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Review article

Open surgery vs. stereotactic radiosurgery for tumour-related trigeminal neuralgia: A systematic review

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ABSTRACT

Background: Secondary trigeminal neuralgia is a facial pain in trigeminal nerve dermatome caused by an underlying disease, such as cerebellopontine angle tumours. Treatment options to relieve the pains were surgical tumour resection and stereotactic radiosurgery of the tumour or trigeminal nerve. This study aims to review the efficacy of open surgery and stereotactic radiosurgery and recommend the treatment of choice for secondary trigeminal neuralgia due to cerebellopontine angle tumours.

Method: The inclusion criteria were studies covering patients with trigeminal neuralgia associated with cerebellopontine angle tumours that were treated with either open surgery or stereotactic radiosurgery and reported pain outcomes after treatment. Non-English articles or studies with a population of less than five were excluded. We systematically searched studies from PubMed, Ebscohost, and Cochrane Library from inception until December 20, 2021. Several works of literature from manual search were also added. Selected articles were appraised using a critical appraisal tool for prognostic studies.

Result: Included articles were 26 retrospective studies and one prospective study comprising 517 patients. Of 127 schwannomas, 226 epidermoids, 154 meningiomas, and ten other tumours, 320 cases received surgical tumour excision with or without MVD, 196 had tumour-targeted radiosurgery, and 22 underwent nerve-targeted radiosurgery. In surgical series, 92.2 % gained pain improvement, 2.8 % were unchanged, and 4.5 % had recurrence; none of the patients had worsened outcomes. In cases treated with tumour-targeted radiosurgery, the improvement rate was 79.1 %, unchanged at 14.3 %, recurrence at 26.5 %, and worse symptoms rate after the intervention was 6.6 %. Six patients with recurrent pain after tumour-targeted radiosurgery received secondary nerve-targeted radiosurgery with improved outcomes. Only one patient in our review underwent primary nerve-targeted radiosurgery, and the result was satisfactory. One study treated 15 patients with a single session of tumour-targeted and nerve-targeted radiosurgery, with an improvement rate of 93.3 % and a recurrence rate of 21.4 %.

Conclusion: Open surgery releasing the nerve root from compressive lesions is advocated to be the first-line treatment to gain satisfactory outcomes. Total removal surgery is recommended if possible. Nerve-targeted radiosurgery should be reserved as a secondary treatment for recurrent cases.

1. Introduction

Trigeminal neuralgia (TN), or tic douloureux, is a chronic yet uncommon disease characterized by recurring facial pain in the trigeminal nerve's dermatome. The fifth nerve (N.V) comprises three subdivisions: ophthalmic, maxillary, and mandibular [1,2]. The International Headache Society (IHS) recently updated TN classification into classical trigeminal neuralgia, secondary trigeminal neuralgia, and idiopathic trigeminal neuralgia. Secondary TN is defined as a condition caused by an underlying disease, with diagnostic criteria of recurrent paroxysms of unilateral facial pain fulfilling the requirements for TN, and an underlying condition has been demonstrated as a cause of the symptom [3].

Abbreviations: CPA, cerebellopontine angle; IHS, International Headache Society; MVD, microvascular decompression; N.V, fifth nerve; REZ, root entry zone; SCA, superior cerebellar artery; SRS, stereotactic radiosurgery; TN, trigeminal neuralgia; VS, vestibular schwannoma.

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Tumour-related facial pain affects between 1 % and 13 % of people with TN symptoms. Although most of these instances are caused by trigeminal schwannomas or petroclival meningiomas, trigeminal nerve symptoms can also be caused by cerebellopontine angle (CPA) tumours, such as vestibular schwannoma (VS) [4]. Meningiomas and epidermoids in the CPA seemed to be the most common causes of tumour-induced TN, accounting for 86–89 % of patients with symptomatic TN [5–8]. Tumour-induced TN is caused by a variety of different processes and is categorized into three types based on surgical anatomical findings: type A, tumour encasing the trigeminal nerve; type B, compression of the trigeminal nerve by the tumour; type C, compression of the trigeminal nerve by both the artery and the neoplasm. Meningiomas tended to displace the nerve with or without vascular compression, whereas epidermoid tumours directly compressed or wrapped the nerve [5]. Irritation of the N.V by the keratin contents has been proposed as a possible etiology for epidermoid-induced neuropathy [9,10].

Several treatment modalities have been reported in treating TN associated with CPA tumour, including tumour resection (with decompression of the N.V if vascular compression is encountered), stereotactic radiosurgery (SRS) of the neoplasm, and SRS of the fifth nerve; however, the results were varied. To our knowledge, studies have yet to review the best treatment for this pathological condition. We aim to review the efficacy of open surgery and SRS and recommend the treatment of choice of secondary TN caused by CPA tumours.

2. Method

2.1. Study search

We performed a study by following the reporting checklist for systematic review based on Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [11]. Available articles were retrieved through search from PubMed, Ebscohost, and Cochrane Library from inception until December 20, 2021. A manual search through other sources was also conducted. We used the keywords "cerebellopontine angle tumour OR acoustic neuroma OR vestibular schwannoma OR meningioma OR epidermoid tumour" AND "trigeminal neuralgia" in MeSH term and text-word format to find journals that matched our criteria. We did not include the outcomes criteria nor filter the study type to broaden our search. There was no limit to the date of the study, but our search was limited to English-only articles.

2.2. Inclusion and exclusion criteria

Inclusion criteria were experimental or observational studies, articles reporting cases of secondary trigeminal neuralgia due to CPA tumours treated with microsurgery or SRS, and the availability of follow-up reports of pain outcomes after therapy. The outcomes were eligible if they indicated whether the pain was improved, the same as before therapy, or worse than before treatment during follow-up. Recurrence was also included in outcomes if the pain was reported to improve initially but then recurred. We excluded non-English articles and studies with populations that met the inclusion criteria of less than five.

If a study contained some population with non-tumoral lesions or tumours outside the CPA region, we only included subjects suitable to our inclusion criteria. For reliability, we agreed to exclude articles if the number of included populations was less than five. We did not include papers that did not directly evaluate outcome of trigeminal pain in CPA tumours. Studies evaluating trigeminal neuropathy or dysfunction without specifically mentioning trigeminal pain or neuralgia were excluded.

2.3. Data extraction and quality assessment

Three reviewers (SWN, SAHP, and MH) independently screened titles and abstracts and read the full text to filter literature that met our research question and inclusion criteria. If inconsistencies were encountered, the problems were resolved through discussion with the first author (SWN). Selected articles were appraised using a critical appraisal tool for prognostic studies (available from https://cebm.net/wp-content/uploads/2018/11/Prognosis.pdf). Discussion between three reviewers or consultation with the first author was conducted if there was any disagreement during evaluation.

3. Result

3.1. Search result and study selection

Fig. 1 presents a detailed process of literature selection. In the initial search of combined keywords, we found 359 articles from PubMed, 463 pieces from Ebscohost, and two from Cochrane Library. Additional literature from manual search was 30; total number of articles initially after removing duplicates was 831. After screening titles and abstracts and assessing full-text eligibility we included 27 studies.(Figs. 2–6).

3.2. Studies Characteristic

Twenty-seven studies were selected, comprising 517 patients with secondary trigeminal neuralgia caused by CPA tumours who underwent microsurgery or SRS. All articles were published between 1986 and 2021, and only one study [12] conducted research prospectively. Of 27 papers, seven studies were conducted in China, [5,8,13–17] six in South Korea, [18–23] four in the United States (US), [4,24–26] three in Japan, [27–29] two in Germany, [30,31] and one in Saudi Arabia, [32] Turkey, [33] Russia, [7] Egypt, [34] and Vietnam [12]. There were 127 schwannoma cases, 226 epidermoids, 154 meningiomas, and ten other tumours. Resection of the tumour without microvascular decompression (MVD) was performed in 220 cases, tumour resection with MVD in 100 instances, tumour-targeted SRS in 196 patients, and trigeminal nerve-targeted SRS in 22 patients. Trigeminal nerve-targeted SRS treatments were done in six patients in Park et al. [18] study whose pain worsened after receiving tumour-targeted SRS, one epidermoid case in Cho et al. [21] study, and 15 patients in Kim et al. [23] study who had tumour-targeted and nerve-targeted SRS in a single session. Of twelve studies that performed tumour-targeted SRS, four had a mean maximum dose of 28.7 Gray (Gy), 25 Gy, 26.1 Gy, and 26.4 Gy, [17,18,20,27] four

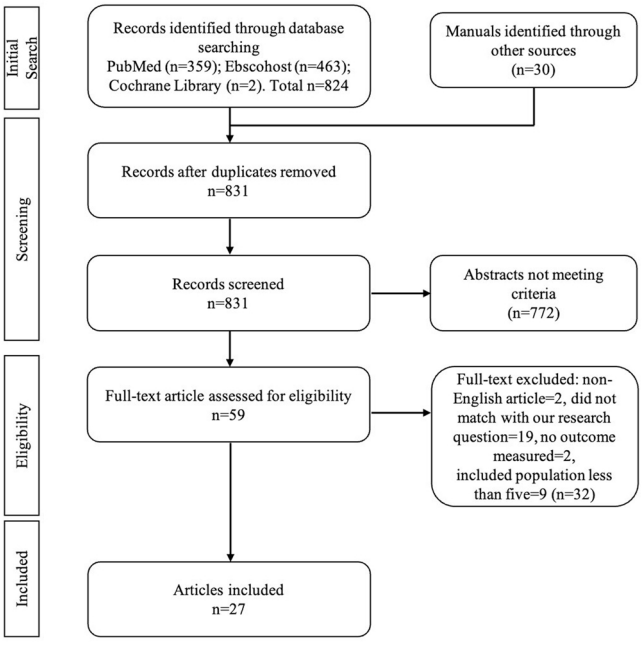

Fig. 1. Flowchart of screening strategy for included studies.

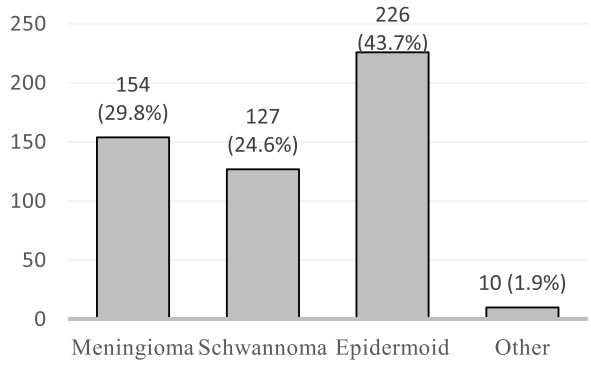

Fig. 2. Types of Tumours Included in This Study.

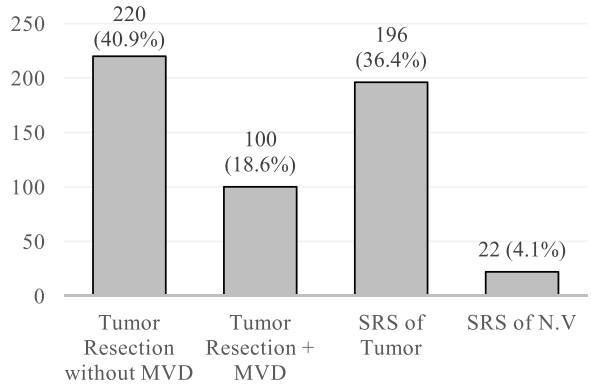

Fig. 3. Treatment Modalities Reported in This Study.

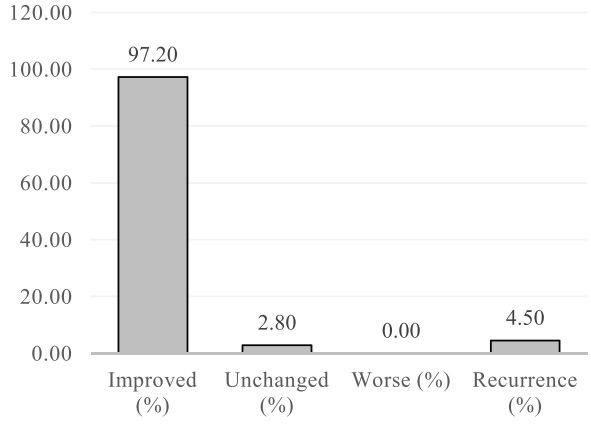

Fig. 4. Tumour Resection Pain Outcomes.

utilized a median marginal dose of 12 Gy, [4,12,26,29] two performed a median marginal dose of 13 Gy, [19,23] and one delivered a median marginal dose of 14 Gy and 11 Gy [21,34]. Three studies that performed trigeminal nerve-targeted SRS administered a maximum dose of 90 Gy and 80 Gy [18,21,23]. The detailed characteristics of the studies are presented in Table 2.

3.3. Pain outcome evaluation

Of 517 cases, three patients from Barker et al.'s study whose outcomes could not be evaluated due to loss of follow-up. [24] Articles in our review described pain outcomes variably; therefore, we divided the pain outcomes category into improved, unchanged, and worse. Patients were included in the improved category if the pain was relieved, even

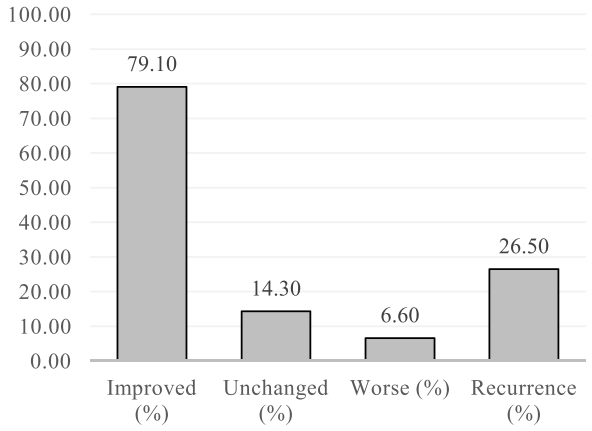

Fig. 5. Tumour-Targeted SRS Pain Outcomes.

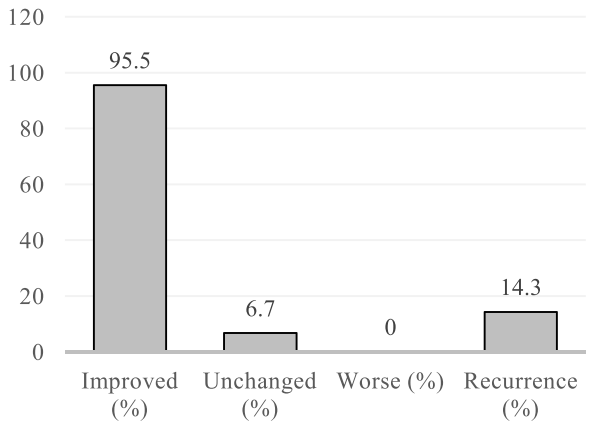

Fig. 6. SRS of Trigeminal Nerve Pain Outcomes.

Table 1
Research question.

Study Component	
Population	Patients with Secondary Trigeminal Neuralgia Associated with CPA Tumour
Intervention/ Exposure	Tumour Resection with or without Microvascular Decompression, SRS of Tumour, SRS of Trigeminal Nerve
Comparison	-
Outcome	Pain Improvement

partially, immediately after treatment or in a defined period. Cases were considered to have a recurrence if there was a recovery period after treatment, but the pain reappeared.

3.3.1. Tumour resection with or without MVD

Three hundred twenty patients underwent tumour resection surgery. As many as 108 cases were found to have offending vessels compressing trigeminal nerve intraoperatively, and 100 patients received microvascular decompression. As many as 197 cases reported underwent total removal surgery, and 89 received subtotal tumour removal. Of all patients who underwent surgical treatment, 97.2 % gained pain improvement after surgery, 2.8 % of patients had their symptoms unchanged, and none had worse pain. As much as 4.5 % of tumour-resected patients suffered recurrence. Of nine patients with the symptoms unchanged, three were subtotal removal cases, including two patients whose tumour capsule was not dissected from trigeminal nerve, and six were unexplained. Of all the recurrent cases, ten were related to tumour residual or regrowth; three were total removal, including one case with arachnoid adhesion; one patient had Teflon displaced with adhesive

Table 2
Characteristics of included studies.

Author	Year Published	Country	Type of Study	Population with Secondary TN due to CPA Tumour	Tumour Type				Treatment Modality				Follow-Up Period (Months)	
					Meningioma	Schwannoma	Epidermoid	Other	Tumour Resection without MVD	Tumour Resection + MVD	SRS of Tumour	SRS of N. V	Surgery	SRS
Kida et al. [27]	2019	Japan	Retrospective Study	9	-	-	9	-	-	-	9	-	-	Mean: 86,1
Neff et al.[4]	2017	US	Retrospective Study	16	-	16	-	-	9	1	6	-	Mean: 30	Mean: 59
Liu et al.[5]	2017	China	Retrospective Study	35	16	4	14	1	20	15	-	-	Mean: 51,6	-
Park et al. [18]	2016	South Korea	Retrospective Study	21	20	1	-	-	-	-	21	6	-	Mean: 43
Barker et al. [24]	1996	US	Retrospective Study	26	14	8	2	2	-	26	-	-	Mean: 112,8	-
Bullitt et al. [25]	1986	US	Retrospective Study	6	3	2	-	1	6	-	-	-	N/A	-
Chang et al. [20]	1999	South Korea	Retrospective Study	28	15	11	-	2	-	-	28	-	-	Mean: 32.1
Samii et al. [30]	1995	Germany	Retrospective Study	9	-	9	-	-	-	9	-	-	< 108	-
Samii et al. [31]	1997	Germany	Retrospective Study	8	8	-	-	-	8	-	-	-	Mean: 32	-
Xia et al.[13]	2014	China	Retrospective Study	12	-	-	-	12	3	9	-	-	< 36	-
Cho et al. [21]	2016	South Korea	Retrospective Study	50	30	18	1	1	-	-	49	1	-	Median: 54,8
Park et al. [19]	2014	South Korea	Retrospective Study	8	8	-	-	-	-	-	8	-	-	Median: 40
Shulev et al. [7]	2011	Russia	Retrospective Study	14	3	1	9	1	8	6	-	-	Mean: 54,8	-
Squire et al. [26]	2012	US	Retrospective Study	21	14	7	-	-	-	-	21	-	-	Median: 45x,6
Zhang et al. [8]	2020	China	Retrospective Study	36	4	5	27	-	30	6	-	-	Mean: 81	-
Guo et al. [14]	2010	China	Retrospective Study	49	-	-	49	-	49	-	-	-	24–60	-
Son et al.[22]	2010	South Korea	Retrospective Study	10	-	-	10	-	9	1	-	-	Mean: 81,6	-
Wei et al. [15]	2016	China	Retrospective Study	39	6	9	23	1	24	15	-	-	Mean: 69,8	-
Jamjoom et al.[32]	1996	Saudi Arabia	Retrospective Study	5	1	1	2	1	5	-	-	-	Mean: 14,4	-
Kobata et al. [28]	2002	Japan	Retrospective Study	28	-	-	28	-	19	9	-	-	Mean: 138	-
Tekkök et al. [33]	1992	Turkey	Retrospective Study	9	1	-	8	-	9	-	-	-	Median: 49,2	-
Meng et al. [16]	2005	China	Retrospective Study	24	-	-	24	-	21	3	-	-	Mean: 38	-
El-Shehaby et al.[34]	2017	Egypt	Retrospective Study	8	-	-	8	-	-	-	8	-	-	Median: 60 months
Hasegawa et al.[29]	2021	Japan	Retrospective Study	6	-	6	-	-	-	-	6	-	-	Median: 152 months
Kieu et al. [12]	2021	Vietnam	Prospective Study	15	-	15	-	-	-	-	15	-	-	< 48 months
Kim et al. [23]	2016	South Korea	Retrospective Study	15	11	4	-	-	-	-	15	15	-	Median: 38 months
Sun et al. [17]	2013	China	Retrospective Study	10	-	10	-	-	-	-	10	-	-	Mean: 61 months

Table 3
Patients Outcomes of Included Studies.

Author	Tumour Size	SRS Dose (Gy)	Tumour Resection (with or without MVD)				SRS of Tumour				SRS of Trigeminal Nerve				Postoperative Trigeminal Hypesthesia
			Improved (%)	Unchanged (%)	Worse (%)	Recurrence (%)	Improved (%)	Unchanged (%)	Worse (%)	Recurrence (%)	Improved (%)	Unchanged (%)	Worse (%)	Recurrence (%)	
Kida et al. [27]	Mean volume: 2.85 cm[3]	Mean max dose: 26,1	-	-	-	-	88,9	11,1	0	11,1	-	-	-	-	-
Neff et al. [4]	Surgery: mean diameter 3.2 cm; SRS: mean diameter 2.1 cm	Marginal dose: 12–13	70	30	0	0	0	16,7	83,3	0	-	-	-	-	-
Liu et al. [5]	NR	-	97.1	2.9	0	8.6	_	_	_	_	-	-	-	-	3 (8,6%)
Park et al. [18]	Mean volume: 2.85 cm[3]	Mean max dose: 25	-	-	-	-	100	0	0	28,6	100	0	0	0	-
Barker et al. [24]	Diameter: 1–5 cm	-	100	0	0	17.4	-	-	-	-	-	-	-	-	13 (50%)
Bullitt et al. [25]	NR	-	67	33	0	0	-	-	-	-	-	-	-	-	-
Chang et al. [20]	Mean volume: 7.5 cm[3]	Mean max dose: 26,4	-	-	-	-	85,7	14,3	0	50	-	-	-	-	3 (10,7%)
Samii et al. [30]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	-
Samii et al. [31]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	4 (44,4%)
Xia et al. [13]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	Number not reported
Cho et al. [21]	Not reported	Median marginal dose: 13,25 (meningioma), 12,5 (vestibular schwannoma), 14 (trigeminal schwannoma)	-	-	-	-	91,8	8,1	0	28	100	0	0	0	-
Park et al. [19]	Median volume: 3 cm[3]	Median marginal dose: 13	-	-	-	-	25	25	50	0	-	-	-	-	-
Shulev et al.[7]	Diameter: 0.5–1.5 cm	-	100	0	0	0	-	-	-	-	-	-	-	-	1 (7,1%)
Squire et al. [26]	Median tumour volume: 2.3 cm[3]	Median marginal dose: 12	-	-	-	-	80,9	19,1	0	29,4	-	-	-	-	
Zhang et al.[8]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	2 (5,6%)
Guo et al. [14]	Not reported	-	95.9	4.1	0	2.1	-	-	-	-	-	-	-	-	33 (67,3%)
Son et al. [22]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	-

(*continued on next page*)

Table 3 (*continued*)

Wei et al. [15]	Diameter: 0.5–4 cm		100	0	0	10.3	-	-	-	-	-	-	-	-	-
Jamjoom et al. [32]	Not reported		80	20	0	0	-	-	-	-	-	-	-	-	-
Kobata et al. [28]	Not reported		100	0	0	7.1	-	-	-	-	-	-	-	-	18 (64,3%)
Tekkök et al. [33]	Not reported	-	100	0	0	0	-	-	-	-	-	-	-	-	-
Meng et al. [16]	Not reported		100	0	0	0	-	-	-	-	-	-	-	-	9 (37,5%)
El-Shehaby et al. [34]	Median volume: 10.5 cm[3]	Median marginal dose: 11 Gy	-	-	-	-	75	25	0	16,7	-	-	-	-	-
Hasegawa et al. [29]	Median volume: 6.7 cm[3]	Median marginal dose: 12 Gy	-	-	-	-	50	50	0	0	-	-	-	-	-
Kieu et al. [12]	Mean diameter: 2.1 cm	Median marginal dose: 12 Gy	-	-	-	-	40	33,3	26,7	0	-	-	-	-	-
Kim et al. [23]	Median volume: 1.7 cm[3]	Median marginal dose: 13 Gy	-	-	-	-	93,3	6,7	0	21,4	93,3	6,7	0	21,4	4 (26,7%)
Sun et al. [17]	Mean volume: 7.2 cm[3]	Mean max dose: 28.7 Gy	-	-	-	-	90	10	0	0	-	-	-	-	-

arachnoid.

3.3.2. Tumour-targeted SRS

Twelve articles reported outcomes of tumour-targeted SRS for secondary trigeminal neuralgia patients [4,12,17–21,23,26,27,29,34]. A total of 196 patients had SRS of tumour; 79.1 % of patients improved, 14.3 % had the symptoms persisted, and 6.6% had their pain worse after therapy. Recurrences were reported in 26.5 % of patients who received SRS of tumour treatment.

3.3.3. Trigeminal Nerve-Targeted SRS

Nerve-targeted SRS was reported in a study by Park et al., Cho et al., and Kim et al. [18,21,23] All six patients in Park et al. study had prior tumour-targeted SRS and initial pain improvement, but then the symptom reappeared and worsened. After the second SRS, all cases reported improvement of pain without recurrence [18]. A single epidermoid case from Cho et al.'s study underwent a single session of Gamma Knife radiosurgery with satisfactory outcomes without recurrence in 37 months of follow-up [21]. Fifteen patients in Kim et al. underwent a single session of radiosurgery of the tumour and trigeminal nerve, with 93.3 % improvement and 21.4 % recurrence [23].

3.4. Postoperative trigeminal hypesthesia

Nine of sixteen studies that performed surgery, with or without MVD, and one study of tumour-targeted SRS, reported postoperative facial hypesthesia [5,7,8,14,16,20,23,24,28,31]. As many as 83 patients had post-surgical numbness. Facial hypesthesia was also reported in seven of 149 stereotactic radiosurgery patients, including four patients who received a single tumour and nerve-targeted radiosurgery session.

4. Discussion

Our review showed that surgical resection of tumour was an effective method to treat trigeminal pain secondary to tumour, with a rate of improvement as high as 97.2 %, and none of the patients complained worse outcomes. The improvement rate of 79,1% indicated the effectiveness of tumour-targeted radiosurgery in relieving pain; however, 14.3 % of patients had worse pain than pre-radiation. Considering the outcomes rates of the two treatments, microsurgery appeared preferable; its recurrence rate also was lower than tumour radiosurgery. In the case of nerve-targeted SRS, it seemed to be an effective method to treat recurrent trigeminal pain, as shown in a report by Park et al. [18].

IHS described trigeminal neuralgia as a disorder characterized by recurrent unilateral brief electric shock-like pains. The diagnostic criteria were recurrent paroxysmal unilateral facial pain, lasting from a fraction second to two minutes with severe intensity and electric shock-like, shooting, stabbing, or sharp in quality. In 2018, they updated the classification into classical trigeminal neuralgia, secondary trigeminal neuralgia, and idiopathic trigeminal neuralgia. [3].

4.1. Mechanism of tumour-related trigeminal neuralgia

Various mechanisms have been proposed to elaborate on the cause of facial pain in patients with intracranial tumours. Surgical anatomy of tumour-induced TN could be divided into the following: Type A, tumour encasing the trigeminal nerve; Type B: compression of the trigeminal nerve by the tumour; Type C: compression of the trigeminal nerve by both the artery and the neoplasm. Meningiomas tended to displace the nerve with or without vascular compression, whereas epidermoid tumours directly compressed or wrapped the nerve [5]. Direct tumour compression on the trigeminal nerve was believed to cause demyelination of pain fibers, resulting in facial pain [4,5,7,10,35,36]. Another mechanism was contact between the N.V and an artery because of tumour displacement. The compression of the artery on the root entry zone (REZ) of the nerve is well understood to be a cause of paroxysmal facial pain [4–6,22,37]. In epidermoid, the tumour encasing the trigeminal nerve may cause chemical irritation and hyperactivity by its keratin contents; therefore, neuralgia may appear even without compression of N.V by tumour or artery [9,10,38]. Our review supported this theory with the intraoperative findings of 81 tumours-encasing trigeminal nerves without any sign of nerve root compression by the tumour.

Epidermoid tumours have been reported in some literature as the most common cause of secondary TN. Shulev et al. wrote the incidence of epidermoid tumours in TN patients was 76.9 %, [7] while Kobata et al. [28] and Wei et al. [15] showed the rates of epidermoids as the cause of TN were 90.6 % and 59 %. Our review showed that of 517 patients from 27 studies, epidermoids were the most common tumour reported among other lesions causing TN, accounting for 43.7 %.

4.2. Efficacy of open surgery for secondary trigeminal neuralgia

Several treatment modalities have been reported for treating secondary TN associated with tumours. Twelve articles of 149 patients in our review wrote SRS as a treatment of choice. These included six cases that underwent SRS of the trigeminal nerve as the second phase of therapy after tumour radiosurgery failed to relieve pain. However, most patients in our study received tumour resection surgery as the primary treatment. As many as 320 patients in 15 studies underwent tumour removal surgery; among them were 100 patients who underwent decompression of N.V from compressing vessels.

We found that 97.2 % of patients who underwent tumour surgery had improved their pain with or without MVD. Only 2.8 % reported having treatment failures, and none of them had the symptom worsened. On the other hand, tumour SRS had a 79.1 % rate of pain improvement, with 14.3 % reported having symptoms unchanged, and even pain in 6.6 % of cases worsened. Microsurgery appeared to have a higher improvement rate, with fewer unchanged or worse outcomes rates than SRS. However, we were unable to perform statistical analysis due to heterogeneous data.

Included study that described comparison of efficacy between surgery and tumour radiosurgery was authored by Neff et al. Of 19 patients with TN and paresthesia secondary to vestibular schwannoma, who underwent surgical tumour resection with a mean follow-up of 30 months, 58 % of cases had better outcomes, while 37 % and 5 % reported having the same and worse outcomes. These results were significantly superior to tumour-targeted radiosurgery, in which none of them improved, and 71 % had worse symptoms with a mean follow-up of 59 months [4].

Decompression of the nerve root, especially the REZ, from the tumour or vessels was sufficient to relieve the neuralgia symptom. Total surgical excision is not always feasible or advised due to the tumour's growth characteristic, extensive extension, and tight adherence to important neurovascular structures [37,39,40]. To cure and avoid recurrence of pain, the adhering tumour capsule and arachnoid membrane must be removed in order to achieve neural axis straightening [22,28]. Neff et al. noted that subtotal tumour removal was sufficient, as long as it relieved the mass effect on the nerve, as four patients whose tumours were left on the N.V had most trigeminal symptoms improved [4]. MVD and tumor excision are advocated if vessels were found intraoperatively compressing the nerve root [28]. In our series, 89 cases were reported had subtotal tumour removal surgery, and only three patients had the pain unrelieved related to tumour residue; these included two cases in which the capsule was not dissected from the nerve root, and the symptom was immediately improved after re-surgery.

Subtotal removal may be sufficient to decompress the nerve root to gain symptom improvement; still it is believed to be associated with increased recurrence rates and the need for additional surgery [14]. Total removal of CPA tumours may result in severe morbidity or mortality; however, partial removal risks recurrence and further surgery,

even though it may occur after a long period as these tumours mostly are slow growing [41,42]. Wei et al., who performed tumour excision on 39 patients suffering secondary trigeminal neuralgia, nine of which were subtotal removal, found that total removal surgery significantly affected the long-term outcomes [15]. Of 14 patients with pain recurrence in our series, ten were related to tumour remnant or regrowth. One recurred case with total removal surgery was found to have arachnoid adhesion to the nerve root during re-exploratory surgery. Another recurred case was due to adhesive arachnoid with displaced Teflon. The regrowth of tumours that re-compress the nerve root and adhesive arachnoid are essential factors that cause pain recurrence.

4.3. Outcomes of stereotactic radiosurgery for secondary trigeminal neuralgia

Regarding exacerbated trigeminal symptoms following SRS, it was thought to result from several factors. Radiosurgery typically did not decrease the tumour; in many cases of SRS treatment for tumours, the patients developed transient tumour enlargement, resulting in temporary or permanent symptoms exacerbation [43]. Direct radiation-induced damage to the N.V or intra-axial trigeminal fibers within the pons could permanently exacerbate pain and numbness; the trigeminal nerve in contact with the tumour capsule would receive a radiation comparable to the prescribed marginal dose to the tumour [44,45].

In our study, three articles described worse trigeminal pain after SRS treatment of the tumour. Neff et al. [4] reported that five (83,3 %) schwannoma patients, who received a marginal dose of 12–13 Gy, had more severe pain after radiosurgery, and four (50 %) meningioma patients in Park et al. [19] study suffered exacerbated pain after receiving a median marginal dose of 13 Gy. Kieu et al., [12] who performed tumour radiosurgery with a median marginal dose of 12 Gy, reported worse outcomes rate was 26.7%. The dose of SRS was comparable with Squire et al. [26] and Cho et al. [21] studies which reported that most patients had pain relief. One study found that marginal dose did not determine the outcome of patients with secondary TN; however, the high maximum dose was associated significantly with a positive initial result in all patients who received a maximum dose of 32.5 Gy or more [46]. The highest maximum dose reported in our review was 28.7 Gy with a pain improvement rate of 90 % without any pain recurrence, [17] compared to 100% improvement of patients who received a mean maximum dose of 25 Gy and a recurrence rate of 28.6 % [18].

Of the cases treated with nerve-targeted SRS, Park et al. reported 20 meningiomas and one schwannoma with clinical features of TN. All patients initially received tumour-targeted SRS, with 71.5 % gaining pain improvement after treatment. The rest had worse symptoms, so they proceeded to second radiosurgery targeting the trigeminal nerve 10 – 114 months after the first therapy. All second-SRS patients, who initially suffered Marseille pain scale V, had satisfactory outcomes [18]. Only one patient in a series by Cho et al. received a satisfactory result of nerve-targeted SRS as a primary treatment. Notably, among patients who suffered pain recurrence after tumour-targeted SRS, one patient underwent a secondary session of SRS targeting the nerve, with an improved outcome [21]. Kim et al. found that one of 15 patients who received radiosurgery for both tumour and nerve in a single session failed to have satisfactory outcomes, and three patients who were initially pain-free suffered recurrence in a median follow-up of 38 months [23]. These findings suggested that radiosurgery of the trigeminal nerve should be reserved for patients who failed to have improvement after tumour-targeted radiosurgery.

A meta-analysis by Florianu et al. [47] showed the effect of SRS on TN secondary to meningioma and vestibular schwannoma. The study reported that in tumour targeting series, pain relief with Barrow Neurological Institute (BNI) intensity score I after SRS was found in 52 (50.5 %) of 103 cases, and pain improvement BNI I-IIIb resulted in 189 (83.8 %) of 228 patients. For tumour and nerve targeting series, in single or multiple sessions, the pain relief BNI I-IIIb rate after SRS was 83.7 % (29 of 36 cases). It showed that the pain improvement rates were higher than our tumour-targeted series but still lower than the relief rate of the surgical series. The recurrence rate was also reported at 34.7% (70 of 205 patients), higher than ours.

4.4. Post-operative complication

Post-treatment facial hypesthesia is the most common complication in our surgical series; 83 patients from nine studies were reported to suffer facial numbness. The highest rate of this complication was reported in Guo et al. study, accounting for 67.3 %. The author mentioned that the complication resulted from nerve handling during tumour resection and capsule dissection [14]. All 83 patients had recovered from the post-surgical facial hypesthesia after several months. The number of facial numbness complications was greatly lower in SRS series, which was believed to be a radiation dose-related brainstem side effect [48,49]. Careful handling of the N.V is mandatory, and even some surgeons prefer not to touch tumour capsule attached to the nerve to preserve the function [15,16,28].

4.5. Recommendations and limitations

This study aims to describe treatment modalities for secondary TN caused by CPA tumours. Trigeminal pain is a disturbing symptom that could affect patients' quality of life; therefore, it is crucial to deliver appropriate treatment so that the patients can resume their daily activities. Our review showed that either surgical resection or radiosurgery could improve trigeminal pain. However, radiosurgery does not directly decompress the nerve root from the lesions, and it also may cause transient tumoral edema that exacerbates the pain. This review showed that tumour-targeted SRS's rate of unchanged, worse, and recurrent pain was higher than in surgical series. We recommend surgical treatment decompressing the trigeminal nerve root from compressing lesions and adhesive arachnoid to be the first line treatment treating tumour-related TN. If it is safe for the patient, total removal surgery is advised; however, if gross total excision is not possible, routine and long-term follow-ups are required to assess the risk of recurrence. SRS targeting N.V can be considered a secondary treatment for recurrent pain after tumour-targeted SRS.

There are several limitations in our systematic review. First, only English articles were included. We only divided outcomes into improved, unchanged, and worse due to the variability of results in included literature. This classification system did not distinguish the degree of improvement. Only one article in our review was a prospective study. We could not proceed to meta-analysis to determine whether the results were statistically significant due to heterogenous patients' composition and non-constant follow-up period. Last, because not all studies disclosed the outcomes based on tumour type, our results could not be categorized accordingly. Our result should be viewed with caution, owing to some limitations.

5. Conclusion

Surgery should be considered a first-line treatment for tumour-related TN if the patients are operable, aiming to release nerve root compression from the tumour, associated vessels, or adhesive arachnoid. Total removal is advised if possible, but surgeons may consider subtotal surgery to prevent injury of neurovascular structures, and long-term follow-ups are essential. SRS of the trigeminal nerve may be the choice for patients with recurrent pain after tumour-targeted radiosurgery.

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CRediT authorship contribution statement

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Declaration of interest

None.

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