Effects of the length of preoperative conservative management on postoperative outcomes after primary microvascular decompression for trigeminal neuralgia

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OBJECTIVE Although trigeminal neuralgia (TN) is initially managed conservatively, approximately half of all patients will eventually undergo surgery. Despite this outcome, there is limited understanding of the relationship between preoperative length of conservative management and pain outcomes after microvascular decompression (MVD). In this study, the authors aimed to describe the relationship between the duration of preoperative conservative management and postoperative outcomes in patients undergoing MVD for TN.

METHODS The electronic medical records of 381 patients with TN who underwent primary MVD at the authors' institution between 2007 and 2023 were reviewed. Patients were dichotomized based on whether the duration of conservative management, defined as the duration of anticonvulsant use, was greater than, or less than or equal to, the median duration of conservative management for the entire cohort. For adjusted analysis, duration of conservative management was also assessed as a continuous variable. Demographic information, comorbidities, clinical TN characteristics, pain recurrence, and pre- and postoperative modified Barrow Neurological Institute (BNI) pain and numbness scale scores were recorded and compared between groups. Differences in pain outcomes were assessed via multivariate ordinal regression, Kaplan-Meier analysis, and Cox proportional hazards analysis.

RESULTS The median preoperative duration of conservative management was 1.74 years. Patients with a prolonged duration of conservative management were significantly more likely to be male (p = 0.028) and less likely to preoperatively use opioids (p = 0.037). At final follow-up, those with a prolonged duration of conservative management had significantly higher reported BNI pain scores (p = 0.021) and higher rates of pain recurrence (p = 0.021). On multivariable ordinal regression analysis, younger age (p < 0.001) and prolonged duration of conservative management, which was assessed as both a dichotomized (p = 0.002) and continuous variable (p = 0.011), were associated with higher BNI pain scores at final follow-up. Patients with a longer duration of conservative management also had a significantly shorter time to pain recurrence, as assessed by Kaplan-Meier survival analysis (p = 0.0037) as well as Cox proportional hazards analysis (p = 0.001, dichotomized; p = 0.008, continuous).

CONCLUSIONS In the setting of primary MVD for patients with TN, a longer duration of preoperative conservative management was associated with higher postoperative BNI pain scores and increased risk of pain recurrence. These findings suggest a potential beneficial role for early surgical intervention.

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KEYWORDS trigeminal neuralgia; microvascular decompression; anticonvulsant; pain; conservative management

TRIGEMINAL neuralgia (TN) is a devastating pathology of the trigeminal nerve characterized by intense, shocklike episodes of pain along the V1–3 branches of the trigeminal nerve.[1–4] TN may be caused by compression of the trigeminal nerve by surrounding vasculature, underlying neuropathology (e.g., multiple sclerosis), or unknown etiologies.[4–8] Regardless of etiology, the anticonvulsants carbamazepine and oxcarbazepine, which are also indicated for use in neuropathic pain, are first-line treatments for TN. Alternative neuropathic pain
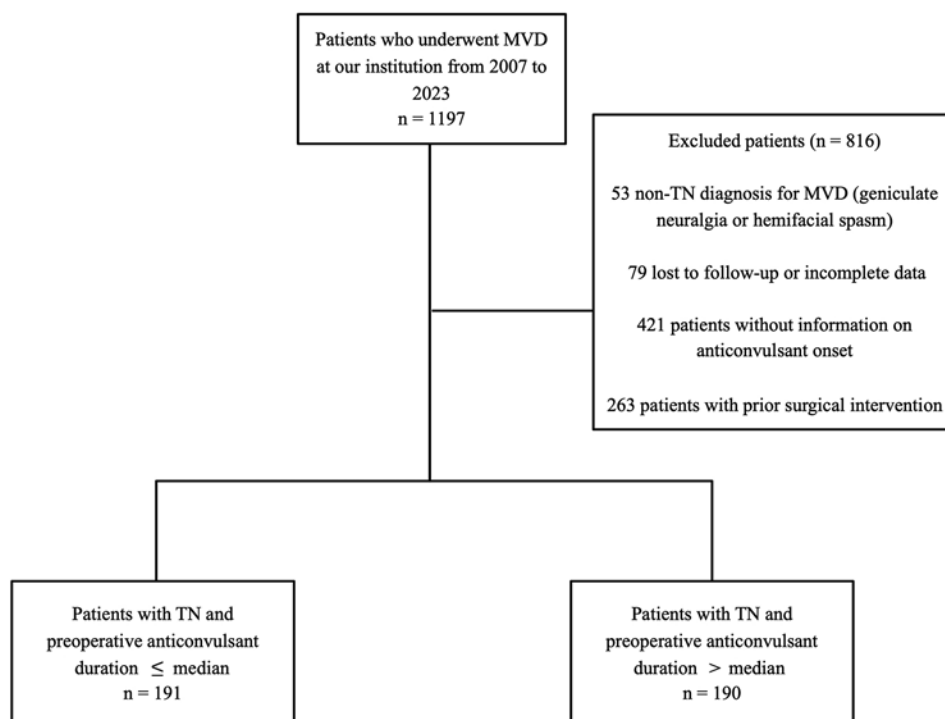
FIG. 1. Flowchart demonstrating selection of the patient cohort.

medications such as pregabalin and lamotrigine may be used instead or as add-on therapies in certain cases.[9–11] For patients who cannot tolerate anticonvulsants or who undergo an unsuccessful trial, other medications such as muscle relaxants and antidepressants may be prescribed, with surgery reserved for those whose pain is poorly controlled with pharmacotherapy.[10] The most common surgical procedure is microvascular decompression (MVD), which relieves vascular compression of the trigeminal nerve and is noted to have high initial rates of pain relief.[12,13]

While all patients with TN are initially managed with pharmacotherapy, it is estimated that up to half will undergo surgery at some point.[5,8,14] Despite the high rates of surgery in these patients, there is little understanding of how the length of conservative management may influence postoperative outcomes. Given the elective nature of surgical intervention for TN, the risks and benefits of medication versus surgery are a common inquiry among patients with TN. While previous studies have suggested that a greater interval between patient-reported symptom onset and date of surgery may be a risk factor for poor outcomes following MVD for TN, these studies are limited due to their small sample size and use of information based on patient recall.[15–18] An important limitation of using patient-reported metrics is the role of recall bias, which can affect the reliability and sensitivity of the data.[19] Thus, in this study, we sought to investigate whether the duration of conservative management, defined as the length of preoperative anticonvulsant use obtained from patients' medication history, was an independent prognostic factor for postoperative outcomes after primary MVD.

Methods

Patient Cohort Selection

We reviewed the electronic medical records of 1197 patients with TN who had undergone MVD for alleviation of symptoms associated with TN at our institution (Johns Hopkins University School of Medicine) between 2007 and 2023. Patients who underwent prior procedures (MVD, Gamma Knife radiosurgery, and rhizotomy; n = 263), patients with non-TN diagnoses (n = 53), and patients with insufficient follow-up data or incomplete medication records (n = 79 and n = 421, respectively) were excluded. A total of 381 patients who underwent primary MVD were included in the final cohort (Fig. 1). Informed consent was waived due to the retrospective nature of the study. The study was approved by the Johns Hopkins IRB.

Medical Record Review

Patient records were reviewed from initial presentation for TN to final follow-up after MVD, defined either based on lack of further follow-up or subsequent neurosurgical intervention. Data on baseline demographic information (age, sex, and race), BMI, comorbidities (coronary artery disease, peripheral vascular disease, hyperlipidemia, chronic kidney disease, hypertension, diabetes, and atrial fibrillation), and clinical TN characteristics (TN type, TN laterality, imaging findings, and intraoperative compression) were abstracted from the records. Additionally, data on preoperative TN medications including anticonvulsants (carbamazepine, oxcarbazepine, gabapentin, pregabalin, phenytoin, lamotrigine, and topiramate), muscle relaxants (tizanidine, baclofen, cyclobenzaprine), antide-
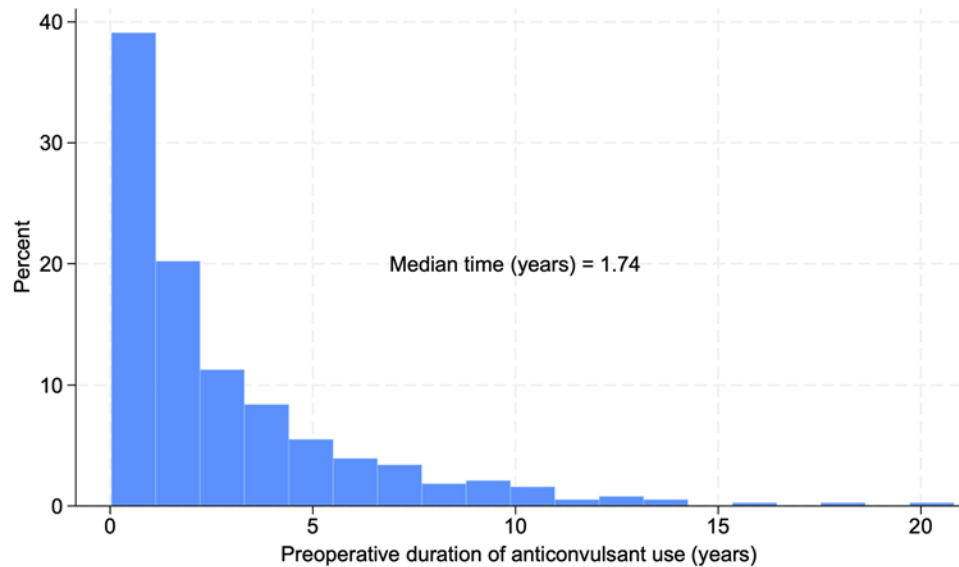
FIG. 2. Histogram depicting duration of conservative management prior to primary MVD. Figure is available in color online only.

pressants, and opioids were recorded. The date of anticonvulsant onset was recorded. Preoperative pain and postoperative pain and numbness were codified based on their respective modified Barrow Neurological Institute (BNI) scale indices, and data on pain recurrence were collected as well.[20]

Statistical Analysis

For statistical analysis, the patient cohort was dichotomized based on whether the duration of conservative management, defined as the duration of anticonvulsant use, was greater than, or less than or equal to, the median duration of conservative management for the entire cohort. Continuous variables in this study were compared using the Student t-test, and ordinal variables were compared via the Mann-Whitney U-test. For categorical variables, chi-square analysis and Fisher's exact test were used for variables with cell counts > or ≤ 5, respectively. To further assess the relationship between duration of conservative management and postoperative modified BNI pain and numbness scores, multivariate ordinal regression was utilized. Kaplan-Meier curves were generated to assess differences in pain-free survival between groups, and Cox proportional hazards analysis was used to evaluate variables associated with increased risk for recurrence. For all adjusted analysis, duration of conservative management was assessed both as a variable dichotomized by the median and as a continuous variable. A p value < 0.05 was used to determine statistical significance for all tests, and all analyses were performed using Stata (version 17, StataCorp LLC).

Results

Duration of Conservative Management, Demographic Characteristics, and Comorbidities

Three hundred eighty-one patients who underwent primary MVD for TN were included in this study (Fig.

1). The median duration of conservative management, defined as the time from onset of anticonvulsant use to surgery, was 1.74 years (Fig. 2). For comparison of baseline demographic and clinical characteristics, patients were stratified into two groups, those with a duration of conservative management less than or equal to the median (n = 191, 50.1%) and those with a duration greater than the median (n = 190, 49.9%, Table 1). The mean (± SD) age in the shorter duration of conservative management group was less than in the longer duration of conservative management group, although the difference was not significant (52.4 ± 14.3 vs 55.0 ± 13.6 years, respectively; p = 0.069). Patients with a shorter duration of conservative management were significantly more likely to be female (71.2% vs 60.5%, p = 0.028). There was no significant difference in race, BMI, smoking history, or assessed comorbidities between groups. Patients in the shorter duration group were more likely to be taking opioids preoperatively (14.7% vs 7.9%, p = 0.037), but there was no difference between groups with respect to use of muscle relaxants, antidepressants, and steroids preoperatively.

Clinical Characteristics and Postoperative Outcomes

There was no significant difference in the type and laterality of TN between patients stratified by duration of conservative management, with type 1 and right-sided TN more common in both groups (Table 2). Patients who had a shorter duration of conservative management also had a significantly shorter median duration of TN symptoms compared with those in the long duration group (0.88 [interquartile range (IQR) 1.56–0.53] vs 4.78 [IQR 7.60–3.09] years, p < 0.001). There was no statistically significant difference in preoperative BNI pain scores between groups, with patients reporting high median preoperative BNI pain scores regardless of having a short or long duration of conservative management (6 [IQR 5–6] vs 5 [IQR 5–6], p = 0.205). Postoperatively, patients who had a lon-

TABLE 1. Demographics and comorbidities of patients with TN stratified by duration of conservative management

Characteristic	Duration of Conservative Mgmt		p Value
	≤ Median	> Median	
Total, n (%)	191 (50.1)	190 (49.9)	
Mean age ± SD, yrs	52.4 ± 14.3	55.0 ± 13.6	0.069
Females, n (%)	136 (71.2)	115 (60.5)	**0.028**
Race, n (%)			0.524
White	149 (78.0)	141 (74.2)	
Black or African American	20 (10.5)	21 (11.1)	
Asian	6 (3.1)	12 (6.3)	
Other	16 (8.4)	16 (8.4)	
Mean BMI ± SD	28.1 ± 5.8	28.6 ± 6.1	0.445
Smoking, n (%)	60 (31.4)	51 (26.8)	0.326
Comorbidities, n (%)			
Coronary artery disease	9 (4.7)	9 (4.7)	0.982
Peripheral vascular disease	3 (1.6)	3 (1.6)	>0.99
Hyperlipidemia	39 (20.4)	53 (27.9)	0.088
Chronic kidney disease	2 (1.0)	1 (0.5)	>0.99
Hypertension	49 (25.7)	38 (20.0)	0.189
Diabetes	12 (6.3)	16 (8.4)	0.424
Atrial fibrillation	3 (1.6)	4 (2.1)	0.724
Preop medications, n (%)			
Muscle relaxant	19 (9.9)	22 (11.6)	0.607
Antidepressant	14 (7.3)	25 (13.2)	0.061
Steroid	1 (0.5)	1 (0.5)	>0.99
Opioid	28 (14.7)	15 (7.9)	**0.037**

Mgmt = management.
Boldface type indicates statistical significance.

TABLE 2. Clinical characteristics and pre- and postoperative pain and numbness outcomes in patients with TN stratified by duration of conservative management

Characteristic	Duration of Conservative Mgmt		p Value
	≤ Median	> Median	
Type of TN, n (%)			0.625
Type 1	162 (84.8)	158 (83.2)	
Type 2	28 (14.7)	32 (16.8)	
Both	1 (0.5)	0 (0.0)	
Side of MVD, n (%)			0.647
Lt	79 (41.4)	83 (43.7)	
Rt	112 (58.6)	107 (56.3)	
Median preop TN symptom duration (IQR), yrs	0.88 (1.56–0.53)	4.78 (7.60–3.09)	**<0.001**
Pain & numbness outcomes			
Median preop BNI pain score (IQR)	6 (5–6)	5 (5–6)	0.205
Median BNI score at final FU (IQR)			
Pain score	1 (1–3)	2 (1–4)	**0.021**
Numbness score	1 (1–1)	1 (1–1)	0.856
Pain recurrence score >3, n (%)	44 (23.0)	64 (33.7)	**0.021**

FU = follow-up.
Boldface type indicates statistical significance.

ger duration of conservative management had significantly higher final follow-up median BNI pain scores (2 [IQR 1–4] vs 1 [IQR 1–3], p = 0.021). There was no difference in BNI numbness scores at final follow-up. Patients with a longer duration of conservative management (33.7%) were significantly more likely to experience pain recurrence, defined as BNI pain score > 3, than those with a shorter duration (23.0%; p = 0.021).

Adjusted Analysis of Postoperative Pain

Dichotomized duration of conservative management, age, sex, preoperative opioid use, and preoperative BNI pain score were incorporated into a multivariate ordinal regression to assess the relationship between duration of conservative management and final follow-up BNI pain and numbness scores (Table 3). Greater length of conservative management (p = 0.002), assessed as a dichotomized variable, and younger age (p < 0.001) were independent predictors of greater postoperative pain. Greater length of conservative management was also associated with greater postoperative pain when assessed as a continuous variable (p = 0.011). There was no association between other assessed covariates and postoperative pain outcomes.

Conservative Management and Pain Recurrence

To assess the relationship between time to pain recurrence and duration of conservative management, Kaplan-Meier survival analysis was performed (Fig. 3). Those with a longer duration of conservative management had a significantly shorter median pain-free survival time (16.5 months) than those with a shorter duration of conservative management (101.1 months; p = 0.0037). A sensitivity analysis performed to assess the patient cohort stratified by various thresholds of duration of conservative management is shown in Fig. 4 and demonstrates that longer duration of conservative management predicted or trended toward predicting shorter pain-free survival across various time thresholds. On multivariate Cox proportional hazards analysis adjusted for age, sex, opioid use, and preoperative BNI pain score, increased duration of conservative management, assessed as a dichotomized variable (p = 0.001), and younger age (p = 0.004) were independent predictors of pain recurrence (Table 4). Increased duration of conservative management was also an independent predictor of pain recurrence when assessed as a continuous variable (p = 0.008). There was no association between other assessed variables and recurrence.

Discussion

TN is a debilitating orofacial pain condition for which a wide array of pharmacological and surgical treatment options may be considered.[10] The initial treatment of TN

TABLE 3. Adjusted multivariate ordinal regression assessing the relationship between duration of conservative management and postoperative outcomes at final follow-up

Models	BNI Pain Score		BNI Numbness Score	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Model 1				
Length of conservative mgmt, dichotomized	1.89 (1.27–2.82)	**0.002**	1.09 (0.57–2.07)	0.792
Age	0.97 (0.95–0.98)	**<0.001**	0.99 (0.97–1.02)	0.501
Male sex	0.73 (0.48–1.12)	0.149	0.78 (0.39–1.57)	0.492
Preop opioid use	1.41 (0.76–2.59)	0.275	0.92 (0.34–2.53)	0.875
Preop BNI pain score	0.73 (0.50–1.08)	0.119	0.76 (0.41–1.41)	0.386
Model 2				
Length of conservative mgmt, continuous	1.08 (1.02–1.15)	**0.011**	0.90 (0.79–1.03)	0.131
Age	0.97 (0.95–0.98)	**<0.001**	1.00 (0.97–1.02)	0.629
Male sex	0.76 (0.50–1.16)	0.204	0.83 (0.41–1.67)	0.607
Preop opioid use	1.41 (0.77–2.59)	0.269	0.83 (0.30–2.27)	0.715
Preop BNI pain score	0.73 (0.50–1.08)	0.114	0.74 (0.39–1.38)	0.337

Model 1 assesses length of conservative management as a dichotomized variable, whereas model 2 assesses length of conservative management as a continuous variable. The length of conservative management was dichotomized by values > or ≤ the median. Boldface type indicates statistical significance.

is generally conservative, with the anticonvulsants carbamazepine and oxcarbazepine prescribed as first-line therapies.[10] Other anticonvulsants, as well as other classes of medications such as muscle relaxants and antidepressants, may also be prescribed as add-on or standalone therapy in certain cases.[9,10] In patients who undergo unsuccessful pharmacological management or who cannot tolerate medication side effects, surgical options may be considered, with approximately half of patients eventually undergoing neurosurgical intervention such as MVD.[5,8,14] Despite the wide use of surgery, however, there is limited understanding of how the preoperative length of conservative management may influence postoperative outcomes. While a few studies suggest that longer symptom duration

may be associated with poor outcomes in patients undergoing MVD for TN, none have specifically examined the length of medical management prior to surgical intervention.[15–17] Thus, in this study, we aimed to determine the association between the duration of preoperative conservative management, defined as the length of preoperative anticonvulsant use, and postoperative pain outcomes in patients with TN who underwent primary MVD. We found that a longer duration of conservative management was associated with worse postoperative outcomes in terms of degree of postoperative pain, pain recurrence, and time to pain recurrence.

The median duration of conservative management in this study was 1.74 years, which aligns with reports sug-
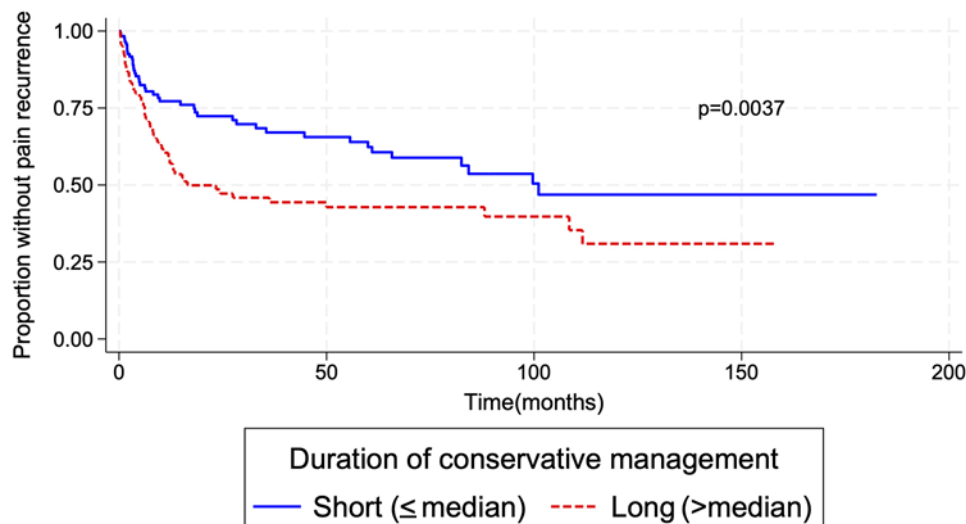

FIG. 3. Kaplan-Meier survival analysis comparing time to recurrence of pain between TN patients with short versus long duration of conservative management. Figure is available in color online only.
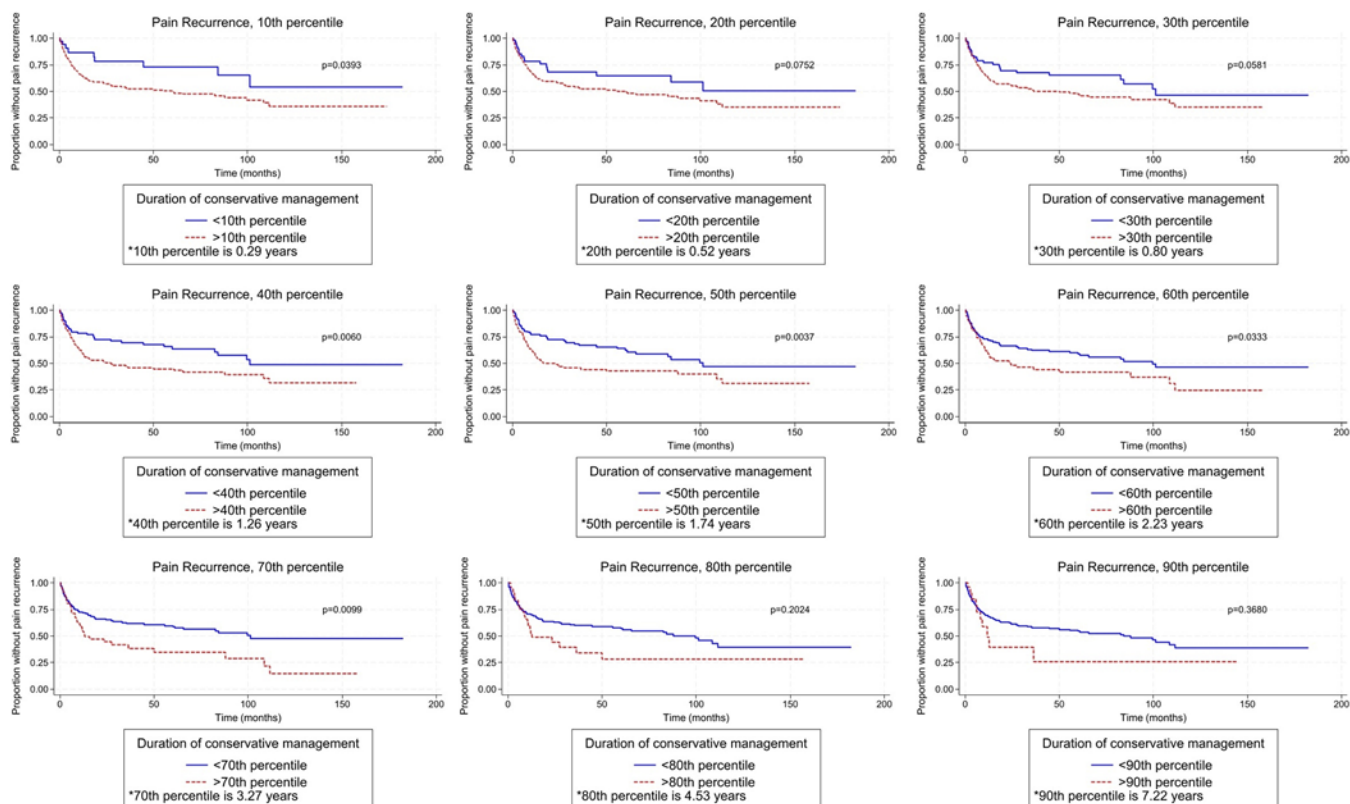
FIG. 4. Exploratory analysis assessing the association between various thresholds of duration of conservative management—divided based on every 10th percentile—and time to pain recurrence. Figure is available in color online only.

TABLE 4. Adjusted Cox proportional hazards model assessing the relationship between duration of conservative management and postoperative pain recurrence at final follow-up

Models	HR (95% CI)	p Value
Model 1		
Length of conservative mgmt, dichotomized	1.92 (1.30–2.84)	**0.001**
Age	0.98 (0.97–0.99)	**0.004**
Male sex	0.96 (0.64–1.45)	0.842
Preop opioid use	1.28 (0.75–2.19)	0.365
Preop BNI pain score	0.93 (0.64–1.36)	0.724
Model 2		
Length of conservative mgmt, continuous	1.08 (1.02–1.15)	**0.008**
Age	0.98 (0.97–0.99)	**0.003**
Male sex	0.94 (0.62–1.43)	0.784
Preop opioid use	1.30 (0.76–2.22)	0.332
Preop BNI pain score	0.93 (0.64–1.35)	0.693

Model 1 assesses length of conservative management as a dichotomized variable whereas model 2 assesses length of conservative management as a continuous variable. The length of conservative management was dichotomized by values > or ≤ the median. Boldface type indicates statistical significance.

gesting that patients with TN often opt for surgical intervention within 2 years of symptom onset.[21–24] Prior studies suggest that a longer duration of TN symptoms may be a poor prognostic factor; for example, in a cohort of 139 patients with TN undergoing MVD, Greve et al. reported that longer TN symptom duration was associated with increased risk for pain recurrence, although this relationship was attenuated when adjusting for age, BNI score, and the American Society of Anesthesiologists grading system of operative fitness status.[15] Similar findings were reported by Herta et al. and Bederson and Wilson in cohorts of 171 and 252 patients, respectively.[16,17] Furthermore, in a systematic review conducted by Holste et al., disease duration ≤ 5 years was shown to predict favorable pain outcomes.[18] While these studies support a role for early neurosurgical intervention, they rely on patient-reported length of symptoms, which are subject to the effect of recall bias and may affect the reliability and sensitivity of data.[19] Thus, in this study, we focus on the length of conservative management. We found that duration of conservative management was a predictor of poor outcomes when assessed as a variable dichotomized by the median or as a continuous variable, suggesting that prolonged conservative management is a robust preoperative risk factor.

Notably, the group with a longer duration of conservative management had a decreased burden of risk factors for poor postoperative pain outcomes that have been established by our group and others, namely female sex

and opioid use.[25–27] This finding is perhaps unsurprising given that female patients and patients who utilize opioids may represent patients with more intense trigeminal pain who elect surgical intervention more quickly; Hung et al. reported that female patients reported greater pain intensity at referral than male patients.[28] However, despite a decreased burden of these risk factors in patients who experienced a longer duration of conservative management, they nevertheless experienced worse pain outcomes compared with patients with shorter conservative management times.

While a role for early surgery has been suggested by other studies, the mechanism by which prolonged duration of conservative management may worsen postoperative outcomes in TN warrants consideration. The precise pathophysiology of TN remains to be elucidated, with the current literature suggesting a central role for nerve compression and inflammation.[29] Prolonged insult via either mechanism may exacerbate pathological changes in the trigeminal nerve, increasing the likelihood of poor pain outcomes. While pharmacological interventions such as anticonvulsants suppress neuronal activity and thus neuropathic pain, they may not directly address the underlying cause of TN, allowing for the progression of pathophysiological changes over time.[30,31] Interventions such as percutaneous rhizotomy, which do not address the underlying compression that often drives TN, have been shown to have decreased efficacy in patients with demonstrated neurovascular compression compared with those without neurovascular compression.[32] In contrast, surgical intervention that attempts to address the underlying cause of TN, such as MVD, may offer a more definitive treatment option in appropriate cases.

Interestingly, studies examining the postoperative experiences of patients with TN who underwent surgery also support a role for early neurosurgical intervention. The majority of patients surveyed postoperatively after MVD report that earlier neurosurgical intervention would have been preferable.[33,34] Zakrzewska et al. reported that 78% of surveyed patients who underwent primary MVD felt that they should have undergone earlier surgical intervention, and 0% reported that their treatment should have been delayed.[33] Coupled with results from this study, these findings suggest that timely surgical intervention may lead to improved pain outcomes and patient satisfaction in appropriate patients undergoing MVD for TN.

Limitations of the Study

One limitation of this study is its retrospective observational nature, which limits our ability to establish a causal relationship between duration of conservative management and postoperative outcomes. Additionally, our sample size was limited to patients with detailed data on the timing of anticonvulsant use and follow-up, thus limiting the power of our analyses. Likewise, all patients were seen by a small group of neurosurgical providers at a single institution, thus limiting the generalizability of this work. Nevertheless, this study establishes a beneficial role of early surgical management in a fairly large patient cohort. Future multi-institutional studies are needed to better characterize this finding.

Conclusions

Treatment options for TN include pharmacological management, primarily anticonvulsants, as well as surgical interventions such as MVD. Although approximately half of patients with TN ultimately undergo some surgical intervention, there is no consensus on the optimal timing of surgery. In this study, we showed that prolonged pharmacological management prior to surgical intervention may be a poor prognostic factor, with patients experiencing greater postoperative BNI pain scale scores and increased pain recurrence compared with those with a shorter duration of conservative management. These findings suggest a potential beneficial role for early surgical intervention in patients with TN.

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Disclosures

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