men with neuralgia are more likely to have neurovascular compression and to be cured with surgical treatment. Moreover, young patients are much less likely to have neurovascular compression, compared to older patients. Furthermore, the posterior fossa in males is larger than the posterior fossa in females. Thus, men and older patients are more likely to be treated with surgical microvascular decompression.

There are also many studies presenting interesting case reports of trigeminal neuralgia. First of all, Zimering et al., 2017 (40) depicted a case of trigeminal neuralgia. A 52-year-old man came for a preoperative MRI, which showed lesions close to Meckel’s cave. He was considered a coroner and a biopsy was sent for histological examination, in which no mitoses were seen, but normal brain tissue. This is the only case with ectopic tissue that caused nerve compression and the corresponding symptoms. Sundararajan et al., 2018 (41) presented a case report of a male patient with classic trigeminal neuralgia in the V3 branch (mandibular nerve). On MRI, followed by a diagnostic protocol, there were no anatomical variations of the brain vessels, but hypoplasia of Meckel's cave. In addition, no examination showed any disease that may be related to neuralgia syndrome. The treatment was surgical. In Peris-Celda et al., 2019 (42), preoperative MRI was performed on a female patient with trigeminal neuralgia syndrome of branches V2 and V3. An enlarged Meckel's cave and a loop of the cerebral artery were found. The next study by Hirata et al., 2019 (43) presented the case of a 46-year-old man with trigeminal neuralgia, in whom computed tomography was performed which showed bone hyperplasia in the area of the left cerebellopontine cistern, resulting in compression of the left trigeminal nerve. The patient underwent surgery (microvascular decompression) and the neuralgia disappeared completely.

Finally, it is very important to be very careful in cases of new emerging neuralgia and to avoid the term "idiopathic" until proven otherwise by validating the newer and more appropriate tests and diagnostic criteria.

Conclusion

The occurrence of trigeminal neuralgia correlates with anatomical variations of the trigeminal nerve and the adjacent anatomical areas and structures, mainly through compression. The enormous development of technology in the field of medicine, especially in terms of imaging and surgical techniques, has changed the therapeutic options for trigeminal neuralgia. However, more research is necessary to address this issue in order to discover innovative and more effective treatment modalities to ameliorate the severity of this disease.

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References

1. Macfarlane TV, Beasley M, Macfarlane GJ. Self-reported facial pain in UK Biobank Study: prevalence and associated factors. J Oral Maxillofac Res. 2014;5(3):2.
2. van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain. 2014;155(4):654-62.
3. Adams H, Pendleton C, Latimer K, Cohen- Gadol AA, Carson BS, Quinones-Hinojosa A. Harvey Cushing's case series of trigeminal neuralgia at the Johns Hopkins Hospital: a surgeon's quest to advance the treatment of the 'suicide disease. Acta Neurochir. 2011;153(5):1043-50.
4. Joo W, Yoshioka F, Funaki T, Mizokami K, Rhoton AL. Microsurgical anatomy of the trigeminal nerve. Clin Anat. 2013;27(1):61-88.
5. Splittgerber R. Snell's Clinical Neuroanatomy. 8th ed. Philadelphia: Lippincott Williams and Wilkins; 2018
6. Thomas KL, Vilensky JA. The anatomy of vascular compression in trigeminal neuralgia. Clin Anat. 2013;27(1):89-93.
7. Leclercq D, Thiebaut JB, Héran F. Trigeminal neuralgia. Diagn Interv Imaging. 2013;94(10):993-1001.
8. Johnson E. Neuroanatomy. 1st ed. Athens: Medical Publication Constantaras; 2012
9. Cruccu G. Trigeminal Neuralgia. Continuum (Minneap Minn). 2017;23(2):396-420.
10. Cheng TM, Cascino TL, Onofrio BM. Comprehensive study of diagnosis and treatment of trigeminal neuralgia secondary to tumors. Neurology. 1993;43:2298-302.
11. Fernández Rodríguez B, Simonet C, Cerdán DM, Morollón N, Guerrero P, Tabernero C, et al. Familial classic trigeminal neuralgia. Neurologia. 2019;34(4):229-33.
12. Devor M, Amir R, Rappaport ZH. Pathophysiology of Trigeminal Neuralgia: The Ignition Hypothesis. Clin J Pain. 2002;18(1):4-13.
13. Love S, Hilton DA, Coakham HB. Central demyelination of the Vth nerve root in trigeminal neuralgia associated with vascular compression. Brain Pathol. 1998;8:1-11.
14. Hilton DA, Love S, Gradidge T, Coakham HB. Pathological findings associated with trigeminal neuralgia caused by vascular compression. Neurosurgery. 1994;35:299-303.
15. Jia D, Li G. Bioresonance hypothesis: A new mechanism on the pathogenesis of trigeminal neuralgia. Med Hypotheses. 2010;74(3):505-7.
16. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629-808.
17. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia – diagnosis and treatment. Cephalalgia. 2017;37(7):648-57.

18. Bašić Kes V, Matovina LZ. Accommodation to Diagnosis of Trigeminal Neuralgia. Acta Clin Croat. 2017;56(1):157-61.
19. Yokosako S, Takahashi Y, Kikuchi A, Yoshimura C, Arai N, Ohbuchi H, et al. Clinical features of bilateral trigeminal neuralgia. No Shinkei Geka. 2015;43(2):127-32.
20. Cruccu G, Biasiotta A, Galeotti F, Iannetti GD, Truini A, Gronseth G. Diagnostic accuracy of trigeminal reflex testing in trigeminal neuralgia. Neurology. 2006;66:139-41.
21. Goh BT, Poon CY, Peck RH. The importance of routine magnetic resonance imaging in trigeminal neuralgia diagnosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;92:424-9.
22. Gronseth G, Cruccu G, Alksne J, Argoff C, Brainin M. Burchiel K, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008;71(15):1183-90.
23. Bowsher D. Trigeminal neuralgia: An anatomically oriented review. Clin Anat. 1997;10(6):409-15.
24. Krmpotić-Nemanić J, Vinter I, Hat J, Jalšovec D. Mandibular neuralgia due to anatomical variations. Eur Arch Otorhinolaryngol. 1999;256(4):205-8.
25. Ray B, Gupta N, Ghose S. Anatomic variations of foramen ovale. Kathmandu Univ Med J. 2005;3(1):64-8.
26. Buch HA, Agnihotri RG. A recurrent variant branch of the inferior alveolar nerve: Is it unique? Clin Anat. 2012;25(4):437-43.
27. Nderitu JM, Butt F, Saidi H. Variant Anatomy of the Nasal and Labial Branches of the Infraorbital Nerve. Craniomaxillofac Trauma Reconstr. 2016;9(4):294-6.
28. Ding W, Chen S, Wang R, Cai J, Cheng Y, Yu L, et al. Percutaneous radiofrequency thermocoagulation for trigeminal neuralgia using neuronavigation-guided puncture from a mandibular angle. Medicine. 2016;95(40):4940.
29. Zdilla MJ, Hatfield SA, Mangus KR. Angular Relationship Between the Foramen Ovale and the Trigeminal Impression. J Craniofac Surg. 2016;27(8):2177-80.
30. Brinzeu A, Dumot C, Sindou M. Role of the petrous ridge and angulation of the trigeminal nerve in the pathogenesis of trigeminal neuralgia, with implications for microvascular decompression. Acta Neurochir. 2018;160(5):971-6.
31. Medélez-Borbonio R, Perdomo-Pantoja A, Serrano-Rubio AA, Tomberlin C, Revuelta-Gutiérrez R, Moreno-Jiménez S. Analysis of morphological measurements of the trigeminal nerve in the linac stereotactic radiosurgery simulation targeting the root entry zone in trigeminal neuralgia. Neurocirugia (Astur : Engl Ed). 2019;30(3):105-14.
32. Tsutsumi S, Ono H, Yasumoto Y, Ishii H. The trigeminal root: an anatomical study using magnetic resonance imaging. Surgical and Radiologic Anatomy. Surg Radio Anat. 2018;40(12):1397-403.
33. Dupont G, Altafulla J, Iwanaga J, Watanabe K, Tubbs RS. Ossification of the roof of the porus trigeminus with duplicated abducens nerve. Anat Cell Biol. 2019;52(2):211-3.
34. Elnashar A, Patel SK, Kurbanov A, Zvereva K, Keller JT, Grande AW. Comprehensive anatomy of the foramen ovale critical to percutaneous stereotactic radiofrequency rhizotomy: cadaveric study of dry skulls. J Neurosurg. 2019;19:1-9.
35. Cleary DR, Handwerker J, Ansari H, Ben-Haim S. Three Cases of Trigeminal Neuralgia with Radiographic Absence of Meckel's Cave. Stereotact Funct Neurosurg, 2019;97(4):249-54.
36. Hardaway FA, Holste K, Ozturk G, Pettersson D, Pollock JM, Burchiel KJ, et al. Sex-dependent posterior fossa anatomical differences in trigeminal neuralgia patients with and without neurovascular compression: a volumetric MRI age- and sex-matched case-control study. J Neurosurg. 2019;132(2):631-8.
37. Yu Grigoryan G, Dreval NO, Sitnikov AR. Anatomical rationale for surgical treatment of trigeminal neuralgia combined with cerebellopontine angle tumors. Zh Vopr Neirokhir Im N N Burdenko. 2019;83(1):53-66.
38. Yousaf T, Dervenoulas G, Politis M. Advances in MRI Methodology. Int Rev Neurobiol. 2018;141:31-76.
39. Bendtsen L, Zakrzewska JM, Abbott J, Braschinsky M, Di Stefano G, Donnet A, et al. EAN guideline on trigeminal neuralgia. Eur J Neurol. 2019;26(6):831-49.
40. Zimering JH, Stone JJ, Paulzak A, Markman JD, Johnson MD, Vates GE. Ectopic brain tissue in the trigeminal nerve presenting as rapid-onset trigeminal neuralgia: case report. J Neurosurg. 2018;129(4):1063-6.
41. Sundararajan S, Loevner LA, Mohan S. Mandibular Myalgia and Miniscule Meckel's Caves. ORL J Otorhinolaryngol Relat Spec. 2018;80(2):103-7.
42. Peris-Celda M, Perry A, Carlstrom LP, Graffeo CS, Link MJ. Intraoperative Management of an Enlarged Suprameatal Tubercle During Microvascular Decompression of the Trigeminal Nerve, Surgical and Anatomical Description: 2-Dimensional Operative Video. Operative Neurosurgery. Oper Neurosurg (Hagerstown). 2019;7(6):247.
43. Hirata S, Kobayashi M, Kamamoto D, Kosugi K, Yoshida K, Fujimaki T. Trigeminal Neuralgia Due to Petrosal Bone Deformity. World Neurosurg. 2019;126:79-82.