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Original Article

A Systematic Review and Meta-Analysis on Trigeminal Neuralgia Linked to Neurovascular Compression Using MRI Analysis

Zygimantas Petronis[1*], Raimundas Golubevas[1], Jan Pavel Rokicki[1], Vesta Guzeviciene[1], Dalius Sakavicius[1], Algirdas Lukosiunas[1]

[1] Department of Maxillofacial Surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania.

***E-mail** ✉ petronis.zygimantas@gmail.com

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ABSTRACT

The exact process underlying the development of trigeminal neuralgia (TN) is not yet fully clarified, with multiple factors potentially contributing to the condition. MRI is a valuable tool in identifying the possible causes. This paper reviews the anatomy of the trigeminal nerve associated with TN, describes the imaging features of vascular compression in TN patients, and examines the correlation between these findings and the TN branch affected. A systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines. The search terms used were ((neurovascular conflict) AND (trigeminal nerve)) AND (neuralgia). Databases such as ResearchGate, ScienceDirect, Google Scholar, and PubMed/Medline were searched. The initial search yielded 3,886 articles, and after applying selection criteria, 4 articles were selected for the analysis. The methodological quality of non-randomized studies was assessed using the MINORS tool. The combination of the second and third trigeminal nerve branches was the most commonly affected, occurring in 55.6% of cases. The comparison between the second and third branches and the most common vessels involved in neurovascular conflict showed no significant statistical difference. MRI remains the primary diagnostic method for detecting NVC in TN. The studies reviewed indicate that the vertebral artery and superior cerebellar artery are the most commonly implicated vessels in NVC. Further research with larger sample sizes is necessary to create an algorithm that can identify the vessel causing compression in TN affecting specific branches.

Keywords: Diagnostic, Trigeminal neuralgia, Magnetic resonance imaging, Neurovascular conflict, Pain.

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Introduction

Facial pain is a common condition with various underlying causes. Trigeminal neuralgia (TN), also known as tic douloureux, stands out as one of the leading causes of facial pain [1]. TN is a type of neuropathic pain that affects one or more branches of the trigeminal nerve (cranial nerve V) [2]. The condition is marked by recurring episodes that last anywhere from a few seconds to several minutes, often described as "shooting" or "electric shock" sensations, with specific areas that trigger these attacks [3]. In the UK, TN is most prevalent in women across all age groups, with the highest incidence occurring between the ages of 45 and 59 years [4]. The V2 and V3 branches are most frequently affected, while the V1 branch is involved in fewer than 5% of cases [5]. It has been reported that approximately 17% of TN patients receive treatment in a hospital setting [6]. The precise mechanism behind the development of TN remains unclear, as multiple factors can contribute to the onset of the disease (**Figure 1**).

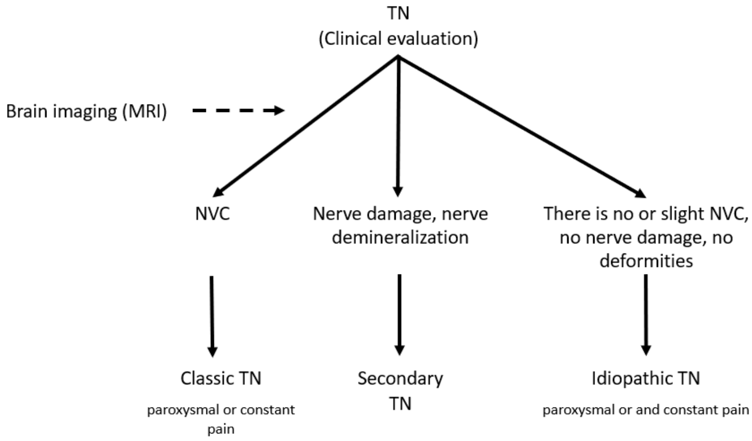


Figure 1. Diagnostic flowchart for trigeminal neuralgia based on various factors [7]; TN: trigeminal neuralgia, MRI: magnetic resonance imaging, and NVC: neurovascular conflict.

Magnetic resonance imaging (MRI) serves as a supplementary tool to identify potential causes of trigeminal neuralgia (TN) [8]. When examining the MRI, neurovascular conflict (NVC), where the nerve is in contact with blood vessels, can be observed. It is believed that the neurovascular pressure from an artery or vein on the trigeminal nerve leads to neuronal disruption, causing neuropathic pain. This pressure damages the myelin sheath and neurons, and as altered nerve impulses are transmitted, the individual perceives and interprets this as pain [9]. In most cases, MRI isn't used to definitively diagnose TN but rather to inform decisions regarding surgery [7]. A patient with TN experienced long-term pain relief after the first microsurgical decompression of the trigeminal nerve, where the superior cerebellar artery was mobilized. This procedure provides favorable and safe outcomes for patients who don't respond to standard treatments [10].

This article aims to review the anatomy of the trigeminal nerve relevant to TN, examine the imaging characteristics of vascular compression in TN patients, and explore the relationship between these findings and the specific TN branch responsible for the condition.

Materials and Methods

Protocol and registration

This systematic review and meta-analysis was carried out following the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines [11]. The study protocol was developed following these standards and registered with PROSPERO (International Prospective Register of Systematic Reviews and Meta-analysis) under the registration number CRD42023334610.

Literature selection

Two reviewers independently conducted searches on the PubMed/MEDLINE, ResearchGate, ScienceDirect, and Google Scholar databases to identify and select original research articles. The review process involved analyzing titles and relevant abstracts. The following search terms were applied: ((neurovascular conflict) AND (trigeminal nerve)) AND (neuralgia). Only English-language studies published between December 2017 and December 2022 were included in the search. There were no limitations based on the publication status or country of origin.

Eligible studies included comparative studies, randomized controlled trials, split-mouth randomized controlled trials with double blinding, and controlled clinical trials involving adult patients. These studies had to explore the relationship between vascular conflict and the pain experienced in different branches of the trigeminal nerve in individuals with TN. Excluded from the review were studies focusing on a single age group, as well as case reports, animal studies, meta-analyses, and systematic reviews.

Data extraction and quality assessment

Data from all selected studies were extracted using a standardized form, and the following key details were collected: the first author's last name and initials, publication year, total number of cases, study design, average age, assessment methods, and the results, including the specific branches and vessels involved for each patient.

Statistical methods

Statistical analysis was performed using SPSS version 27, while MedCalc (Statistical Software version 17.1) was utilized for the meta-analysis. Due to significant clinical heterogeneity among the studies, a random-effects model was applied. The chi-square and I-square tests were used to evaluate statistical heterogeneity, with I2 values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. A P-value of < 0.05 was considered statistically significant. The mean difference (MD) and its corresponding 95% confidence interval (CI) were calculated to assess the effect of the evaluation.

Results and Discussion

Literature search

A total of 3886 articles were identified from the initial database search using the specified criteria. After reviewing the full texts of 24 articles, 20 were excluded for not meeting the inclusion requirements. Only studies presenting individual patient data were considered for inclusion. Ultimately, 4 articles were selected for the review (**Figure 2**).

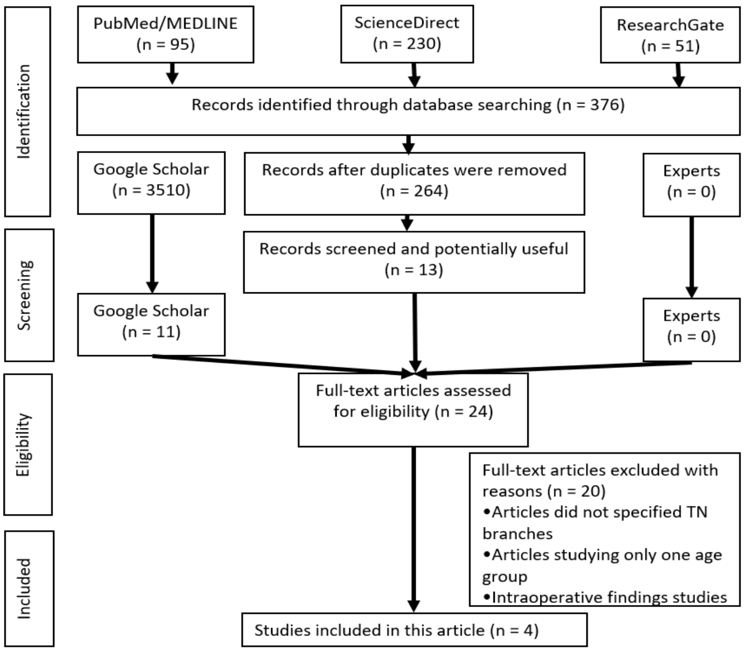


Figure 2. Diagram illustrating the process of literature search and selection criteria.

The studies included in the review had sample sizes ranging from one to 22 patients. All four studies reported the detection of NVC through MRI [12-15]. Upon examining the articles, it was observed that the sample sizes in these studies were relatively small (**Table 1**).

Quality assessment (Risk of bias)

Table 1. Data of interest

No	Study	Number of patients	Age of patients (years)	Methods of Determining Neurovascular Conflict
1	Wang *et al.* [12]	8	59.4 (42–71)	GE 1.5T MR scanner; a time-of-flight (TOF) sequence was used to capture the pictures (TE minimum full bandwidth, 25 kHz; field of view, 24 cm; slice thickness, 1.0 mm).
2	Son *et al.* [13]	1	68 (68)	3.0T MR machine
3	Liu *et al.* [14]	22	63 (44-80)	MR machine and computer tomography
4	Moon *et al.* [15]	14	49 (36–64)	7.0T MR machine

MR: Magnetic resonance

Each article was evaluated for potential bias after assessing the risk of errors. The MINORS methodology for non-randomized studies [16] was employed. The risk of bias was independently assessed by two reviewers, with a third reviewer resolving any disagreements. The results are displayed in Figure 3.

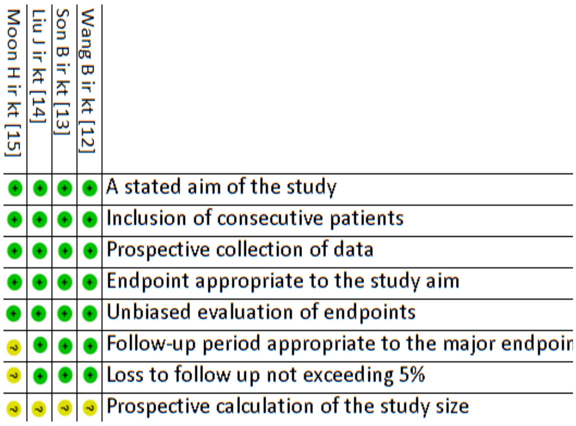


Figure 3. Assessment of error likelihood in the reviewed articles.

Outcomes

Wang *et al.* [12] examined 8 patients and determined that the 2nd and 3rd branches were most commonly affected by TN, with the superior cerebellar artery being the most frequently involved vessel in NVC. Son *et al.* [13] identified NVC in a single patient. In Liu et al.'s study [14], the vertebral artery was the primary vessel implicated in neurovascular conflict or combination with other vessels (17 cases), followed by the superior cerebellar artery (12 cases), veins (1 case), and the anterior inferior cerebellar artery (6 cases). Notably, after using a special biomedical adhesive technique, 20 of the 22 patients (91%) experienced recovery. Moon *et al.* [15] reported that the superior cerebellar artery is the most common vessel involved in NVC, with 11 out of 14 cases affected (**Table 2**).

Table 2. The findings from the studies on trigeminal nerve neuralgia included in this review [12-15]

Study	No.	Sex	Age	Side	Pain region	NVC vessel
Wang *et al.* [12]	1	M	65	L	V 2+3	VA
	2	M	55	R	V 2+3	SCA, SPV
	3	F	71	R	V 2+3	SCA
	4	F	43	L	V 3	SCA
	5	F	63	R	V 2+3	AICA
	6	M	53	L	V 1+2+3	SCA
	7	M	68	R	V 2+3	VA, SCA
	8	F	58	R	V 2+3	AICA
Son *et al.* [13]	1	F	68	R	V 3	AICA
Liu *et al.* [14]	1	M	60	L	V 3	VA, SCA
	2	D	74	L	V 2+3	VA, SCA
	3	M	44	L	V 2+3	VA
	4	M	68	R	V 2+3	BA, AICA
	5	F	80	L	V 2+3	VA, SCA
	6	M	78	L	V 2+3	BA, SCA
	7	F	74	R	V 2+3	BA
	8	M	64	L	V 2+3	VA, vein
	9	F	50	L	V 2	BA
	10	F	62	L	V 2+3	VA, SCA
	11	M	75	R	V 2+3	VA, SCA
	12	F	67	R	V 2+3	VA, SCA, AICA
	13	F	66	L	V 2+3	VA, AICA
	14	M	64	L	V 1+2+3	VA, AICA
	15	F	56	L	V 2+3	VA
	16	F	55	R	V 2+3	VA, AICA
	17	F	61	L	V 2+3	VA
	18	F	57	L	V 1+2+3	VA, SCA
	19	F	65	R	V 1+2+3	VA, SCA
	20	M	51	R	V 2+3	BA, SCA
	21	F	45	L	V 2	VA, SCA, AICA
	22	M	64	R	V 2	VA, SCA
Moon *et al.* [15]	1	F	50	L	V 2	SCA
	2	F	53	R	V 2	SCA
	3	M	36	L	V 3	SCA
	4	F	59	L	V 2	AICA
	5	F	31	R	V 1+2+3	SCA
	6	M	43	R	V 2	AICA
	7	F	48	R	V 2+3	SCA
	8	F	46	L	V 2+3	AICA
	9	F	62	R	V 2	SCA
	10	F	62	L	V 2	SCA
	11	M	64	L	V 2	SCA
	12	F	60	L	V 2+3	SCA

13	M	36	R	V 2	SCA
14	F	40	L	V 2+3	SCA

F: female; M: male; L: left, R: right; VA: vertebral artery; SCA: superior cerebellar artery; SPV: superior petrosal vein; BA: basilar artery; AICA: anterior inferior cerebellar artery; V: trigeminal nerve

Upon reviewing all the articles, it was observed that the most frequently affected branches in TN were the 2nd and 3rd branches, accounting for 55.6%. This combination typically occurs when NVC involves the trigeminal nerve, vertebral artery, or superior cerebellar artery. It was also noted that the second branch of TN was often associated with NVC from the superior cerebellar artery.

Meta-analysis outcomes

All studies included in the meta-analysis [12-15] (Figures 4 and 5) showed no significant statistical difference when comparing the 2nd and 3rd trigeminal nerve branches with the most commonly involved NVC vessels. This research highlights the value of high-resolution MRI for assessing NVC. However, there is a lack of comprehensive global research that fully explores NVC and creates an algorithm capable of easily identifying the blood vessels in contact with a specific trigeminal nerve branch in TN cases. It was observed that larger studies don't specify which trigeminal nerve branch is in contact with which blood vessel, posing challenges for drawing significant conclusions in this study. While some articles mentioned using magnetic resonance imaging to diagnose neurovascular conflict, others only reported intraoperative findings, which were not applicable for inclusion in this review [17, 18].

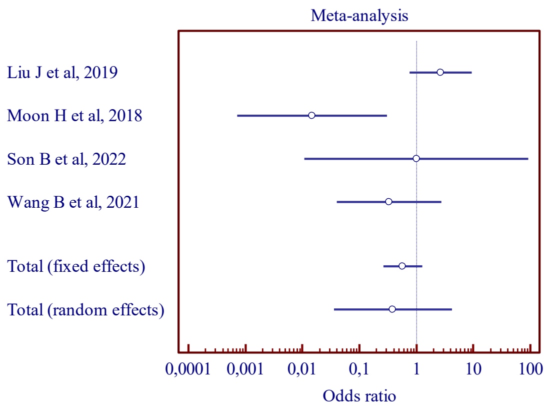
There is still a tendency for radiologists to occasionally miss NVC during MRI examinations. A study by Singhal and Danks [19] showed that radiologists' evaluations can be accurate in 88% of cases when examining arterial NVC. Recent studies highlight the use of multispiral computed angiography as a potential alternative to magnetic resonance imaging for detecting NVC [20], along with magnetic resonance imaging angiography [21].

It has been observed that MRI provides high sensitivity and specificity in identifying NVC, particularly in patients presenting with "classic" TN. Spanish research indicates that the presence of an identified NVC on an MRI is a strong predictor of long-term pain relief following nerve decompression surgery [22].

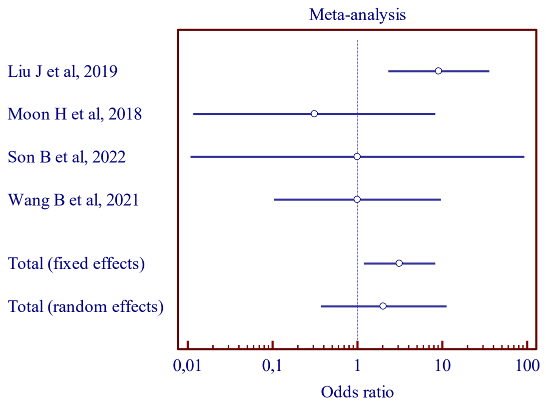
Brinzeu *et al.* [23] reported that MRI exhibits a sensitivity of 97% and a specificity of 50% when detecting NVC. It performs particularly well in terms of specificity across different tesla strengths, with higher values yielding better outcomes. The ability to identify the vessel type is considered highly reliable, while the assessment of NVC grade has shown moderate or poor reliability. When deciding on nerve decompression, the degree of pressure exerted on the nerve is noted as the most significant factor for predicting long-term pain relief following surgery.

The primary cause of TN is often attributed to artery compression of the nerve [24]. However, recent studies suggest that venous compression is less commonly involved in TN [25, 26]. According to a study by Dumot *et al.* [27] and Wang *et al.* [28], venous compression may be responsible for approximately 10% of cases. In our study, no cases of isolated venous compression were observed. Compared to arterial NVC, venous involvement in TN has not been as extensively studied, particularly in terms of its clinical characteristics and surgical outcomes [28].

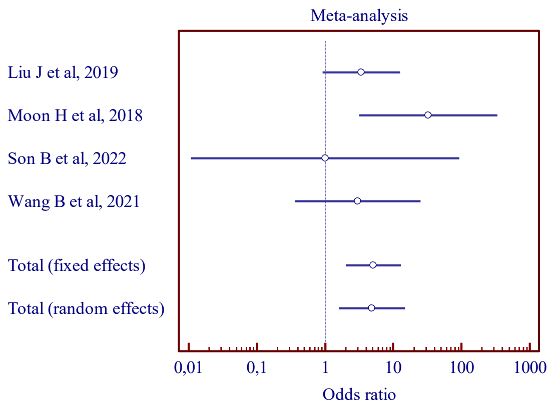
Understanding NVC and determining whether the conflict involves an artery or a vein is crucial, yet the pattern of trigeminal neuralgic pain varies greatly depending on where the neurovascular compression occurs around the trigeminal nerve root [29]. Consequently, TN is associated with neurovascular compression, which can lead to atrophy of the trigeminal nerve. Research has demonstrated that prolonged and severe NVC can result in trigeminal nerve atrophy, along with demyelination and loss of axons in the affected nerve [15, 30].



a) (MD, 0.386; 95% CI, 0.0357 to 4.172)

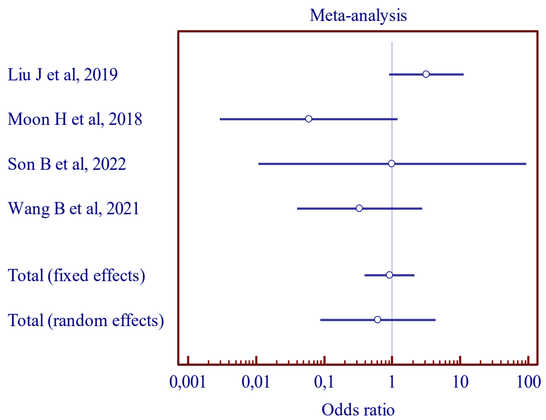


b) (MD, 2.035; 95% CI, 0.372 to 11.130)

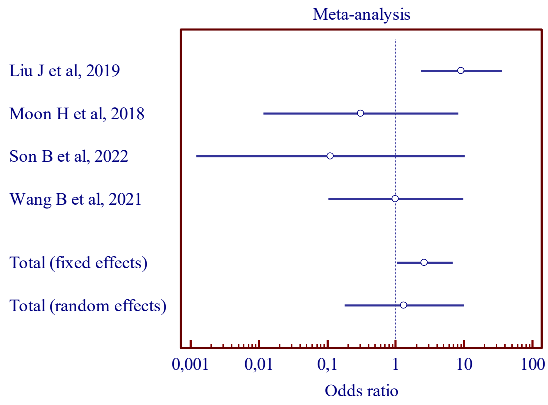


c) (MD, 4.824; 95% CI, 1.569 to 14.827)

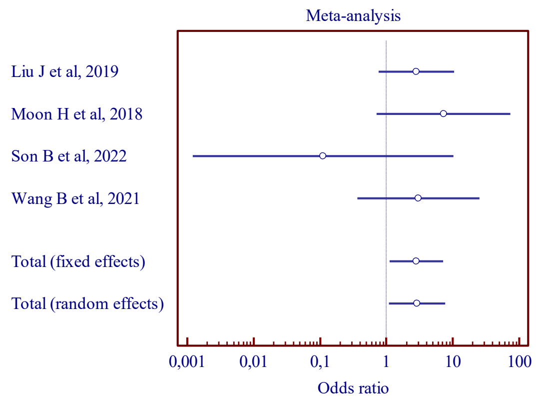
Figure 4. Meta-analysis outcomes comparing the second branch of the trigeminal nerve with the vertebral artery and superior cerebellar artery (a), vertebral artery and anterior inferior cerebellar artery (b), and superior cerebellar artery and anterior inferior cerebellar artery (c).



a) (MD, 0.613; 95% CI, 0.0874 to 4.297)



b) (MD, 1.327; 95% CI, 0.179 to 9.850)



c) (MD, 2.916; 95% CI, 1.098 to 7.744)

Figure 5. Meta-analysis results comparing the third trigeminal nerve branch with the vertebral artery and superior cerebellar artery (a), vertebral artery and anterior inferior cerebellar artery (b), and superior cerebellar artery and anterior inferior cerebellar artery (c).

Conclusion

MRI remains the primary method for assessing neurovascular conflict (NVC) in trigeminal neuralgia (TN). The reviewed studies indicate that the vertebral and superior cerebellar arteries are the most commonly involved vessels in NVC. However, due to the limited sample sizes of these studies, no definitive conclusions can be drawn. To create a more effective diagnostic approach, larger-scale studies are necessary to develop an algorithm that can reliably identify the vessel causing contact in cases of branch TN. Additionally, a collaborative diagnostic framework involving radiologists, neurologists, and maxillofacial/oral surgeons should be established.

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approved the manuscript, and no other individuals meet the criteria for authorship.

Conflict of Interest: None

Financial Support: None

Ethics Statement: This study complies with the ethical standards set by the Lithuanian University of Health Sciences.

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