▪ Headache Medicine 2025, 16(4): 244-258 ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

▪ DOI: 10.48208/HeadacheMed.2025.38

Review

Trigeminal neuralgia in multiple sclerosis patients: a systematic review and meta-analysis of minimally invasive surgical procedures, decompression, and the pain outcomes

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Edited by:
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Background
Trigeminal neuralgia is characterized by episodes of severe, recurrent, and debilitating facial pain that can occur in 1 to 2% of the patients who are diagnosed with multiple sclerosis throughout their lives. Trigeminal neuralgia can be described as ranges of intense facial pain, like electric shocks, involving the trigeminal nerve. The aim is to demonstrate the effectiveness of various minimally invasive procedures for controlling trigeminal neuralgia pain in patients with multiple sclerosis, ranging from conservative to surgical treatment.

Methods
The review focused on surgical clinical outcomes and treatment modalities related to trigeminal neuralgia in patients with multiple sclerosis treated with MISS, stem cells as a modern treatment. The comprehensive search was conducted in several databases, including ScienceDirect, PubMed/MEDLINE, Google scholar, and the EMBASE Database, of systematic review using the PRISMA guidelines, R software, and Excel. PROSPERO ID: 1173874 terms, only studies published in English up to January 1987 and September 2025.

Results
In our systematic review and meta-analysis, we included a total of N=1559 patients with trigeminal neuralgia caused by multiple sclerosis. These were broken down into N=836 patients, or 53%. Among these, N=867 procedures accounted for 55% of the total. Ch2 192-193.34, df=13, $p < .010000$.

Conclusion
Trigeminal neuralgia, which can be caused by multiple sclerosis, is a double combination to the patient's pain. The most common treatments are percutaneous rhizotomies, including radiofrequency rhizotomy, glycerol rhizotomy, and percutaneous balloon compression, and anatomical microvascular decompression and treatment therapy on stem cells.

Keywords:
Trigeminal neuralgia
Multiple sclerosis
Stem cells
Gamma knife radiosurgery
Percutaneous balloon compression
Microvascular decompression
Pain outcomes

Received: October 25, 2025
Revised: December 14, 2025
Accepted: December 26, 2025

Introduction

Trigeminal neuralgia (TN) is characterized by episodes of severe, recurrent, and debilitating facial pain that can occur in 1 to 2% of patients diagnosed with multiple sclerosis throughout their lives (1). The incidence of trigeminal neuralgia in patients diagnosed with multiple sclerosis is 149/100,000 in the general population per year (95% CI: 108-190), although some authors in the literature have found an incidence of 9.9/100,000 (95% CI: 9.5-10.3). Trigeminal neuralgia: It can be idiopathic or secondary in origin, with multiple sclerosis (MS) being a triggering factor. Multiple sclerosis can be treated with minimally invasive procedures, such as a gamma knife or radiosurgery, which can be managed as a targeted, noninvasive, and effective treatment (2). Trigeminal neuralgia is defined as an instantaneous, brief, stabbing pain that can recur in the different branches of the trigeminal nerve. Intermittent type 1 and constant type 2 may consist of clinical manifestations or pathological types and prognoses in different origins. Trigeminal neuralgia can also stimulate multiple peripheral pathological mechanisms of the compressed or tractioned root, with alterations or dysfunctions of the brainstem, basal ganglia, and other cortical pain-modulating mechanisms, such as the most accepted vascular theory.

Diagnosis will be based on clinical grounds, with MRI secondarily used to detect the injured and neurovascularly compressed root. Carbamazepine is considered the drug of choice; like oxcarbazepine, baclofen, lamotrigine, phenytoin, and topiramate are also manageable. In trigeminal neuralgia, microvascular decompression is the surgical treatment of choice. However, for some patients with trigeminal neuralgia and multiple sclerosis, the procedures to be performed after choosing are gamma knife radiosurgery, percutaneous balloon compression, glycerol rhizotomy, and radiofrequency thermocoagulation (3).

Trigeminal neuralgia develops in patients with multiple sclerosis, showing high comorbidity in multiple sclerosis. Therefore, the rate is 20 times higher in the general population. TN goes from a single classification to a secondary one; the relationship between TN and MS is more than complex, resulting in an intense pain syndrome (4). MS primarily affects white matter as a type of diffuse neurodegeneration with the presence of myelin in the gray matter and its alterations. There is an exacerbating relationship between multiple sclerosis and gray matter, which could lead to new pain markers that could be clearly demonstrated in imaging studies (5).

Methods

A systematic review was conducted following the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). This review focused on surgical clinical outcomes and treatment modalities related to pain in trigeminal neuralgia in patients with multiple sclerosis treated with stem cells as a modern treatment. A comprehensive systematic review, was searched and conducted in several databases, including ScienceDirect, PubMed/MEDLINE, Google Scholar, and the EMBASE Database of systematic reviews, using the PRISMA guidelines, R software, and Excel. PROSPERO ID: ID:1173874 Search terms included "trigeminal neuralgia in patients with multiple sclerosis treated with stem cells" along with terms specifying management and surgical techniques, rehabilitation methods, and associated pathologies such as demyelination. We are considering only studies published in English up to January 1987 and September 2025.

The PICO (Population, Intervention, Comparison, Outcome) framework was used to define the overall study population. Framework includes N = 1,559 patients with trigeminal neuralgia secondary to multiple sclerosis, patients (46%). Pain control was achieved between minimally invasive procedures: conservative vs. surgical. Outcome: pain control via BNI scale. It was used to define the overall study population, focusing on patients aged 18 to 85 years experiencing facial pain due to trigeminal neuralgia (Figure 1).

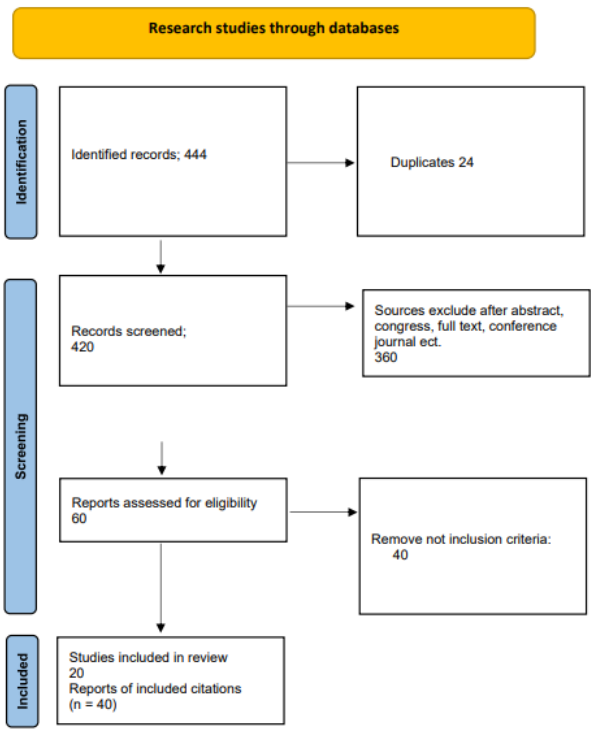

Figure 1: PRISMA flow diagram for the selection of studies on trigeminal neuralgia in patients with multiple sclerosis.

A structured literature search was conducted using Medical Subject Headings (MeSH) related to trigeminal neuralgia

in patients with multiple sclerosis. The search strategy was designed to ensure comprehensive retrieval of studies addressing clinical aspects, including cerebrospinal fluid findings, complications, diagnosis, diagnostic imaging, diet therapy, pharmacological treatment, epidemiology, etiology, pathology, pathophysiology, prevention and control, psychological aspects, radiation therapy, rehabilitation, surgical management, and therapeutic approaches. Search Strategy: The search strategy incorporated MeSH (Medical Subject Headings) terms related to Trigeminal neuralgia in Patients with Multiple sclerosis, ensuring comprehensive coverage of relevant studies.

("Trigeminal Neuralgia"[Mesh]) AND ("Trigeminal Neuralgia/classification"[Mesh] OR "Trigeminal Neuralgia/complications"[Mesh] OR "Trigeminal Neuralgia/congenital"[Mesh] OR "Trigeminal Neuralgia/diagnosis"[Mesh] OR "Trigeminal Neuralgia/diagnostic imaging"[Mesh] OR "Trigeminal Neuralgia/diet therapy"[Mesh] OR "Trigeminal Neuralgia/drug therapy"[Mesh] OR "Trigeminal Neuralgia/embryology"[Mesh] OR "Trigeminal Neuralgia/epidemiology"[Mesh] OR "Trigeminal Neuralgia/etiology"[Mesh] OR "Trigeminal Neuralgia/genetics"[Mesh] OR "Trigeminal Neuralgia/history"[Mesh] OR "Trigeminal Neuralgia/immunology"[Mesh] OR "Trigeminal Neuralgia/metabolism"[Mesh] OR "Trigeminal Neuralgia/mortality"[Mesh] OR "Trigeminal Neuralgia/pathology"[Mesh] OR "Trigeminal Neuralgia/physiopathology"[Mesh] OR "Trigeminal Neuralgia/prevention and control"[Mesh] OR "Trigeminal Neuralgia/psychology"[Mesh] OR "Trigeminal Neuralgia/rehabilitation"[Mesh] OR "Trigeminal Neuralgia/surgery"[Mesh] OR "Trigeminal Neuralgia/therapy"[Mesh]) ("Multiple Sclerosis/classification"[Mesh] OR "Multiple Sclerosis/complications"[Mesh] OR "Multiple Sclerosis/congenital"[Mesh] OR "Multiple Sclerosis/diagnosis"[Mesh] OR "Multiple Sclerosis/diagnostic imaging"[Mesh] OR "Multiple Sclerosis/diet therapy"[Mesh] OR "Multiple Sclerosis/drug therapy"[Mesh] OR "Multiple Sclerosis/embryology"[Mesh] OR "Multiple Sclerosis/epidemiology"[Mesh] OR "Multiple Sclerosis/etiology"[Mesh] OR "Multiple Sclerosis/genetics"[Mesh] OR "Multiple Sclerosis/history"[Mesh] OR "Multiple Sclerosis/immunology"[Mesh] OR "Multiple Sclerosis/mortality"[Mesh] OR "Multiple Sclerosis/pathology"[Mesh] OR "Multiple Sclerosis/physiopathology"[Mesh] OR "Multiple Sclerosis/prevention and control"[Mesh] OR "Multiple Sclerosis/psychology"[Mesh] OR "Multiple Sclerosis/radiotherapy"[Mesh] OR "Multiple Sclerosis/rehabilitation"[Mesh] OR "Multiple Sclerosis/surgery"[Mesh] OR "Multiple Sclerosis/therapy"[Mesh]).

Keywords / Other Keywords: "Trigeminal neuralgia", "multiple sclerosis", "facial pain", "microvascular decompression", "gamma knife", "radiofrequency thermocoagulation", "percutaneous rhizotomy", "percutaneous balloon compression", "stem cell therapy" and “pain control”.

Inclusion criteria

-Age range: 18 to 85 years;
-Patients receiving stem cell-based approaches or treatments for trigeminal neuralgia in multiple sclerosis, including neural repair and regeneration;
-Magnetic resonance imaging strategies for evaluating trigeminal neuralgia in Multiple sclerosis patients;
-Indicators of symptoms of trigeminal neuralgia with neurological facial compression;
-Patients who are eligible for microvascular decompression for the trigeminal nerve in the context of Multiple sclerosis;
-Postoperative neurological outcomes in patients with trigeminal neuralgia diagnosed with multiple sclerosis.

Exclusion criteria

-Patients not diagnosed with multiple sclerosis, or those with facial paralysis due to other causes, such as trauma, herpes, or other demyelinating diseases (e.g., Guillain-Barré syndrome);
-Pediatric patients without an established diagnosis;
-Patients with trigeminal neuralgia vs. multiple sclerosis alone.

Data collection

Data were extracted from the included studies, covering various aspects of trigeminal neuralgia in patients with multiple sclerosis, including diagnosis, management, and treatment outcomes. Physical examinations and clinical data considered factors influencing TN in MS patients, including facial or spinal pain. Details on surgical, clinical, and conservative management strategies were recorded, including early decompression, pharmacological therapy (e.g., carbamazepine), gamma knife radiosurgery, microvascular decompression, stereotactic surgery, and percutaneous procedures such as balloon compression or rhizotomy.

Data extraction and analysis

We performed data extraction using standardized systems and a rigorous analysis of research manuscripts relevant to trigeminal neuralgia in patients with multiple sclerosis with both diagnoses. Detailed information on the studies was collected, including demographic characteristics, interventions, control parameters in comparative studies, authorship, year of publication, and the current year's study design.

Results

In our systematic review and meta-analysis, N=444 publications were included in this study, but only N=100 were eligible; N=340 were excluded because they did not meet the inclusion criteria, while of N= 60 we had to remove N=40 and only work with N=20 articles for the main text. A total of N=1,559 patients with trigeminal neuralgia secondary to multiple sclerosis were included. Among these, N=836 patients (53%) underwent treatment, with a total of N=867 procedures performed (55%). Of these procedures, N= 160 involved stereotactic radiosurgeries, accounting for 10% of the total. Complete pain control was achieved in N=499 patients (32%), while partial pain control or relief was observed in N=213 patients (13%) of the conservative treatment. Heterogeneity was assessed as follows: Chi^2=35.83, df=14, P<0.001 vs. I^2=61%, test for overall effect: Z= 0.73, P=0.; Tau^2 = 0.01; Chi^2=34.68, df=14, P<0.002; I^2=60%, confidence interval test for overall effect: Z=0.34, P=0.74, (see Table 1, Figures 1–2,5, 6, 7).

Table 2 summarizes outcomes for N=723 patients (46%). Pain control was achieved in N =205 (13%), complications occurred in N=79 (5%), and microvascular decompression was performed in N=10 (0.6%). Balloon microcompression was performed in N=217 patients (14%). Additional procedures included rhizotomy in N=184 (12%), stereotactic radiosurgery in N = 59 (4%), and gamma knife radiosurgery in N=56 (3%), Heterogeneity was assessed as follows: Chi^2=37.74, df=14, P<0.0006 vs. I^2=63%, test for overall effect: Z=0.75, Risk ratio P<0.45, (see Table 2, 3, 4 Figures 3–4, 8, 9 10).

A randomized, double-blind, placebo-controlled study conducted in 2006–2007; included patients with neuropathic pain due to diabetic peripheral neuropathy, postherpetic neuralgia, traumatic or surgical nerve injuries, incomplete spinal cord injuries, and trigeminal neuralgia (including MS-related TN) or peripheral neuropathy associated with immunocompromising diseases such as HIV. Eligible patients had a mean weekly pain score ≥ 4/11 and received a single dose of lamotrigine (200, 300, or 400 mg daily; n = 111) or placebo (n=109) for at least 14 weeks, including 8 weeks of dose escalation. This study mirrored earlier trials of gabapentin and tricyclic antidepressants. There was no significant difference in pain reduction between lamotrigine and placebo (P=0.67). Pain was assessed using the McGill Short Form, the Clinical Global Impression of Change scale, and the Patient Global Scale of Change. Lamotrigine (up to 400 mg/day) and gabapentin were generally well tolerated (6).

Table 1. Management, approach and control of pain in patients with trigeminal neuralgia in patients with multiple sclerosis

Authors	Kind of study	Year	Patients No.	Procedure	Stereotactic radio surgery (SRS)	Complete pain control	Relief of pain	Follow up	P=Value
Holland et al.(7)	Retrospective	2017	17	10	7	12	9	N/A	p=0.04
Kanpolat et al.(8)	Retrospective	2000	17	25	N/A	12	14	60 months (range: 6-141 months	N/A
Mallory et al.(9)	Retrospective	2012	95	67	69	55	27	13 months (range, 0.25-132 months)	P < .001
Berk et al.(10)	Retrospective	2022	13	13	N/A	N/A	10	52 months	N/A
Kondziolka et al.(11)	Retrospective	1994	53	27	N/A	29	8	36 months	N/A
Pickett et al.(12)	Review	2005	53	97	N/A	38	7	81 months	P < 0.05
Mohammad-Mohammadi et al.(13)	Retrospective	2013	96	277	52	N/A	N/A	(median, 5.7 years)	P = .04
Kouzounias et al.(14)	Retrospective	2010	47	66	N/A	40	17	20 months	N/A
Montano et al.(15)	Retrospective	2012	21	21	N/A	8	N/A	N/A	p = 0.042
Mathieu et al.(16)	Retrospective	2012	45	18	27	18	22	60 months (range 12-276 months)	N/A
Alvarez-Pinzon et al.(17)	Retrospective	2017	202	78	N/A	175	48	24 months	P = 0.03
Bergenheim et al.(18)	Retrospective	2013	100	100	N/A	77	23	28 months	P = 0.2
Rogers et al.(19)	CT	2002	15	10	5	12	3	17 months (range 6-38 months)	N/A
Weller et al.(20)	Retrospective	2014	35	35	N/A	N/A	13	N/A	p = 0.04
Conti et al.(21)	Cohort study	2017	27	23	N/A	23	12	37 (18-72) month	

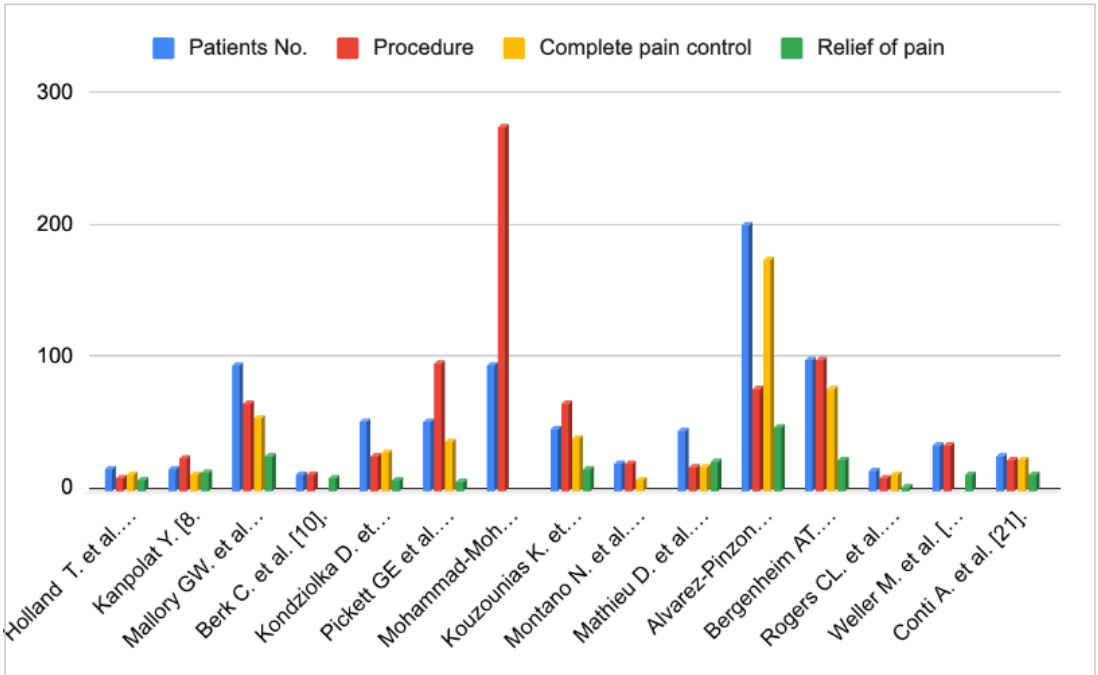

Figure 2. Management and procedures for pain control vs. relief in patients with trigeminal neuralgia in patients with multiple sclerosis.

Table 2. Multiple research on patients with trigeminal neuralgia caused by patients with multiple sclerosis as a trigger point

Author	Research	Year	Patients No	Procedures or surgical techniques	Pain control	Complications	Follow up	P=value
Paulo et al.(22)	Retrospective	2020	33	Microvascular decompression	22	N/A	53.5 months	0.006
Worm et al.(23)	Prospective study	2023	18	microvascular decompression, glycerol rhizolysis or balloon compression	2	3	3-6 months	N/A
Gündüz et al.(24)	Retrospective	2023	215	percutaneous radiofrequency thermocoagulation	N/A	51	36 months	0.065
Patel et al.(25)	Case series	2021	20	radiofrequency thermocoagulation	12	N/A	5 years	0.275
Helis et al.(26)	Retrospective	2019	74	Gamma Knife Radiosurgery	61	3	2-4 years	<.01
Tyurnikov et al.(27)	Retrospective	2015	28	percutaneous rhizotomy	4	4	3 months to 14 years	
Yang et al.(28)	Retrospective	2024	101	microvascular decompression (MVD) and gamma knife radiosurgery (GKRS)	N/A	9	12 months	0.037
Ariai et al.(29)	Retrospective	2014	10	Microvascular decompression (MVD)	5	4	4 months (range, 1-23 months)	N/A
Tuleasca et al.(30)	prospective case series	2014	43	Radiosurgery using the Gamma Knife	39	N/A	53.8 months (12-157.1)	N/A
Sandell and Eide(31)	Retrospective	2010	15	Microvascular decompression	7	N/A	55 months (range, 17-99 months)	N/A
Zorro et al.(32)	Retrospective	2009	37	Gamma knife	32	N/A	56.7 months (range, 6-174)	N/A
Martin et al.(33)	Retrospective	2015	80	Percutaneous balloon	N/A	N/A	43 months	p< 0.01
Eldridge et al.(34)	Retrospective	2003	9	microvascular decompression (MVD)	4	3	N/A	N/A
Athanasiou et al.(35)	Case series	2005	5	trigeminal ganglion percutaneous injection and radio-frequency l	4	N/A	38.75 months; range 8-59 months)	N/A
Broggi et al.(36)	Cohort study	2004	35	microvascular decompression (MVD)	13	2	44 months (range, 6-108 mo)	N/A

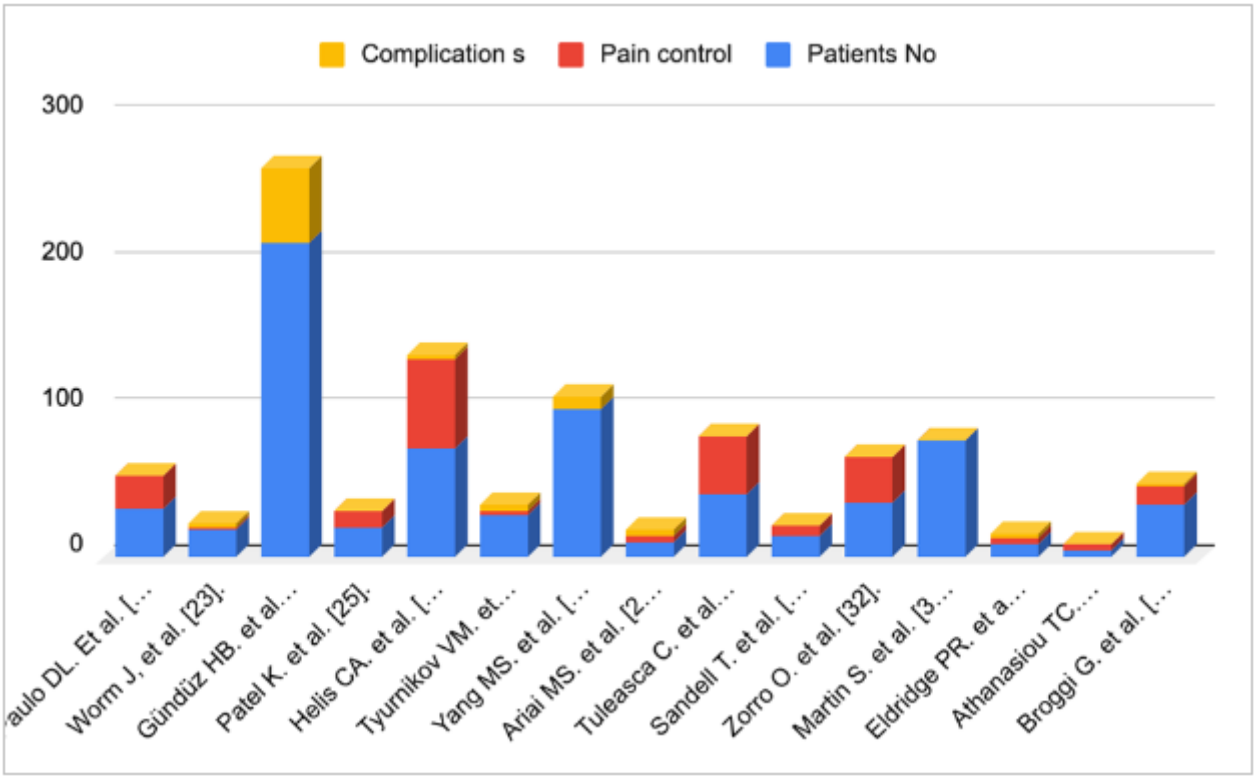

Figure 3. Analysis of groups of patients with trigeminal neuralgia in multiple sclerosis.

Table 3. Recently surgical procedures in patients with trigeminal neuralgia secondary to multiple sclerosis

Reference	Rhizotomy	Stereotactic radiosurgery	Gamma Knife radiosurgery (GKRS)	Microvascular decompression (MVD)	Balloon microcompression
Mousavi et al.(37)	0	0	29	0	0
Holland et al.(7)	10	7	0	0	0
Mallory et al.(9)	67	0	0	0	69
Mohammad-Mohammad et al.(13)	89	52	0	10	82
Kouzounias et al.(14)	0	0	0	0	66
Mathieu et al.(16)	18	0	27	0	0

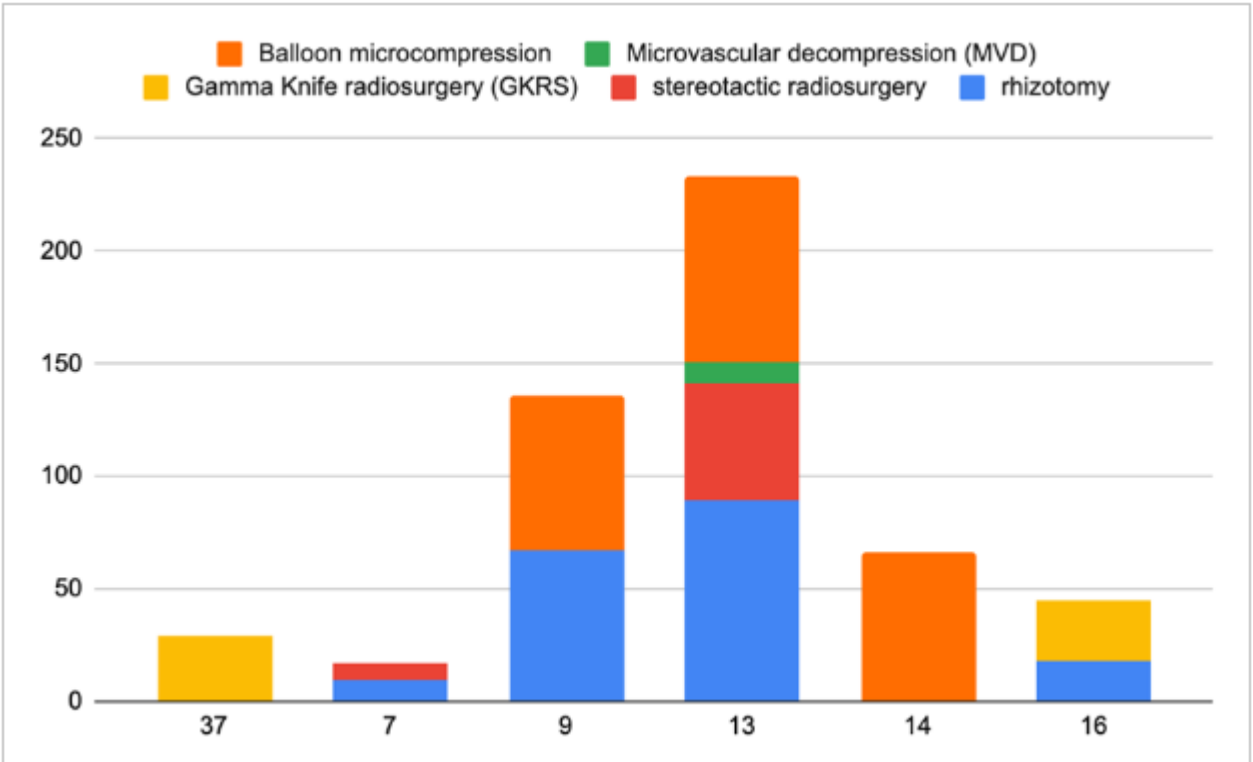

Figure 4. Graphs of study groups of the most commonly used surgical management in patients with multiple sclerosis causing trigeminal neuralgia (TN).

Table 4. Barrow Neurological Institute Pain Intensity Score

Score	Pain evaluation
I	No pain, no conservastive treatments
II	Variant pain, no treatment required
III	Some pain, good control with medications
IV	Some pain, not good control with medications
V	Stremely pain or not letting the pain

Trigeminal neuralgia (TN) is a well-recognized clinical manifestation of multiple sclerosis (MS), yet the symptomatology associated with specific MS subtypes remains understudied. A recent retrospective study spanning 2007 to 2022 aimed to identify patients diagnosed with both MS and TN. Pain was assessed using the Barrow Neurological Institute (BNI) pain scale, where categories I–III indicated good pain control and IV–V indicated poor control.

In the study, eight patients with TN caused by MS were evaluated, including four with relapsing MS (RMS) and eleven with secondary progressive MS; the outcomes in the latter group were unclear. Three patients with secondary relapsing and progressive MS were followed for 11 to 18 years. A total of 30 patients transitioned to progressive MS. Treatment-refractory neuralgia included nine patients with RMS and 22 with progressive MS ($p = 0.001$). The median duration of analgesic use was lower in patients with TN compared with those with progressive MS ($p = 0.014$). MRI revealed demyelinated lesions in the trigeminal sensory pathway in 27 patients, while 14 patients had negative MRI findings. Patients with preexisting conditions were more likely to experience treatment failure (74% vs. 36%, $p = 0.017$) and to require surgical intervention (55% vs. 7%, $p = 0.003$). TN was not observed in patients with primary progressive MS, indicating that neuralgia in these cases was more amenable to treatment (37).

A systematic review and meta-analysis further investigated the etiology of TN, including idiopathic cases and secondary cases triggered by MS, and assessed the contribution of minimally invasive procedures such as Gamma Knife radiosurgery (GKRS) as precise, effective, and noninvasive primary treatments. Approximately 30 patients with TN and MS were treated with GKRS, with efficacy evaluated using pain scores and the BNI scale. Outcomes included numbness, irritating pain, facial pain, and recurrent pain.

Fourteen studies encompassing over 752 GKRS procedures for post-MS TN were analyzed. Initial pain was present in 83% of cases, with an overall treatment success rate of 51%. Facial numbness occurred in 19% of cases, bothersome or irritating pain in 4.1%, and recurrent pain in 40%. The odds ratio for a positive response to initial pain was 0.83 (95% CI: 0.76–0.89), while treatment success had an odds ratio of 0.51 (95% CI: 0.379–0.639). The odds ratio for facial numbness was 0.196 (95% CI: 0.130–0.262), for bothersome or irritating numbness 0.041 (95% CI: 0.013–0.069), and for recurrence 0.403 (95% CI: 0.254–0.551) (38).

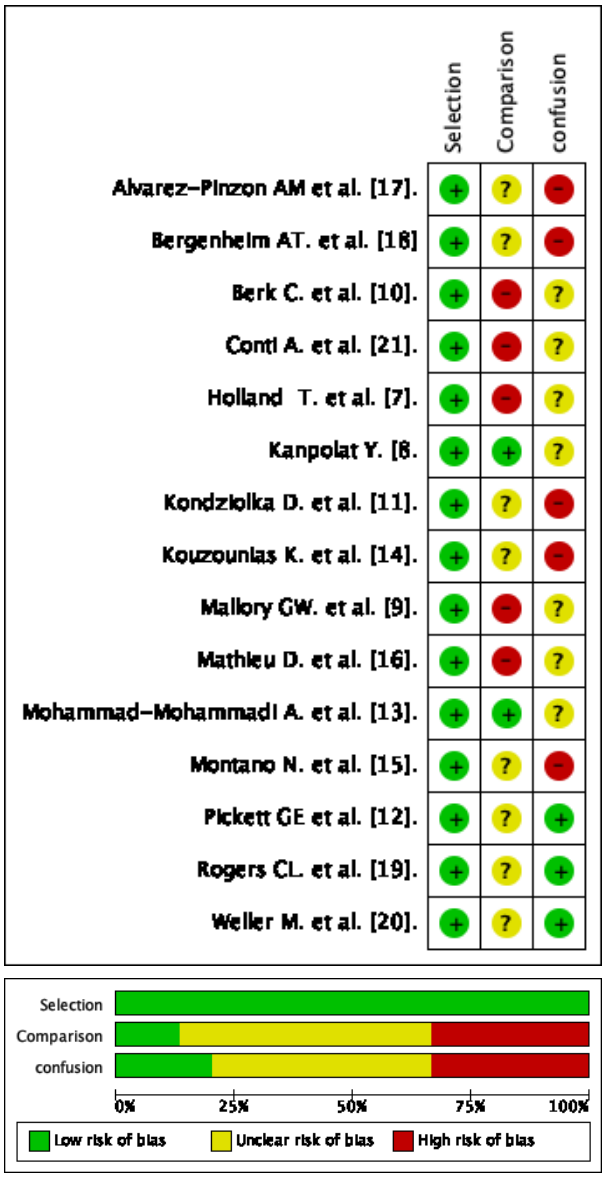

Figure 5. Risk of bias graph of the patients with TN-MS.

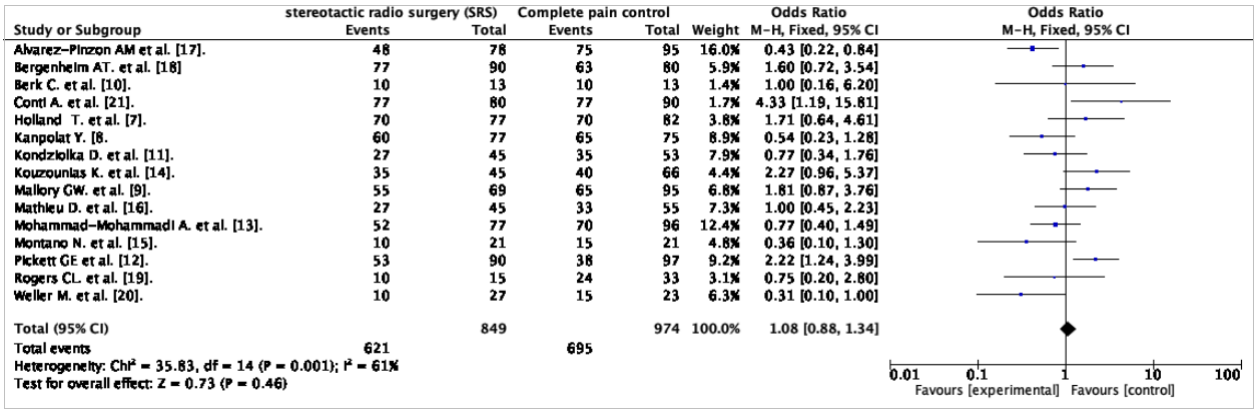

Figure 6. Florest Plot: Odds- ratio in patients with multiple sclerosis causing by trigeminal neuralgia (TN).

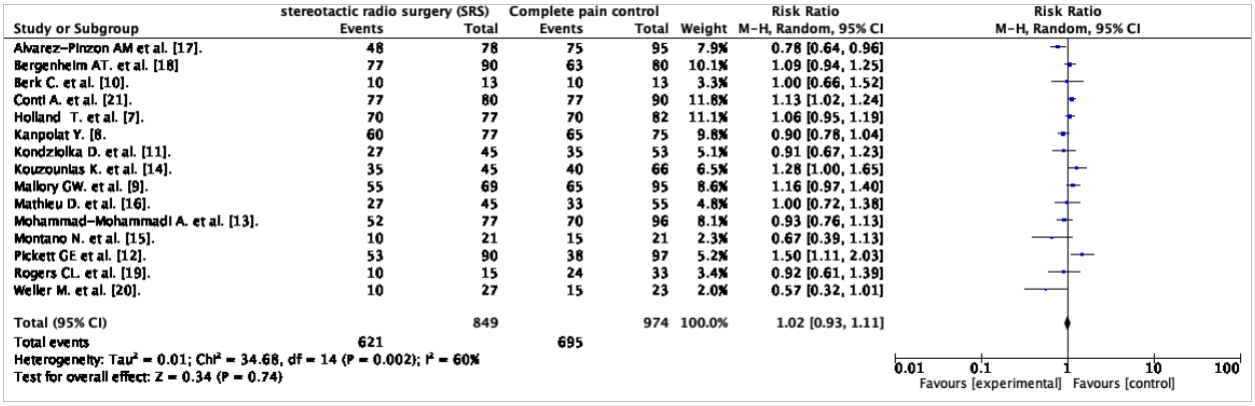

Figure 7. Florest Plot: Risk- ratio Patients with Trigeminal neuralgia in multiple sclerosis.

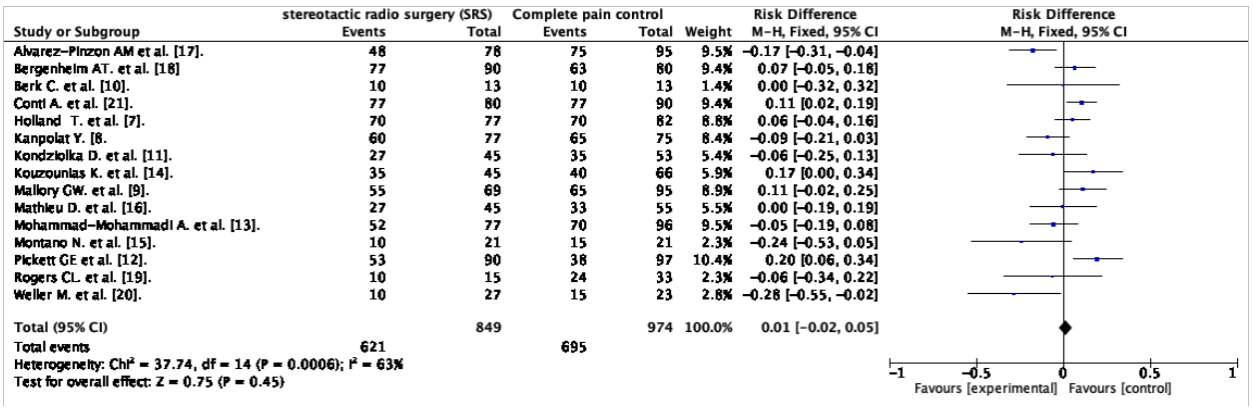

Figure 8. Forest plot illustrating management strategies in patients with multiple sclerosis causing trigeminal neuralgia (TN), showing the risk difference in pain management and control.

A recent retrospective study evaluated the efficacy of onabotulinumtoxinA (BTX-A) in primary trigeminal neuralgia (TN), noting that the effects in secondary TN remain less defined. The study included 53 patients, of whom 42% had primary TN and 58% had TN associated with multiple sclerosis (TN-MS). Treatment with BTX-A was effective in 52% of TN-MS patients and in 45% of those with primary TN (10 patients).

BTX-A demonstrated particular efficacy in patients with persistent pain and those previously treated, though its effectiveness varied. The results were statistically significant (p = 0.007; odds ratio [OR]: 0.020–0.53; and p = 0.047; OR: 0.046–0.98) in the treatment of trigeminal ganglion pain. Clinical characteristics, demographics, and pain intensity were assessed two weeks prior to BTX-A administration. The treatment is usually delivered subcutaneously and submucosally. Efficacy was evident, with a ≥50% reduction in pain intensity and frequency reported in treated patients (39).

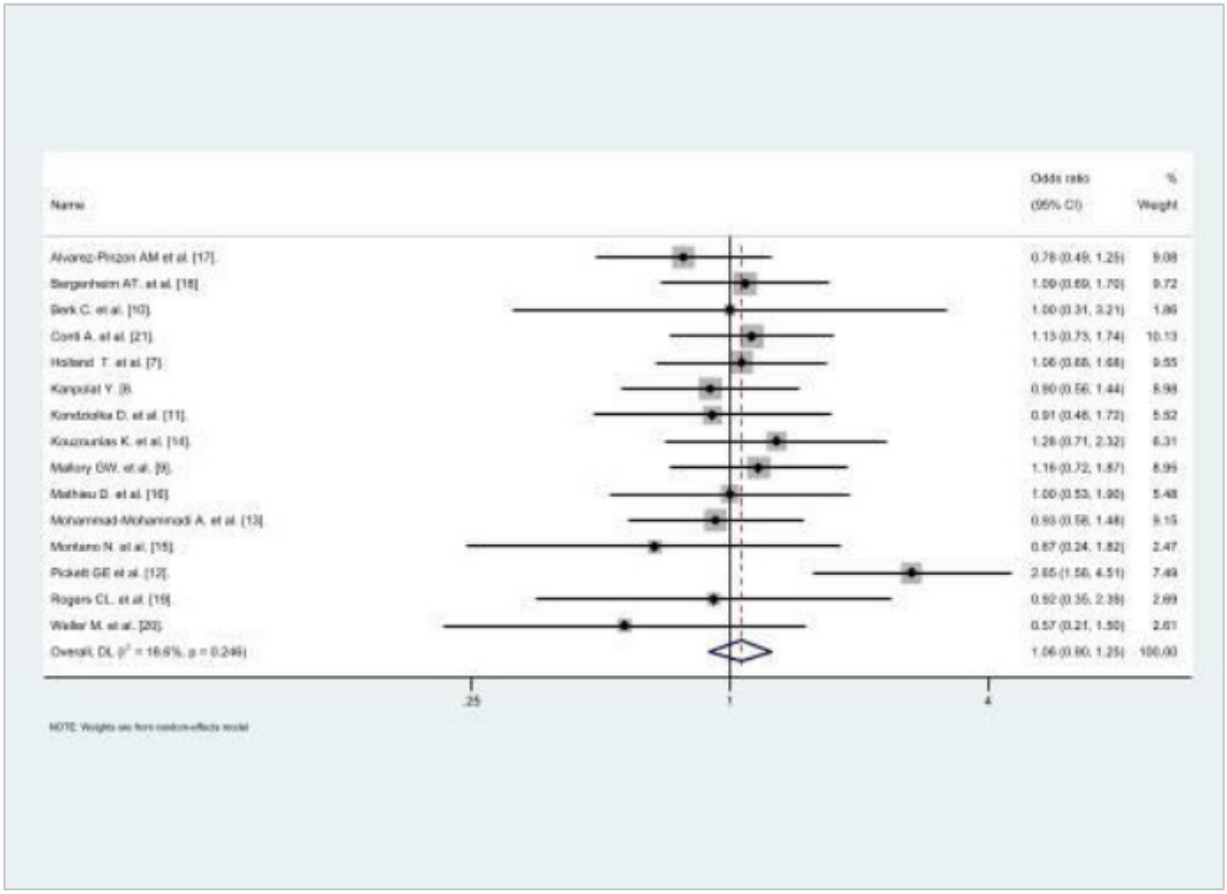

Figure 9. Forest Plot illustrating the effect of minimally invasive surgery and radiotherapy over conservative therapy in managing the Trigeminal Neuralgia in Multiple sclerosis patients.

Discussion

The International Classification of Headache Disorders and guidelines from the International Association for the Study of Pain classify trigeminal neuralgia (TN) based on neuropathic pain characteristics. TN can arise from vascular compression of the trigeminal nerve and pathophysiological changes in the nerve root, or as secondary TN due to idiopathic neurological diseases, which requires careful investigation (40,41).

In patients with TN associated with multiple sclerosis (MS), the incidence ranges from 11% to 30%, often resulting in a high rate of bilateral TN. Typical pharmacological treatment with carbamazepine may lose efficacy in these patients, who can also present with muscle weakness, gait disturbances, and dizziness (42). Pregabalin is another therapeutic option for neuropathic pain, though its efficacy has not been fully validated (43).

Surgical interventions are available for TN in MS patients, including microvascular decompression (MVD), stereotactic radiosurgery, and percutaneous lesions of the Gasserian (trigeminal) ganglion. Some authors have recommended radiofrequency (RF) thermocoagulation of the Gasserian ganglion due to its rapid, reliable results and lower recurrence rate (44). Although surgical outcomes in MS-related TN are generally less favorable than in typical TN, clinical experience remains a critical factor in achieving effective pain management (45).

Pathophysiology associated with TN-MS

The literature identifies an association between pontine demyelinating plaques and trigeminal neuralgia (TN). Anatomically, these lesions affect the intrapontine segment of the trigeminal nerve, specifically the ventrolateral pons between the trigeminal root entry zone (REZ) and the primary intrapontine afferent pathways (46). Demyelinating plaques are implicated in tensor abnormalities observed on imaging in both classic and idiopathic TN, particularly in the cisternal and REZ segments of the trigeminal nerve in the pons (47). These plaques may also coincide with trigeminal root compression in TN-MS patients, sometimes serving as the sole clinical manifestation, suggesting that pontine plaques can affect intra-axial primary afferents as well as the compressed nerve itself (48). TN secondary to MS may involve a "double crush" mechanism, resulting from mechanical and inflammatory demyelinating injury of first-order neurons (49).

Pharmacological management includes baclofen, a muscle relaxant and presynaptic modulator, which is used for trigeminal nerve pain. However, prolonged use can lead to tolerance and diminished effectiveness. In such cases, symptomatic neurolesional surgery is indicated. Radiofrequency thermorhizotomy is considered the procedure of choice, with intraoperative monitoring or evoked potentials of the trigeminal nerve, as it is appropriate given the injury severity and anatomical location (50).

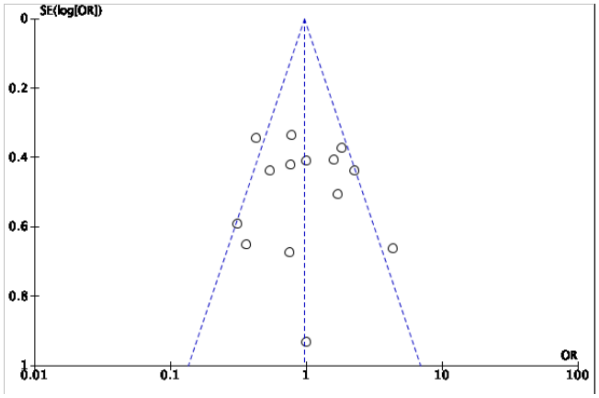

Figure 10. Funnel splot of the Patients, with TN-SM, Managements, treatments and outcomes.

Surgical techniques for TN in MS patients include percutaneous balloon compression (PBC), percutaneous glycerol retrogasserian rhizolysis (PRGR), radiofrequency rhizotomy (RFR), and glycerol rhizotomy (GR). Asplund et al. note that, despite over 30 years of clinical use, PBC and PRGR have demonstrated comparable efficacy in treating TN. Both procedures carry a risk of postoperative hypoesthesia, though PBC is associated with lower incidences of dysesthesia, corneal hypoesthesia, and technical complications (51). Percutaneous rhizotomies—including RFR, GR, and PBC—are minimally invasive options for MS-related TN (52). No single technique consistently outperforms the others, although PBC has been associated with higher rates of postoperative masticatory weakness than GR. Lozouet et al.(53) reported that, among 18 patients followed for three months, RFR provided pain relief in approximately three-quarters of cases compared to PBC. Similarly, Noorani et al.(54) found that RFR and PBC provided longer-lasting pain relief than GR ($P = 0.013$).

Endoscopic decompression techniques

The retrosigmoid endoscopic keyhole approach, following completion of vascular decompression, offers significant advantages, particularly in navigating the complex anatomy of the transscapular cerebellar artery. The use of an endoscope allows for precise mapping of the root entry zone (REZ) and the trigeminal cerebellar artery (TCA). In cases where the vasculature is restricted due to dense perforating arteries, interposing a Teflon sponge enables effective and accurate decompression without compromising these critical structures. Additionally, the presence of multiple trigeminal nerve sites and spiral TCA configurations can be addressed through combined transpositional techniques, tailored to the patient's individual anatomical variations (56).

Management of Spasticity in MS Patients

We go over both pharmaceutical and non-pharmacological methods for treating and controlling multiple sclerosis patients' spasticity. Spasticity is treated with botulinum toxin A (BoNT-A). The most popular antispasmodic medications include tizanidine, diazepam, dantrolene, and baclofen. But like all drugs, they are costly and have few effects. Despite the complexity of MS, treatment and rehabilitation must be patient-centered, with an emphasis on symptom reduction, increasing physical activity, and improving both active and passive involvement and quality of life (57).

Limitations and future directions

There is an exacerbating relationship between multiple sclerosis (MS) and gray matter, which may give rise to novel pain markers detectable through imaging studies. In clinical trials, no significant difference was observed between lamotrigine and placebo in managing TN ($p = 0.67$). Another limitation noted was that the median duration of analgesic use was shorter in patients with TN compared with those with progressive MS ($p = 0.014$). Patients with preexisting conditions were more likely to experience treatment failure (74% vs. 36%, $p = 0.017$) and a higher likelihood of requiring surgical intervention.

Regarding pharmacological management, onabotulinumtoxinA (BTX-A) is not recommended for primary TN, as its efficacy in secondary TN remains unclear. Baclofen, a muscle relaxant and presynaptic modulator, is commonly used for trigeminal nerve pain, but prolonged use may lead to tolerance and reduced effectiveness. In cases where tolerance develops, symptomatic neurolesional surgery is indicated as a definitive treatment option.

Conclusion

Trigeminal neuralgia associated with multiple sclerosis (MS) represents a compounded source of pain for the patient. Common treatments consist of percutaneous rhizotomies, including radiofrequency rhizotomy, glycerol rhizotomy, and percutaneous balloon compression, all of which are minimally invasive techniques. Anatomical microvascular decompression is a commonly employed surgical intervention for managing pain in trigeminal neuralgia associated with multiple sclerosis (TN-EM) and for stem cell therapy.

This study emphasizes the intricate nature of the TN-EM relationship and the necessity for customized management strategies, encompassing conservative, pharmacological, and surgical approaches. Carbamazepine is considered the standard treatment for trigeminal neuralgia, even after Gasserian ganglion blockade. Combining various treatment modalities for TN and MS-related pain has demonstrated effectiveness, with outcomes frequently evaluated using validated pain scales, particularly the Barrow Neurological Institute (BNI) scale. No significant difference was observed between minimally invasive approaches in patients with trigeminal neuralgia and multiple sclerosis (10%) and conservative treatment for pain control (13%). The primary distinction is that trigeminal neuralgia necessitates nerve decompression, as it is unresponsive to conservative treatment; following decompression, pain intolerance will not be managed by medication.

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Conflicts of interest: There is no conflict of interest.
Funding: No.