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CLINICAL ARTICLE

Earlier radiosurgery leads to better pain relief and less medication usage for trigeminal neuralgia patients: an international multicenter study

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OBJECTIVE Trigeminal neuralgia (TN) is a chronic pain condition that is difficult to control with conservative management. Furthermore, disabling medication-related side effects are common. This study examined how stereotactic radiosurgery (SRS) affects pain outcomes and medication dependence based on the latency period between diagnosis and radiosurgery.

METHODS The authors conducted a retrospective analysis of patients with type I TN at 12 Gamma Knife treatment centers. SRS was the primary surgical intervention in all patients. Patient demographics, disease characteristics, treatment plans, medication histories, and outcomes were reviewed.

RESULTS Overall, 404 patients were included. The mean patient age at SRS was 70 years, and 60% of the population was female. The most common indication for SRS was pain refractory to medications (81%). The median maximum radiation dose was 80 Gy (range 50–95 Gy), and the mean follow-up duration was 32 months. The mean number of medications between baseline (pre-SRS) and the last follow-up decreased from 1.98 to 0.90 ($p < 0.0001$), respectively, and this significant reduction was observed across all medication categories. Patients who received SRS within 4 years of their initial diagnosis achieved significantly faster pain relief than those who underwent treatment after 4 years (median 21 vs 30 days, $p = 0.041$). The 90-day pain relief rate for those who received SRS ≤ 4 years after their diagnosis was 83.8% compared with 73.7% in patients who received SRS > 4 years after their diagnosis. The maximum radiation dose was the strongest predictor of a durable pain response (OR 1.091, $p = 0.003$). Early intervention (OR 1.785, $p = 0.007$) and higher maximum radiation dose (OR 1.150, $p < 0.0001$) were also significant predictors of being pain free (a Barrow Neurological Institute pain intensity score of I–IIIA) at the last follow-up visit. New sensory symptoms of any kind were

ABBREVIATIONS BNI = Barrow Neurological Institute; MVD = microvascular decompression; SRS = stereotactic radiosurgery; TN = trigeminal neuralgia.

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seen in 98 patients (24.3%) after SRS. Higher maximum radiation dose trended toward predicting new sensory deficits but was nonsignificant (p = 0.075).

CONCLUSIONS TN patients managed with SRS within 4 years of diagnosis experienced a shorter interval to pain relief with low risk. SRS also yielded significant decreases in adjunct medication utilization. Radiosurgery should be considered earlier in the course of treatment for TN.

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KEYWORDS Gamma Knife radiosurgery; trigeminal neuralgia; carbamazepine; stereotactic radiosurgery; pain

TRIGEMINAL neuralgia (TN) is a chronic pain condition that is difficult to control with medical management.[1,2] Carbamazepine is the recommended first-line drug (level A) for pain management in TN; however, patients often require additional agents such as oxcarbazepine, gabapentin, or baclofen, among others.[3] Disabling side effects are common, with at least one adverse event reported in 66% of patients taking carbamazepine.[4] Furthermore, since the efficacy of medical management typically decreases over time, many patients turn to surgical intervention for more durable pain relief.[5] Surgical options include microvascular decompression (MVD), stereotactic radiosurgery (SRS), partial sensory neurectomy, and percutaneous procedures (glycerol rhizotomy, radiofrequency ablation, and balloon compression).[6]

MVD, when successful, is known to provide the longest period of pain relief. The hallmark study by Barker et al. showed that, after MVD, 70% of patients had pain- and medication-free status for 10 years, and the annual rate of pain recurrence was less than 1%.[7] Although MVD is effective when feasible, patient selection is critical for its success, and patients are still exposed to the operative risks associated with open cranial surgery. Additionally, many TN patients do not meet surgical criteria for MVD, such as those who lack evidence of vascular compression on imaging. Finally, some patients prefer less invasive interventions, such as SRS.

In this study, the authors conducted a multicenter retrospective review of patients diagnosed with type I TN at 12 international Gamma Knife centers. All patients in this study (n = 404) had no prior surgical intervention or irradiation. Indications for SRS included medication intolerance, failure of medical management, or both. The purpose of this study was to determine how SRS affects reliance on pain medication regimens and to evaluate pain outcomes based on the time interval between diagnosis and SRS.

Methods

Under IRB approval, an international group of 12 Gamma Knife centers retrospectively reviewed patients diagnosed with type I TN who underwent SRS as their primary surgical intervention. Patient demographics, disease characteristics, treatment plans, medication histories, and relevant outcomes (with an emphasis on pain outcomes) were reviewed and documented for analysis.

Inclusion Criteria

The patients included in this study had no prior open or percutaneous surgical intervention. All patients included were referred for SRS due to medication intolerance, failed medical management, or both. Patients with atypical TN, multiple sclerosis, tumor-related TN, and prior surgery were excluded.

Gamma Knife Radiosurgery Technique

All patients underwent single-session radiosurgery treatment. Patients were placed in a stereotactic head frame under local anesthesia and/or conscious sedation. Detailed brain MRI with and without contrast was then conducted. Radiosurgery was performed using the Leksell Gamma Knife model U, model 4C, Perfexion, or ICON (Elekta Instruments, Inc.). Radiosurgical plans in all cases were developed by a team composed of a neurosurgeon, radiation oncologist, and medical physicist.

Outcomes

Data were collected at the first and last clinical visits post-SRS. The primary outcome was time to initial pain response after SRS. Initial pain response was defined as either partial or complete improvement in pain. Based on prior evidence suggesting that clinically significant intervention with SRS may occur at either 3 years[8] or 5 years[9] from initial TN diagnosis, data in this study were stratified for analysis by patients who received SRS ≤ 4 years and > 4 years from TN diagnosis. Additional data collected included pain recurrence, pain recurrence grade, and pain grade on the given day of follow-up. Secondary outcomes included whether the patient experienced durable pain relief, treatment failure, or changes in medication utilization. Durable pain relief was defined as experiencing pain relief without subsequent failure or pain recurrence. Failure was defined as needing to undergo additional surgical treatment after pain recurrence, not experiencing any initial pain relief, or reporting a Barrow Neurological Institute (BNI) pain intensity score of IIIB, IV, or V at last follow-up. Additional surgical treatments included MVD, radiofrequency ablation, glycerol injections, balloon decompressions, nerve lesioning, or additional radiosurgery.

Detailed medication usage data were collected. The total number of pain medications patients required since the time of diagnosis was recorded. Baseline number of medications were those being used at the time of SRS. Specific medication names and total prescribed dosages per day were measured at baseline and last follow-up. Medication usage was subsequently analyzed both collectively and according to the following categories: carbamazepine, oxcarbazepine, GABAergics (gabapentin, pregabalin), muscle relaxants (baclofen, cyclobenzaprine), benzodiazepines, opioids, anticonvulsants (phenytoin, lamotrigine,

topiramate, lacosamide, valproic acid, leviticeratem), and antidepressants.

New sensory deficits, as well as their time to occurrence and time to resolution, were measured. A new sensory deficit was defined as any new sensory loss, paresthesia, dysesthesia, and deafferentation pain.

Statistical Analysis

All statistical analysis was performed using SAS version 9.4 (SAS Institute Inc.). Univariable analyses for continuous variables were performed using the independent-samples t-test, and chi-square and Fisher's exact tests were employed for categorical univariable comparisons as appropriate. Paired analyses were performed using the paired t-test and the categorical McNemar's test. To determine predicting variables for outcomes of interest, multivariable logistic regressions were performed for predefined categorical outcomes. In logistic regression models, variables with a significance of $p < 0.3$ in relevant univariate analyses were tested in the models according to a stepwise method, and those with a significance of contribution of $p < 0.05$ were retained. Time-to-pain relief analyses were plotted using product-limit failure Kaplan-Meier curves and analyzed using the Cox proportional hazards model. As in our logistic regressions, all variables with a univariable significance of $p < 0.3$ were tested in the Cox proportional hazards model in a stepwise fashion and retained if their contributing significance was $p < 0.05$ to perform an appropriately adjusted analysis.

Results

Baseline Patient Characteristics

In total, 404 patients met the inclusion criteria (Table 1). The mean age at radiosurgery was 70 years, with 60% female and 40% male patients. Nearly 75% of patients experienced symptoms in the V_2 and/or V_3 distributions, with the largest group of patients presenting with combined V_2/V_3 disease (36.1%), mostly localized to the right side (61.4%). The most common indication for SRS was pain refractory to medical management (81.0%). Fewer than 10% of patients had known nerve course distortion from vascular compression. The mean length of follow-up was 32 months (SD ± 1.85, range 1–254 months).

TABLE 1. Characteristics of 404 patients with TN

Parameter	Value (%)
Age in years (mean ± SEM)	69.69 ± 0.58
Sex	
Male	163 (40.4)
Female	241 (59.7)
Pain distribution	
V_1	13 (3.2)
V_1+V_2	59 (14.6)
$V_1+V_2+V_3$	29 (7.2)
V_1+V_3	3 (0.7)
V_2	84 (20.8)
V_2+V_3	146 (36.1)
V_3	70 (17.3)
Lateralization	
Rt	247 (61.4)
Lt	155 (38.6)
Time from diagnosis to SRS (yrs)	
≤4	197 (48.8)
>4	207 (51.2)
Max radiation dose (Gy)	
Mean ± SEM	81.25 ± 0.20
<80	44 (10.9)
≥80	360 (89.1)
Radiation dose rate (cGy/min)	2.60 ± 0.03
Vascular compression	
No vessel	145 (39.8)
Vessel adjacent	183 (50.3)
Vessel + nerve distortion	36 (9.9)
Indication for SRS	
Medically refractory	324 (81.0)
Medication intolerance	60 (15.0)
Both	16 (4.0)
Baseline no. medications	1.98 ± 0.05
Baseline medications	
Carbamazepine	211 (52.2)
Oxcarbazepine	72 (17.8)
GABAergics	202 (50.0)
Antispasmodics	42 (10.4)
Benzodiazepines	9 (2.2)
Opioids	20 (5.0)
Anticonvulsants	69 (17.1)
Antidepressants	28 (6.9)

Values are presented as the number (%) of patients or as the mean ± SEM.

SRS and Medication Use

Prior to SRS, patients were taking an average of 2 pain medications; carbamazepine (52.2%) and GABAergic (50.0%) medications were the most commonly used, followed by oxcarbazepine (17.8%) and anticonvulsants (17.1%). Other medications used included muscle relaxants (10.4%), antidepressants (6.9%), opioids (5.0%), and, most infrequently, benzodiazepines (2.2%).

Post-SRS medication utilization at last follow-up was significantly decreased from baseline presurgical usage (Table 2). The mean number of pain medications decreased from 1.98 ± 0.05 to 0.90 ± 0.04 ($p < 0.0001$). Dependence on the most commonly used agents at baseline decreased by nearly half: carbamazepine (52.2% pre-SRS vs 27.5% post-SRS, $p < 0.0001$), GABAergics (50.0% pre-SRS vs 28.96% post-SRS, $p < 0.0001$), and oxcarbazepine (17.82% pre-SRS vs 10.64% post-SRS, $p < 0.0001$). This trend of highly significant reduction in medication usage was consistent across all medication categories (Table 2).

SRS and Facial Sensory Symptoms

New sensory symptoms of any kind were seen in 98 patients (24.3%). In multivariable analysis (Supplemental Table A), being on carbamazepine (OR 0.575, 95% CI 0.350–0.943, $p = 0.028$) or having known vascular involvement or compression of the trigeminal nerve ($p = 0.050$ overall) were protective from developing a new sensory deficit

TABLE 2. Medication utilization before and after SRS

Parameter	No. of Patients (%)		p Value
	Pre-SRS	Post-SRS	
No. of medications*			
Mean ± SEM	1.98 ± 0.05	0.90 ± 0.04	**<0.0001**
Medications†			
Carbamazepine	211 (52.2)	111 (27.5)	**<0.0001**
Oxcarbazepine	72 (17.8)	43 (10.6)	**<0.0001**
GABAergics	202 (50.0)	117 (29.0)	**<0.0001**
Antispasmodics	42 (10.4)	19 (4.7)	**<0.0001**
Benzodiazepines	9 (2.2)	2 (0.5)	**<0.0001**
Opioids	20 (5.0)	7 (1.7)	**<0.0001**
Anticonvulsants	69 (17.1)	33 (8.2)	**<0.0001**
Antidepressants	28 (6.9)	11 (2.7)	**<0.0001**

Boldface type indicates statistical significance.
* Comparison of paired means by paired t-test.
† Comparison of paired proportions by McNemar's test.

TABLE 3. Sensory deficits and recurrence

Parameter	No. of Patients (%)
New sensory deficit	98 (24.3)
Pain recurrence or initial treatment failure	170 (42.1)
Treatment after recurrence/initial failure	
None	79 (46.5)
MVD	30 (17.7)
Radiofrequency ablation	1 (0.6)
SRS	41 (24.1)
Glycerol	22 (12.9)
Balloon compression	4 (2.4)
Nerve lesion	1 (0.6)

after SRS. The maximum radiation dose, while trending toward positively predicting new sensory symptoms, was not significant (OR 1.055, 95% CI 0.995–1.119, p = 0.075), and time to SRS from diagnosis (≤ 4 years vs > 4 years) was also nonsignificant (OR 0.996, 95% CI 0.960–1.032, p = 0.227). One hundred seventy patients (42.1%) either experienced recurrence of their preoperative pain after SRS or never experienced any pain relief. While the largest group of these patients (46.5%) did not seek further surgical treatment, the most common second-line surgical intervention was additional SRS (24.1%), followed by MVD (17.7%) (Table 3).

Time Course to Pain Relief

The median time to pain relief after SRS for the whole cohort was 27 days (IQR 21–30 days) with a 78.6% pain relief rate at 90 days (Fig. 1 left). When stratified by time to SRS from diagnosis, patients who received SRS within 4 years of initial TN diagnosis achieved significantly faster pain relief than those who received SRS beyond 4 years (median 21 days [IQR 15–30 days] vs 30 days [IQR 23–31 days]; HR = 1.23 favoring ≤ 4 years, p = 0.041, unadjusted) (Fig. 1 right). The 90-day pain relief rate for those who received SRS ≤ 4 years from diagnosis was 83.8% versus 73.7% in patients who received SRS > 4 years from diagnosis. After adjusting for the only other major contributing variable, maximum radiation dose, Cox proportional hazards showed a consistent significant difference in time to pain relief favoring earlier SRS within 4 years of initial diagnosis (HR = 1.24 favoring ≤ 4 years, p = 0.033, adjusted) (Supplemental Table B).

Radiosurgery Dose Response

The median maximum dose was 80 Gy (range 50–95 Gy), at a mean dose rate of 2.60 cGy/min. A durable pain response was defined as having achieved an initial pain response (389 patients, 96.3%) and never experiencing recurrence of pain during follow-up (235 patients, 58.2% of total cohort). In both univariable and multivariable analyses, higher maximum radiation dose was the strongest predictor of achieving a durable pain response (OR 1.131, 95% CI 1.050–1.219, p = 0.001) (Table 4). Notably, time to last follow-up was not a significant effect modifier of these results (Table 4). Correspondingly, a lower maximum dose was the strongest predictor of failure (OR 0.850, 95% CI 0.794–0.909, p < 0.0001) (Supplemental Table C). Furthermore, at last follow-up, both early intervention with SRS within 4 years (OR 1.785, 95% CI 1.169–2.725, p = 0.007) and higher maximum dose (OR 1.150, 95% CI 1.076–1.230, p < 0.0001) were strong and significant predictors of being pain free (BNI score I–IIIA) at last follow-up (Table 5).

Discussion

This large, multicenter, retrospective study successfully demonstrates the utility of early SRS in type I TN, in particular within 4 years of initial TN diagnosis. Prior to this study, two key publications had similarly aimed to define how timing influences response to radiosurgery in TN; the first, by Mousavi et al., demonstrated that type I TN patients who received SRS within 3 years of pain onset likewise experienced a shorter interval to pain relief and longer duration of pain control.[8] However, while only 42% of patients in the Mousavi et al. study were referred for SRS after becoming refractory to medical management, in our study, those refractory to medications comprised the vast majority of the cohort (81%). This difference in patient population likely contributes to the overall earlier (within 3 vs 4 years of pain onset) and faster (within 7 vs 21 days of SRS) pain response to SRS seen in the Mousavi et al. study; the progression of TN over time, especially when it is becoming increasingly refractory to medical management, is related to the development of demyelination and gliosis within the nerve, which likely also affects its response to radiosurgery.[10] Interestingly, a second landmark study, Lee et al. looked at the response to SRS in a cohort of TN patients who, at baseline, were all already medically refractory to medications or had failed prior surgical intervention.[9] In this study, the time to SRS from diagnosis that predicted faster pain relief was even longer than what was reported in our study (within 5 vs 4 years of pain onset), which is consistent with the thought that these patients might be more pathologically resistant to radiosurgery in their initial symptomatic years. Additionally,

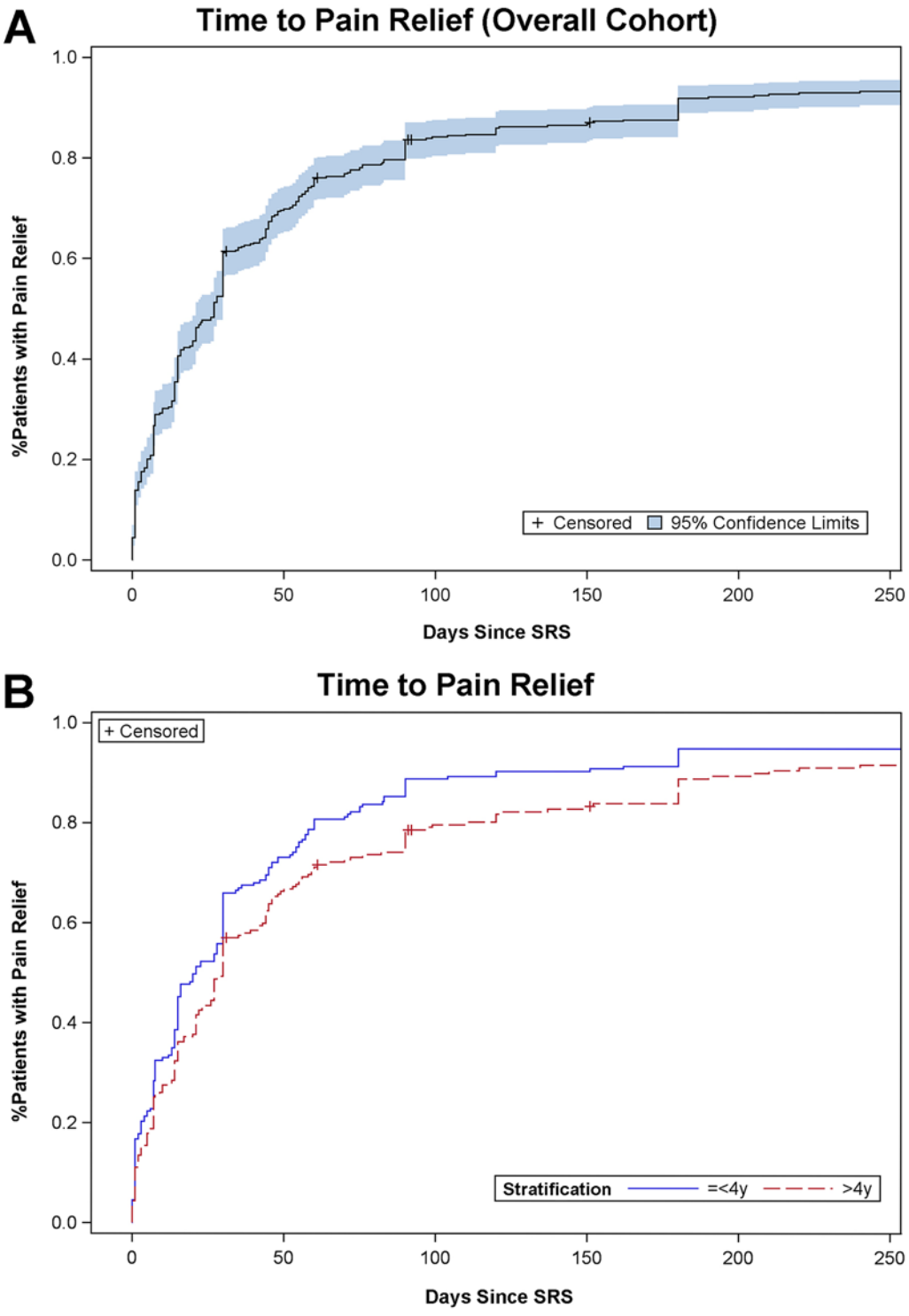

FIG. 1. Time to pain relief (in days since SRS) shown on product-limit failure Kaplan-Meier curves for the overall cohort (**A**), with 95% CIs shown, and stratified by patients who received SRS within 4 years of their initial diagnosis (*blue*) or beyond 4 years of their initial diagnosis (*red*, **B**). *Hashmarks* indicate censored values where follow-up ended. Figure is available in color online only.

in the Lee et al. study, a pain history of ≤ 5 years was a significant predictor of durable pain relief, consistent with our findings. Nevertheless, this cohort is fundamentally different than that in the Mousavi et al. study and in our study patients in whom prior surgical therapy failed were included. Prior surgery is known to contribute to scar tissue formation, fibrosis, and subsequent nerve effect, which all likely influence a patient's response to SRS.

TABLE 4. Multivariate logistic regression for durable pain response

Parameter	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p Value	OR	95% CI	p Value
Age	0.994	0.974–1.015	0.593			
Sex						
F vs M	1.618	0.993–2.637	**0.053**	—	—	—
Lateralization						
Rt vs lt	1.143	0.696–1.877	0.597			
Time to SRS	1.008	0.972–1.045	0.666			
Maximum dose (Gy)	1.137	1.055–1.225	**0.0008**	**1.131**	**1.050–1.219**	**0.001**
Dose rate (cGy)	0.964	0.663–1.400	0.846			
Vascular compression			0.379			
Vessel vs none	1.465	0.846–2.539				
Vessel+torsion vs none	1.084	0.487–2.413				
Baseline carbamazepine	0.993	0.615–1.605	0.978			
Baseline oxcarbazepine	1.526	0.838–2.781	**0.167**	—	—	—
Baseline GABAergics	0.571	0.351–0.929	**0.024**	**0.601**	**0.365–0.989**	**0.0449**
Baseline anticonvulsants	1.727	0.826–3.609	**0.146**	—	—	—
Time to last follow-up	0.945	0.792–1.127	0.527			

Multivariate regressions performed by stepwise addition of all variables with a significance of $p < 0.3$ in the univariate analysis; contributing variables with a significance level of $p < 0.05$ remained in the multivariate model. — = not found to be significant in the multivariate model. Boldface type indicates statistical significance.

The reported median maximum radiation doses in the aforementioned studies were 80 Gy in Mousavi et al. and 90 Gy in Lee et al., and the rates of new-onset facial numbness were 15% and 55%, respectively. The latter reported rate is relatively high compared to a reported median rate of new sensory symptoms of 19% in a systematic review across all TN subtypes.[11] In our study, we reported a 24% new sensory symptom rate. Although a higher maximum radiation dose is known to correlate with improved and more durable pain control, as seen in our multivariable

TABLE 5. Multivariate logistic regression for outcome of BNI score of ≤ 3A at last follow-up

Parameter	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p Value	OR	95% CI	p Value
Age	0.992	0.974–1.009	0.344			
Sex						
F vs M	1.147	0.759–1.733	0.514			
Lateralization						
Rt vs lt	1.130	0.745–1.714	0.564			
Time to SRS	0.976	0.946–1.007	**0.127**	—	—	—
≤4 yrs vs >4 yrs	1.696	1.124–2.558	**0.012**	**1.785**	**1.169–2.725**	**0.007**
Maximum dose (Gy)	1.144	1.071–1.222	**<0.0001**	**1.150**	**1.076–1.230**	**<0.0001**
Dose rate (cGy/min)	0.971	0.690–1.367	0.868			
Vascular compression			0.444			
Vessel vs none	1.247	0.789–1.971				
Vessel+torsion vs none	0.831	0.395–1.747				
Baseline no. of medications	0.946	0.769–1.165	0.603			
Baseline carbamazepine	1.201	0.800–1.803	0.378			
Baseline oxcarbazepine	1.078	0.632–1.839	0.783			
Baseline GABAergics	0.918	0.611–1.377	0.679			
Baseline antispasmodics	1.296	0.651–2.578	0.461			

Multivariate regressions performed by stepwise addition of all variables with a significance of $p < 0.3$ in the univariate analysis; contributing variables with a significance level of $p < 0.05$ remained in the multivariate model. — = not found to be significant in the multivariate model. Boldface type indicates statistical significance.

analysis as well, it is also associated with a higher incidence of new sensory symptoms.[12,13] Interestingly, new-onset facial numbness following radiosurgery has been suggested to actually be predictive of a successful pain response and the durability of pain relief.[14,15]

Another critical goal of applying SRS to TN patients is to reduce pain medication dependence. It is well known that rates of pain medication failure in TN increase with time due to both tolerance and the increasing severity of the disease.[5] Additionally, adverse effects caused by these medications are common, particularly since tolerance stipulates that the dose required to maintain adequate pain control increases over time. Our study is the first to describe the influence of SRS on pain medication utilization of TN patients. In our study, the most commonly used medications prior to SRS were carbamazepine and GABAergics (gabapentin and pregabalin). Compared to pre-SRS baseline, the dependence on these medications reduced nearly by half across all patients (i.e., carbamazepine usage reduced from 52.2% to 27.5%, GABAergic usage reduced from 50.0% to 29.0%). This trend of highly significant reductions in usage was consistent both in the aggregate (mean number of medications pre-SRS vs last follow-up: 1.98 to 0.90, $p < 0.0001$) and across all pain medication subcategories (see Table 2). A critical focus of surgical intervention in TN should be the reduction of the patient's reliance on pain medications and, in doing so, the reduction of the medication side effects experienced. According to our data, SRS is of value to achieving this goal.

While compelling, this study has several limitations that must be considered. First and foremost, its retrospective nature introduces inherent selection bias. Additionally, in an effort to control for a specific patient population (type I TN patients, in this case) to isolate treatment effect, these findings cannot be generalized to those with atypical TN, multiple sclerosis, or tumor-related TN. In atypical TN and TN related to multiple sclerosis, the response rate to SRS has been reported to be low.[15,16] The relationship between tumor-related TN and pain relief is still being study. Inconsistent pain outcomes have been reported in patients who undergo SRS targeting the tumor alone; there is a small body of literature that advocates for the simultaneous treatment of tumor and nerve with SRS for more effective pain relief, but further study in this space is warranted.[17–19] Lastly, the mean follow-up period in this cohort was 32 months, which is on par with previously series (i.e., 17 months,[9] 36 months[8]), but it is limited in clarifying the true long-term durability of SRS for pain relief in these cases beyond a few years. Further long-term follow-up regarding SRS and the durability of pain relief would be particularly beneficial for this type I TN population whose patients tend to be older (mean age 70 years in this series) and are already otherwise experiencing polypharmacy.[20]

Our findings support the use of SRS earlier in the treatment of typical TN, especially within 4 years of initial pain onset and diagnosis. Treatment outcomes and the durability of pain response to SRS are related to the maximum radiation dose used. Additionally, the maximum dose was not a predictor of developing new sensory symptoms after SRS ($p = 0.075$), indicating that the median 80-Gy dose used in this cohort can be applied for durable pain relief and low risk. Our study is also the first to provide evidence that SRS reduces pain medication dependence in type I TN and thereby a reduction in medication-related side effects. We therefore advocate for earlier consideration of radiosurgery in the treatment course for typical TN and, to further verify these findings, call for additional research both in the context of a higher level of evidence (i.e., a randomized trial) and with longer-term follow-up.

Conclusions

In summary, the evidence presented in this study supports using SRS in the early management of patients with typical TN. Patients who underwent SRS within 4 years of diagnosis experienced a shorter interval to pain relief, with low risk of adverse sensory events, and were more likely to experience overall pain relief at their last follow-up. SRS also yielded significant decreases in adjunct medication utilization. We encourage physicians caring for patients with type I TN to refer for neurosurgical evaluation sooner rather than increasing medications to doses that lead to debilitating side effects.

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Disclosures

Dr. Lunsford reports being a consultant for Insightec (DSMB); he owns stock in Elekta AB. Dr. Kondziolka reports receiving support for non–study-related research or clinical efforts that he oversees from Brainlab.

Author Contributions

Conception and design: Kondziolka, Mureb, Benjamin. Acquisition of data: Mureb, Strickland, Zada, Chang, Urgošík, Liščák, Warnick, Speckter, Eastman, Kaufmann, Patel, Feliciano, Carbini, Mathieu, Leduc, Nagel, Hori, Hung, Ogino, Faramand, Kano, Lunsford, Sheehan. Analysis and interpretation of data: Kondziolka, Mureb, Golub, Benjamin. Drafting the article: Kondziolka, Mureb, Golub. Critically revising the article: Kondziolka, Mureb, Golub, Benjamin, Gurewitz, Urgošík, Feliciano. Reviewed submitted version of manuscript: Kondziolka, Mureb, Golub, Benjamin, Gurewitz, Strickland, Zada, Chang, Liščák, Warnick, Speckter, Eastman, Kaufmann, Patel, Carbini, Mathieu, Leduc, Nagel, Hori, Hung, Ogino, Faramand, Kano, Lunsford, Sheehan. Statistical analysis: Kondziolka, Golub. Study supervision: Kondziolka, Mureb, Benjamin.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplemental Tables A–C. https://thejns.org/doi/suppl/10.3171/2020.4.JNS192780.

Previous Presentations

The New York University data included in this study were presented as an electronic poster at the 2019 Annual Meeting of the American Association of Neurological Surgeons, San Diego, California, April 13–17. This study was also accepted as an oral presentation at the 2019 Congress of Neurological Surgeons meeting in San Francisco, California, October 19–23.

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