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Treatment Utilization Patterns and Long-term Prognosis of Trigeminal Neuralgia: Insights from a Nationwide Study

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Purpose: This nationwide retrospective study aimed to examine treatment utilization patterns, including pharmacological and surgical interventions, and evaluate the long-term prognosis of trigeminal neuralgia (TN). This study also aimed to provide accurate epidemiologic information on TN.

Methods: Claims data from the Health Insurance Review and Assessment Service (HIRA) in Korea from 2007 to 2018 was utilized. Incidence rates, healthcare utilization, remission periods, and treatment durations of TN. Furthermore, pharmacological and surgical treatment patterns were also evaluated.

Results: A total of 28,669 patients were included, with an annual crude incidence rate of 7.0 per 100,000 persons. Findings showed that incidence increased with age, peaking in the 60s. Patients utilized about two healthcare institutions, with neurology having the highest visit rate among the specialties. Remission duration decreased initially but stabilized with repeated episodes. Approximately half of the patients initially received analgesics. For monotherapy, carbamazepine (CBZ, 49.3%) and gabapentin (46.9%) were the most frequently prescribed drugs. Among those patients receiving CBZ monotherapy, the mean (standard deviation) daily dose was 333.2 (167.8) mg, with a slight increase over time. Surgery was performed in 12.7% of the study population, with the ganglion procedure as the most frequent and repeated. Microvascular decompression had low reoperation rates, and fewer patients resumed medication.

Conclusions: Korean patients with TN exhibited similar demographics and epidemiologic features as those from other countries. The stable decrease in remission duration and insignificant increase in CBZ dosage over time suggests a favorable prognosis for TN. However, deviations from the international guidelines, such as the use of ineffective medications and early surgery decisions, were observed. Further education for clinicians is necessary to improve understanding and treatment of TN.

Keywords: Epidemiology; Insurance claim review; Prognosis; Therapeutics; Trigeminal neuralgia

INTRODUCTION

Trigeminal neuralgia (TN) is a condition characterized by sudden, electric shock-like pain that occurs on one side of the face and is limited to one or more divisions of the trigeminal nerve [1]. Although rare, TN causes severe pain that can significantly impact the activities of daily living for many patients. These pain patterns and the nature of chronic diseases are often accompanied by depression and anxiety. Without proper treatment, this can significantly reduce the patients' quality of life [2,3].

The general recommendation for the treatment of TN is

to start pharmacological therapy first and consider surgical intervention if the patient is refractory to medical treatment or if severe side effects prevent continued pharmacological therapy [4,5]. The European Academy of Neurology (EAN) guideline strongly recommends carbamazepine (CBZ) or oxcarbazepine (OXC) as the first-line therapy for TN treatment [4]. Medications including lamotrigine (LTG), gabapentin (GBP), botulinum toxin type A, pregabalin (PGB), baclofen (BCF), and phenytoin (PHT) could be considered for treating TN as either a single therapy or as an add-on therapy, which is based on low to very low quality of evidence. However, in clinical practice, the guideline for the pharmacological therapy seemed not to be consistently followed. A recent study that analyzed health insurance claims data in the United States found that TN patients received a range of drugs, including opioids and anti-inflammatory drugs [6]. Cases of inappropriately titrated drugs are also commonly experienced. More data from diverse study population are needed to better understand medication utilization in clinical practice for TN, including information on the types, combination patterns, dosages, and duration of frequently used drugs.

Surgical treatment for TN can be performed at three levels: Trigeminal nerve root in the posterior fossa including microvascular decompression (MVD) and stereotactic radiosurgery (SRS), gasserian ganglion including percutaneous sensory rhizotomy, and trigeminal nerve branches distal to the ganglion (peripheral procedures) [7,8]. Among these surgical options, MVD is considered to have the best pain relief effects and fewer side effects [8-10]. However, studies comparing the effectiveness of different surgical options are still lacking. Clinicians seem to manage TN patients surgically in various ways, frequently resulting in inadequate pain management.

TN has been thought to be a progressive disease with poor prognosis over time [11,12], but some of the recent studies showed different results from the traditional notion [13-16]. Long-term data on the prognosis of TN is lacking.

Given the severity of pain, chronicity, and progressive nature of TN, providing a comprehensive management program is important that includes optimizing drug therapy, providing continuous advice and support, and considering surgical options for the medically intractable patients, in order to achieve a favorable prognosis. While understanding treatment utilization patterns of TN patients during a long-term follow-up is important, large-scaled studies on this topic are still lacking, particularly within domestic researches [17-19]. Therefore, a retrospective, nationwide study was designed to identify real-world treatment utilization patterns for TN patients, including various pharmacological and surgical interventions, and to evaluate the progress of TN through long-term follow-up. This study also aimed to investigate the epidemiology of TN patients on a national scale.

MATERIALS AND METHODS

1. Study Design and Data Source

This study is a retrospective cohort analysis using claims data from Health Insurance Review and Assessment Service (HIRA) databases from January 1, 2007 to December 31, 2018 to analyze the epidemiology and treatment patterns of Korean patients with TN.

Since HIRA data is provided in anonymized form, this study protocol was exempted from review by the Institutional Review Board Committee of Dankook University Dental Hospital in accordance with the guidelines.

2. Patient Population

Using the HIRA database from 2007 to 2018, this study included patients aged ≥20 years, newly diagnosed as TN identified by the diagnostic code of G50.0 from the Korean Standard Classification of Diseases. Newly diagnosed TN patients were defined as those who had not made any claims with G50.0 in the year prior to the index date. The index date was defined as the date upon which the diagnostic code of TN first appeared in the patient's claims data.

To improve the accuracy of the diagnosis, only patients who were diagnosed with TN by neurologists, neurosurgeons, or specialists of oral medicine and orofacial pain at least once and who had a treatment period of more than 3 years since the index date were included in this study. This duration also provides sufficient time to analyze treatment patterns, based on previous research [6]. This study also included patients who received surgical treatment among those who had a treatment period of <3 years (Appendix 1).

3. Outcome Measures

1) Demographics and epidemiology

Demographic data were collected including age and sex of patients with TN at the index date. To obtain the annual crude incidence rate (per 100,000 persons), the total number of TN patients newly diagnosed between 2008 and 2015 was divided by the sum of the total population of Korea by year according to Statistics of Korea [20] and then divided again by eight. As the inclusion criteria in this study required a treatment period of at least 3 years, data for new patients from 2016 to 2018 was limited to those who underwent surgery. Crude incidence rate was adjusted for age to the world standard population (WHO 2000-2025) [21] using direct method.

2) Healthcare utilization patterns

Patient distribution was investigated based on the specialty of the healthcare provider (e.g., neurology, neurosurgery) at the first visit and throughout the entire treatment period. In addition, this study examined the number of hospitals that the patients visited during the entire treatment period. In this study, entire treatment period refers to the duration from the index date to the last prescription date.

3) Remission

Treatment episode was defined as the duration of a series of treatment courses [22]. In this study, the endpoint of a single treatment episode was set by adding the days of drug supply to the last prescription date, when no additional prescription was given for ≥90 days [9,23]. In this study, since TN is difficult to tolerate without any treatment during the pain period, the gap of ≥90 days between two adjacent treatment episodes was designated to be the remission. The number of remission and treatment episodes, as well as changes in their duration over time, were examined to evaluate the prognosis of TN.

4) Pharmacological treatment patterns

To investigate pharmacological treatment patterns for TN patients, those who underwent surgical treatments or peripheral procedures (nerve block or destruction of trigeminal peripheral nerve branch or sympathetic plexus or ganglion) were excluded.

The study extracted the active ingredient codes of medications prescribed throughout the entire treatment period to the total study population from the HIRA database.

For the nine drugs which included the seven study medications, tricyclic antidepressants (TCAs), and analgesics, the proportion of patients receiving each drug was calculated. The term “study medications” refers to the seven drugs that are generally recommended for TN treatment based on the clinical guidelines [4]: CBZ, OXC, GBP, PGB, LTG, BCF, and PHT. The analysis included TCAs and analgesics because TCAs are commonly used for neuropathic pain management [24] and analgesics are widely used for pain control in clinical practice. The type of combination used in patients receiving combination treatment was identified, and the proportion of prescription for each combination type was investigated. Moreover, for patients who received monotherapy with CBZ, changes in daily dose and treatment duration were monitored by treatment episodes.

5) Surgical treatment patterns

In this study, surgery refers to posterior fossa surgery such as MVD, SRS (including gamma knife surgery), gasserian ganglion block or destruction, and radiofrequency thermocoagulation (RFTC). Data regarding the surgical procedure that the patients underwent were collected using the procedure code (Korean Classification of Procedures in Medicine).

The frequency, mean number of surgeries during the entire treatment period, and duration from initial diagnosis to the first operation was examined based on the type of surgery. To evaluate the efficacy of surgical treatment, the frequency of reoperation, interval between surgical interventions, whether medication was resumed after surgery, and the duration of medication suspension after surgery, all related to the type of surgery, were also investigated. When evaluating whether medication was resumed, prescriptions received within 90 days after surgery were not considered as a restart of pharmacological treatment.

4. Statistical Analyses

SAS Enterprise Guide (version 6.1, SAS Institute Inc.) was used for data extraction, computation, linkage, processing, and sampling. All the other statistical analyses were

performed using the R statistical software (version 4.0.3, The R Foundation for Statistical Computing). All p-values of <0.05 were considered to be statistically significant.

T-test was used to compare age and gender between patients who underwent surgery and those who did not. Using Tukey's multiple comparison test, the comparison of changes in the duration of remission and treatment period as well as the doses administered per episode were analyzed.

RESULTS

1. Demographic and Epidemiologic Characteristics

This study included a total of 28,669 patients, of whom 3,652 (12.7%) patients underwent surgery. The mean (standard deviation [SD]) age at the index date was 57.7 (13.9) years, and around 70.2% (n=20,133) of the patients were female. The mean (SD) age of the patients who underwent surgery was found to be significantly higher than those who did not [58.3 (13.8) and 57.6 (13.9), respectively, p=0.03], and the proportion of women was found to be significantly lower [68.2% (n=2,490) and 70.5% (n=17,642), respectively; p=0.004].

During the period from 2008 to 2015, the annual crude incidence rate (per 100,000 persons) was 7.0, and the age-adjusted incidence was 5.3. The incidence rate of TN showed an increasing trend across different age groups until the 60s, after which it reached a peak (Appendix 2).

2. Healthcare Utilization Patterns

On average, TN patients visited about two different hospitals, with a mean (SD) of 1.9 (1.3).

The specialty types for the first visit were ranked in the following order: Neurology (53.9%), neurosurgery (16.6%), dentistry (8.3%), otolaryngology (5.2%), internal medicine (4.8%), and anesthesiology (2.8%). Throughout the entire treatment period, neurology (37.6%) was accounted to have the largest proportion, followed by neurosurgery (16.2%),

Table 1. Distribution of patients with trigeminal neuralgia by medical specialty and number of hospitals visited during treatment

Number[a] of various medical facilities	n (%)	
1	15,347 (53.5)	
2	7,714 (26.9)	
≥3	5,608 (19.6)	
Mean (standard deviation, range)	1.9 (1.3, 1–15)	
Medical specialty type	Proportion of patient numbers, %	
	First visit	Entire treatment period
Neurology	53.9	37.6
Neurosurgery	16.6	16.2
Dentistry	8.3	6.1
Otolaryngology	5.2	5.3
Internal medicine	4.8	8.4
Anesthesiology	2.8	6.9
Orthopedic surgery	2.5	4.9
Korean medicine	2.1	6.3
Others[b]	4.0	8.3

[a]Multiple visits to the same hospital were counted as once.
[b]Others include psychiatry, general surgery, family medicine, emergency medicine, etc.

Table 2. Changes in duration of remission and treatment by episode and numbers of remissions

Variable	Episode				
	1st	2nd	3rd	4th	5th
Treatment period (d)	138.0±308.5	137.2±268.7	128.9±237.8	126.7±232.2	114.5±193.4
Remission period (d)	992.2±857.2	556.2±562.5*	416.5±417.3*	356.2±350.4*	312.4±299.9
Number of remissions	Number of patients (%)				
0	2,275 (7.9)				
1	10,983 (38.3)				
2	6,524 (22.8)				
3	3,826 (13.4)				
4	2,282 (8.0)				
≥5	2,779 (9.7)				

Values are presented as mean (standard deviation) or number (%).
p-values were obtained using Tukey's multiple comparison test. *p<0.05.

internal medicine (8.4%), anesthesiology (6.9%), Korean medicine (6.3%), and dentistry (6.1%) (Table 1).

3. Changes in Remission and Treatment Period

Out of the total number of patients, 2,275 patients (7.9%) did not experience any remission. Additionally, about 10% of patients was found to have experienced more than five remissions. The remission period significantly decreased after the first remission ($p<0.05$), followed by a slight decrease after subsequent remissions, which eventually stabilized after the fourth remission. The average treatment duration for each episode was approximately 4 months, with a slight but insignificant decrease over time (Table 2).

4. Pharmacological Treatment Patterns

Excluding patients who underwent surgery or peripheral procedures, 22,922 (80.0%) patients received only pharmacological treatment throughout the entire treatment period. Among them, about 90% (n=20,244) were prescribed with at least one of the seven study medications. Upon examining the prescription patterns for TN patients during their first visit, out of a total of nine medications (including seven study medication, TCAs and analgesics), analgesics were found to be the most prescribed medication (nearly 50%), followed by CBZ (38.4%) and GBP (32.4%). These findings are presented in Table 3.

Among the patients who received the study medications, monotherapy was the most common (59.3%), followed by

Table 3. Proportions of prescribed medication for patients with trigeminal neuralgia

Proportion[a] of prescribed medication among the nine drugs at the first visit	
Analgesics	11,319 (49.4)
CBZ	8,808 (38.4)
GBP	7,417 (32.4)
TCAs	2,786 (12.2)
BCF	447 (2.0)
PGB	369 (1.6)
OXC	331 (1.4)
PHT	105 (0.5)
LTG	12 (0.1)

Proportion of seven study medications by number of medications prescribed throughout the entire treatment period			
	1 drug	2 drugs	≥3 drugs
CBZ	5,923 (49.3)	5,222 (87.8)	2,184 (95.2)
GBP	5,630 (46.9)	4,992 (84.0)	2,134 (93.0)
PGB	219 (1.8)	778 (13.1)	1,179 (51.4)
BCF	124 (1.0)	489 (8.2)	940 (41.0)
OXC	88 (0.7)	333 (5.6)	842 (36.7)
PHT	20 (0.2)	66 (1.1)	205 (8.9)
LTG	-	12 (0.2)	50 (2.2)
Total	12,004 (59.3)[b]	5,946 (29.4)[b]	2,294 (11.3)[b]

CBZ, carbamazepine; GBP, gabapentin; TCAs, tricyclic antidepressants; BCF, baclofen; PGB, pregabalin; OXC, oxcarbazepine; PHT, phenytoin; LTG, lamotrigine.
Values are presented as number (%). The patients could contribute more than one drug; therefore, the sum exceeds 100%.
The nine drugs include seven study medications (BCF, CBZ, GBP, LTG, OXC, PGB, PHP) as well as analgesics and TCAs. Analgesics include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and tramadol.
[a]Denominator=total number of patients in the pharmacological treatment group (22,922).
[b]Denominator=total number of patients receiving more than one drug of the seven study medications (20,244).

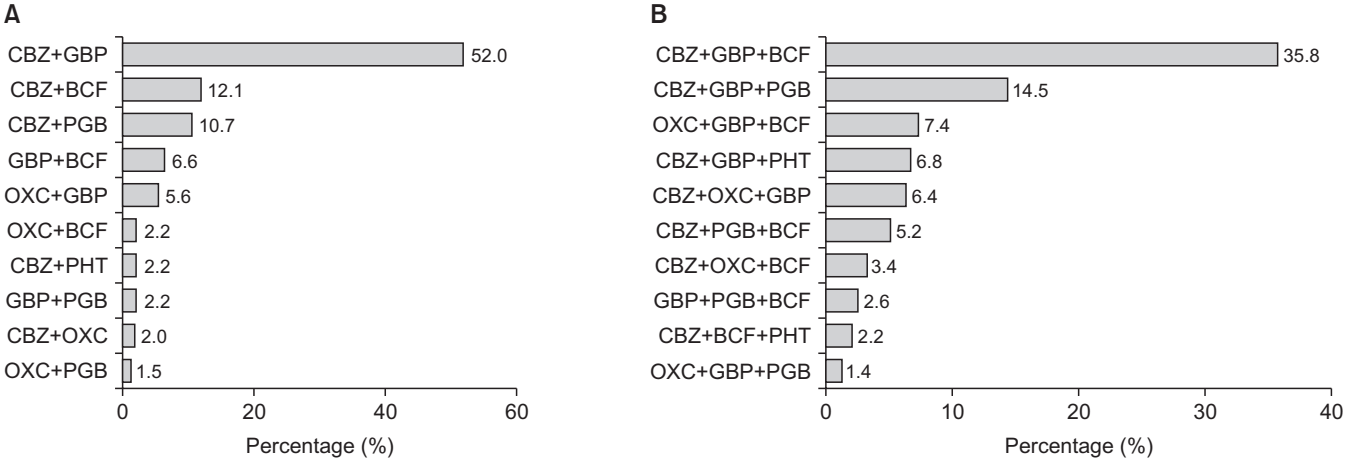

Fig. 1. Proportion of prescription patterns by combination of two drugs (A) and three or more drugs (B): Top 10 most prescribed combination types. Values are presented as percentage. CBZ, carbamazepine; GBP, gabapentin; BCF, baclofen; PGB, pregabalin; OXC, oxcarbazepine; PHT, phenytoin.

the patients who received two (29.4%) or three or more drugs (11.3%). CBZ and GBP were the most frequently prescribed medications in both monotherapy and combination therapy (Table 3, Fig. 1). BCF and OXC were more commonly used as adjuvant therapy in the combination regimens than as monotherapy (Fig. 1).

Changes in daily dose and treatment duration for CBZ monotherapy in each treatment episodes are presented in Table 4. A significant but small increase in the mean daily dose of CBZ was observed from the 4th treatment episode, with an increase range of only 30 mg. Treatment duration per episode showed a significant decrease from the 2nd episode, followed by a slight decreasing trend, but remained largely unchanged.

5. Surgical Treatment Patterns

The pattern of surgical treatment for TN patients is presented in Table 5. A total of 3,652 TN patients underwent surgical intervention, and the mean (SD) number of surgeries was 2 (2.8). On average, the first surgery was performed about 2 years after the initial diagnosis, while for those cases receiving a ganglion procedure, the average was the shortest, about 1.6 years. Of all the patients who received surgical treatment, 50% underwent ganglion procedure, and almost 50% of them had more than one ganglion procedure. Only a small number of patients underwent the same surgery twice or more in case of MVD (2.1%) or SRS (5.3%). A total of 3,035 patients received pharmacological treatment with any of the seven study medications for an average duration of 340 days (total prescription days) prior to their first surgery. After each surgery (MVD, ganglion

Table 4. Daily dose and treatment duration by treatment episode in patients with trigeminal neuralgia treated with carbamazepine monotherapy throughout the entire treatment period

Variable	Treatment episode				
	1st (n=5,923)	2nd (n=3,987)	3rd (n=2,031)	4th (n=1,059)	≥5th (n=580)
Dose (mg/day)	323.1±150.1	324.9±149.0	335.2±158.6	353.6±177.5*	374.7±264.7*
Treatment duration (d)	133.3±380.2	102.1±266.9*	102.5±242.8	101.7±233.1	90.5±180.2

Values are presented as mean±standard deviation.
During the entire treatment period, the mean daily dose was 333.2±167.8 mg.
The p-value was obtained using Tukey's multiple comparison test. *p<0.05.

Table 5. Surgical treatment patterns for patients with trigeminal neuralgia

Total number of surgeries	MVD (n=988)	SRS (n=805)	Ganglion procedure (n=1,852)	RFTC (n=546)	Total (n=3,652)
1	967 (97.9)	762 (94.7)	979 (52.9)	371 (68.0)	2,439 (66.8)
2	20 (2.0)	40 (5.0)	383 (20.7)	105 (19.2)	548 (15.0)
3	1 (0.1)	3 (0.3)	171 (9.2)	34 (6.2)	238 (6.5)
≥4	-	-	319 (17.2)	36 (6.6)	427 (11.7)
Mean (standard deviation)	1.0 (0.2)	1.1 (0.3)	2.5 (3.6)	1.6 (1.2)	2.0 (2.8)
Duration from initial diagnosis to the first surgery (y)					
	2.5 (2.4)	2.4 (2.5)	1.6 (2.3)	2.5 (2.4)	1.9 (2.3)
Number of patients received ≥90 days pharmacotherapy after the first surgery					
	358 (36.2)	471 (58.5)	534 (28.8)	181 (33.2)	
Duration from the first surgery to restart of medication (y)					
	1.4 (1.5)	1.1 (1.3)	1.3 (1.4)	1.2 (1.3)	

MVD, microvascular decompression; SRS, stereotactic radiosurgery; Ganglion procedure, ganglion block or destruction procedure; RFTC, radiofrequency thermocoagulation.
Values are presented as number (%) or mean (standard deviation). The number of patients receiving the study medication before surgery was 3,035, and the mean (standard deviation) total prescription duration was 340.1 (455.5) days.

Table 6. Number of patients who underwent reoperation for each surgical method and time interval between surgeries

Previous surgery	Reoperation				Interval between surgery and reoperation (mo)			
	MVD	SRS	Ganglion procedure	RFTC	MVD	SRS	Ganglion procedure	RFTC
MVD	21	27	18	12	22.2 (24.7)	31.2 (26.4)	20.2 (30.1)	19.1 (19.2)
SRS	28	38	58	24	27.5 (21.6)	33.2 (24.5)	18.3 (17.7)	25.5 (23.3)
Ganglion procedure	64	54	2,275	238	16.1 (19.9)	14.6 (19.4)	3 (8.7)	5.2 (11.5)
RFTC	19	26	145	252	19.4 (22.6)	13.8 (13.1)	11 (15.0)	13.9 (15.5)

MVD, microvascular decompression; SRS, stereotactic radiosurgery; Ganglion procedure, ganglion block or destruction procedure; RFTC, radiofrequency thermocoagulation.
Values are presented as number only or mean (standard deviation).

surgery, and RFTC), approximately 30% of patients resumed drug treatment about 1 year later, whereas more than 50% of patients who underwent SRS resumed medication after the procedure.

The number of reoperations for each surgical intervention and the interval between surgical treatments are presented in Table 6. In the case of two or more surgeries, the frequency in reoperation for the ganglion procedure after a previous ganglion procedure was overwhelmingly high. The frequency of reoperation for MVD or SRS was low, and vice versa. In the case of those receiving the ganglion procedure after the previous ganglion procedure, the interval was as short as 3 months, and in the case of those receiving SRS after previous SRS, the interval was as long as 2.7 years.

DISCUSSION

The incidence rate of TN has been reported in many studies, with a wide range of 4.3-26.8 per 100,000 persons per year [25-27], which may be dependent on population size and composition of the surveyed group. Using the nationwide claims database in Korea, this study indicates that the crude incidence per 100,000 per year was 7.0, and it was decreased by 5.3 following adjustment by age (Appendix 2). It was comparable to 4.8 and 8.0 from a US and a UK study, respectively [25,27]. Female-to-male ratio was about 2:1, and incidence increased up to the 60s with a peak and decreased afterward (Appendix 2), which were similar to previous studies [7,26].

At the initial visit, out of the nine drugs, analgesics were the most frequently prescribed, followed by CBZ, GBP, and TCAs (Table 3). Furthermore, throughout the entire treatment period, analgesics were the most prescribed pain-related drugs among the top 50 medications, although the data for these drugs is not presented here. Out of the seven study medications prescribed as monotherapy, CBZ was the most frequently used drug (49.6%). However, GBP was also used with a high rate of 46.9%, which was comparable to CBZ (Table 3). These findings, consistent with those from previous studies [6,28], were surprising given that analgesics are known to have no efficacy in treating TN and that GBP has a lower effect [4]. Although GBP is widely used in neuropathic pain and is known to have fewer side effects [29], it is considered as second- or third-line therapy for TN due to the lack of high-quality evidence [4,8,9,30,31], despite some studies reporting its efficacy in pain relief for TN patients [32,33]. However, highly prevalent use of GBP among clinicians in this study may have resulted from the difficulty in differentiating TN from other neuropathic pain conditions, familiarity with using this drug, and its relatively fewer side effects [29]. The relatively high prescription rate of PGB and TCAs may also be understood in similar context. Although it is considered as a first-line therapy due to its similar effectiveness and fewer side effects than CBZ [4,8,9,30,31], OXC was rarely prescribed in this study, possibly because insurance benefits only cover its use for patients who are refractory or intolerant to CBZ.

In this study, the most prevalent treatment approach was monotherapy using one of the seven study medications (59.3%), followed by combination of two or three drugs (29.4% and 11.3%, respectively). Among combination therapies, GBP was the most frequently used drug followed by BCF (Fig. 1). Previous studies [2,6,34] have reported rates of monotherapy ranging from 36.2% to 84%. Although there are few studies on commonly used drug combination regimen, some studies have suggested the therapeutic benefits

of combination therapy [35-37]. Scrivani et al. [36] suggested that combination therapy may enhance the therapeutic response for a patient who is partially responsive to monotherapy and experience side effects at the effective dose. Merrill and Graff-Radford [35] and Sindrup and Jensen [37] also reported that drug combination of CBZ and BCF had synergistic analgesic effect among TN patients. BCF may be used combined with CBZ or OXC, but its evidence has been proven to be weak [4].

In 5.923 patients treated with CBZ monotherapy in this study, the mean (SD) daily dose was 333.2 (167.8) mg (Table 4), which is relatively low compared to the reported maintenance dose range of 300-800 mg/day [9,10]. Studies on Japanese [38] and Korean patients [19] found similar effective doses to this study, indicating comparable physical constitutions.

For monotherapy with CBZ, the mean dose of CBZ remained relatively low with a modest increase over time, and the duration of treatment episode remained largely unchanged, although it decreased significantly between the first and second episodes (Table 4). These facts imply a good prognosis for patients receiving CBZ monotherapy and, conversely, suggest that CBZ monotherapy was feasible for these reasons.

This study showed that 16.9% of patients received surgical treatment as the first-line therapy without receiving any medication (Table 5), which was a similar to the finding of a 21.6% rate in a study using claims data in US population [6]. This may be partially attributed to lack of clinicians' knowledge on the international clinical guideline [4] or the preference of clinicians and/or patients for early surgery. According to the EAN guidelines [4], surgical treatment for TN is recommended for patients who are refractory or intolerant to pharmacological treatment. However, they also suggested that early surgery would be effective if neurovascular compression with morphologic change is confirmed upon MRI, and some studies have supported this idea [11,29,39]. Further research is necessary to establish the optimal timing for surgical intervention.

This study found that surgeries were performed within an average of 2 years after diagnosis (Table 5), which was earlier than expected. The ganglion procedure was the most frequently performed, likely due to its high availability. However, these findings differ from a previously reported study [6], possibly due to differences in definition of the ganglion procedure used in this study. According to the Korean procedure code, the ganglion procedure included destruction or blocking of the trigeminal ganglion, as well as the maxillary nerve or mandibular nerve, which are peripheral procedures. The least frequency of RFTC in this study probably results from serious adverse effects such as sensory loss [40,41].

The efficacy of surgical treatment was evaluated by time to resume medication after the first surgery, frequency of reoperation, and intervals between surgery and reoperation. The ganglion procedure was found to be the most frequently repeated with the shortest interval (Table 6). Patients who received the ganglion procedure had the least proportions of pharmacological therapy and took the 2nd longest duration to resume medication, following MVD (Table 5). These findings suggest that patients who underwent ganglion procedure may prefer reoperation to medication when pain recurs despite poor efficacy and acceptable side effects.

SRS had high numbers of patients resuming medication within the shortest duration, indicating poor efficacy [42]. Conversely, MVD had the longest duration to resume medication and the 2nd lowest numbers of patients resuming medication. Consistent with other studies [4,7,26,39,40], this finding indicates that MVD has better prognosis over other ablative surgical treatments. However, MVD is the most invasive procedure with the possibility of serious side effects including hearing loss or death, and elderly patients may be restricted to undergo MVD [40,43]. Also, Lopez et al. [41] pointed out that in the case of ablative surgery, more nerve destruction is required to increase the pain reduction effect, leading to higher likelihood of side effects. Therefore, the surgical options should be selected considering patients' satisfaction as well as the effect of the surgery and patients' condition.

Generally, TN has an alternating period of pain attacks and remission. To assess the long-term prognosis of TN, this study has investigated changes in treatment duration and remission periods per episode. The mean (SD) remission period was 0.8 (0.8)-2.7 (2.3) years per episode (Table 2). Previous studies [2,44-47] have reported varying remission period from weeks to years. In this study, the duration

of remission period significantly decreased after the first remission ($p<0.05$) until the 4th remission but remained similar thereafter (Table 2). This finding is consistent with the results from previous studies indicating shorter remissions over time [2,11,44], suggesting that the initial remission period may be relatively long. In contrast to remission, no significant changes were found in the duration of treatment episodes. These findings are consistent with the result of Di Stefano et al. [13], who found that pain frequency and duration did not worsen over time in most TN patients. As previously mentioned, insignificant increase in doses of CBZ as monotherapy throughout the entire treatment period suggests a better, or at least tolerable, prognosis of TN.

This study has several limitations inherent to the methodology of analyzing insurance claims data. Claims data do not include information on TN type (i.e., classical or idiopathic, pure paroxysmal or concomitant continuous pain) and disease severity, treatment effectiveness, and side effects. Moreover, due to the unavailability of medical records, accuracy of TN diagnosis cannot be confirmed. To mitigate errors, the study population was limited to those diagnosed only by neurologists, neurosurgeons, or specialists of oral medicine and orofacial pain. Despite these limitations, this study provides valuable long-term data on the epidemiology and treatment patterns of TN patients at the national level, offering insights into TN management and prognosis.

In conclusion, the findings reveal that Korean patients with TN share similar demographic and epidemiological characteristics with patients from other countries. A decrease in the duration of remission was also observed, but as the episodes were repeated, the duration of remission gradually stabilized without a significant decrease. Furthermore, the insignificant increase in daily dose and treatment duration for patients receiving CBZ monotherapy suggests a relatively favorable prognosis of TN. However, the study identified deviations from the international guidelines, including the frequent use of drugs with little or no evidence of efficacy such as analgesics and TCAs, as well as early decisions of surgery. This might be due to the lack of knowledge about TN. Therefore, these findings indicate clinicians' need for further education to improve their understanding and appropriately manage TN. Furthermore, considering that TN patients often seek dental care, dentists should be acknowledgeable about the differential diagnosis and management of TN.

CONFLICT OF INTEREST

Hye-Kyoung Kim has been the Editor-in-Chief of the *Journal of Oral Medicine and Pain* since April 1, 2022. Mee-Eun Kim serves as an editor of the *Journal of Oral Medicine and Pain*. However, they have no role in the decision to publish this article. Except for that, the authors have no potential conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The datasets used in this study are available from the corresponding author upon reasonable request.

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None.

AUTHOR CONTRIBUTIONS

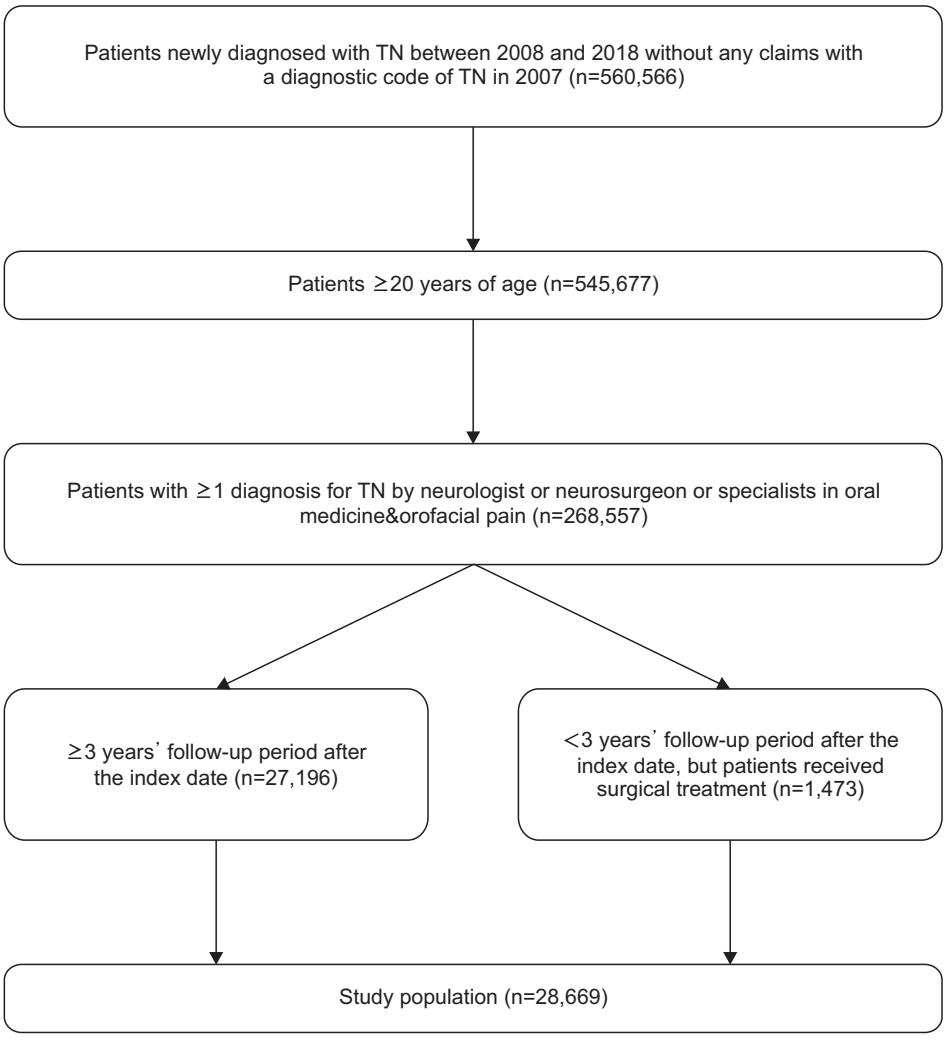
Conceptualization: JEP, MEK. Methodology: JEP, MEK. Writing original draft and visualization: JEP, HKK, MEK. Writing review and editing: JEP, HKK, MEK.

REFERENCES

1. Cruccu G, Finnerup NB, Jensen TS, et al. Trigeminal neuralgia: New classification and diagnostic grading for practice and research. Neurology 2016;87:220-228.
2. Zakrzewska JM, Wu J, Mon-Williams M, Phillips N, Pavitt SH. Evaluating the impact of trigeminal neuralgia. Pain 2017;158:1166-1174.
3. Melek LN, Devine M, Renton DT. The psychosocial impact of orofacial pain in trigeminal neuralgia patients: a systematic review. Int J Oral Maxillofac Surg 2018;47:869-878.
4. Bendtsen L, Zakrzewska JM, Abbott J, et al. European academy of neurology guideline on trigeminal neuralgia. Eur J Neurol 2019;26:831-849.
5. Gronseth G, Cruccu G, Alksne J, et al. Practice Parameter: The diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review). Neurology 2008;71:1183-1190.
6. Zakrzewska JM, Wu N, Lee JYK, Werneburg B, Hoffman D, Liu Y. Characterizing treatment utilization patterns for trigeminal neu-

ralgia in the United States. Clin J Pain 2018;34:691-699.
7. Vasappa CK, Kapur S, Krovvidi H. Trigeminal neuralgia. BJA Education 2016;16:353-356.
8. Cruccu G. Trigeminal neuralgia. Continuum (Minneap Minn) 2017;23:396-420.
9. Al-Quliti KW. Update on neuropathic pain treatment for trigeminal neuralgia. The pharmacological and surgical options. Neurosciences (Riyadh) 2015;20:107-114.
10. Obermann M. Treatment options in trigeminal neuralgia. Ther Adv Neurol Disord 2010;3:107-115.
11. Zakrzewska JM, Patsalos PN. Long-term cohort study comparing medical (oxcarbazepine) and surgical management of intractable trigeminal neuralgia. Pain 2002;95:259-266.
12. Prasad S, Galetta S. Trigeminal neuralgia: historical notes and current concepts. Neurologist 2009;15:87-94.
13. Di Stefano G, La Cesa S, Truini A, Cruccu G. Natural history and outcome of 200 outpatients with classical trigeminal neuralgia treated with carbamazepine or oxcarbazepine in a tertiary centre for neuropathic pain. J Headache Pain 2014;15:34.
14. Heinskou TB, Maarbjerg S, Wolfram F, et al. Favourable prognosis of trigeminal neuralgia when enrolled in a multidisciplinary management program-a two-year prospective real-life study. J Headache Pain 2019;20:23.
15. Maarbjerg S, Gozalov A, Olessen J, Bendtsen L. Concomitant persistent pain in classical trigeminal neuralgia–evidence for different subtypes. Headache 2014;54:1173-1183.
16. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L. Association between neurovascular contact and clinical characteristics in classical trigeminal neuralgia: A prospective clinical study using 3.0 Tesla MRI. Cephalagia 2015;35:1077-1084.
17. Han SH, Lee KH, Kim ME, Kim KS. Treatment pattern of patients with neuropathic pain in Korea. J Oral Med Pain 2009;34:197-205.
18. Nam CO, Park JS, Ko MY. A stusy on the clinical feature and treatment outcome of patients with trigeminal neuralgia. J Oral Med Pain 1999;24:315-323.
19. Ko YJ, Kim KY, Hur YK, Choi JK. A study on clinical features pharmacologic treatment outcomes of patients with trigeminal neuralgia. J Oral Med Pain 2009;34:207-216.
20. Statistics Korea. Future Population Estimation. Available from: https://kosis.kr/statHtml/ statHtml.do?orgId=101&tblId=DT_1BPA001&conn_path=I3. Accessed Dec. 6, 2020.
21. National Cancer Institution. Standard Population Data. World (WHO 2000-2025) Standard [Internet]. National Cancer Institution [cited 2020 Dec 6]. Available from: https://seer.cancer.gov/stdpopulations/world.who.html
22. Hornbrook MC, Hurtado AV, Johnson RE. Health care episodes: Definition, measurement and use. Med Care Rev 1985;42:163-218.
23. Van Wijk BLG, Klungel OH, Heerdink ER, de Boer A. Refill persistence with chronic medication assessed from a pharmacy database was influenced by method of calculation. J Clin Epidemiol 2006;59:11-17.
24. Finnerup NB, Sindrup SH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. Pain 2010;150:573-581.
25. Katusic S, Beard CM, Bergstralth E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. Ann Neurol 1990;27:89-95.
26. Zakrzewska JM, Kinskey ME. Trigeminal neuralgia. BMJ 2014;348:474.
27. MacDonald BK, Cockerell OC, Sander JWAS, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain 2000;123:665-676.
28. Hall GC, Carroll D, Parry D, McQuay HJ. Epidemiology and treatment of neuropathic pain: The UK primary are perspective. Pain 2006;122:156-162.
29. Bennetto L, Patel NK, Fuller G. Trigeminal neuralgia and its management. BMJ 2007;334:201-205.
30. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia-diagnosis and treatment. Cephalalgia 2017;37:648-657.
31. Jones MR, Urits I, Ehrhardt KP, et al. A comprehensive review of trigeminal neuralgia. Curr Pain headache Rep 2019;23:74.
32. Yuan M, Zhou HY, Xiao ZL, et al. Efficacy and safety of gabapentin vs. carbamazepine in the treatment of trigeminal neuralgia: a meta-analysis. Pain Pract 2016;16:1083-1091.
33. Cheshire WP. Defining the role for gabapentin in the treatment of trigeminal neuralgia: a retrospective study. J Pain 2002;3:137-142.
34. Heinskou T, Maarbjerg S, Rochat P, Wolfram F, Jensen RH, Bendsten L. Trigeminal neuralgia-a coherent cross-specialty management program. J Headache Pain 2015;16:66.
35. Merrill RL, Graff-Radford SB. Trigeminal neuralgia: how to rule out the wrong treatment. J Am Dent Assoc 1992;123:63-68.
36. Scrivani SJ, Mathews ES, Maciewicz RJ. Trigeminal neuralgia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100:527-538.
37. Sindrup SH, Jensen TS. Pharmacotherapy of trigeminal neuralgia. Clin J Pain 2002;18:22-27.
38. Sato J, Saitoh T, Notani KI, Fukuda H, Kaneyama K, Segami N. Diagnostic significance of carbamazepine and trigger zones in trigeminal neuralgia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;97:18-22.
39. Barker FG, Jannetta PJ, Bissonette DJ, Larkins MV, Jho HD. The long-term outcome of microvascular decompression for trigeminal neuralgia. N Engl J Med 1996;334:1077-1083.
40. Tatli M, Satici O, Kanpolat Y, Sindou M. Various surgical modalities for trigeminal neuralgia: literature study of respective long-term outcomes. Acta Neurochir (Wien) 2008;150:243-255.
41. Lopez BC, Hamlyn PJ, Zakrzewska JM. Systematic review of ablative neurosurgical techniques for the treatment of trigemial neuralgia. Neurosurgery 2004;54:973-982.
42. Sivakanthan S, Van Compel JJ, Alikhani P, van Loveren H, Chen R, Agazzi S. Surgical management of trigeminal neuralgia: Use and cost-effectiveness from and analysis of the medicare claims database. Neurosurgery 2014;73:220-226.
43. Degn J, Brennum J. Surgical treatment of trigeminal neuralgia. Results from the use of glycerol injection, microvascular decompression, and rhizotomia. Acta Neurochir (Wien) 2010;152:2125-2132.

44. Zakrzewska JM. Assessment and treatment of trigeminal neuralgia. Br J Hosp Med (Lond) 2010;71:490-494.
45. Garvan NJ, Siegfried J. Trigeminal neuralgia–earlier referral for surgery. Postgrad Med J 1983;59:435-437.
46. Rushton JG, MacDonald HNA. Trigeminal neuralgia; special considerations of nonsurgical treatment. J Am Med Assoc 1957; 165:437-440.
47. Maarbjerg S, Gozalow A, Olesen J, Bendsten L. Trigeminal neuralgia–a prospective systematic study of clinical characteristics in 158 patients. Headache 2014;54:1574-1582.



Appendix 1. Flow chart of data collection from patients with trigeminal neuralgia (TN) in this study.

Appendix 2. Proportion of newly diagnosed patients with TN by age-gender group and annual incidence rate (per 100,000 persons)

Variable	2008	2009	2010	2011	2012	2013	2014	2015	2008-2015[a]	Incidence [b]
Number of newly diagnosed patients	4,957	4,451	4,219	3,897	3,437	2,967	2,573	1,680	3,523	7.0 (5.3)
Sex										
Female	71.8	70.7	70.6	70.1	71.4	68.2	68.7	67.9	70.3	9.9
Male	28.2	29.3	29.4	29.9	28.5	31.8	31.3	32.1	29.7	4.2
Age group (y)										
20-29	2.8	2.8	2.9	2.9	3.0	3.0	2.8	2.8	2.9	1.5 (1.7)
30-29	8.2	8.3	7.7	8.5	8.5	7.4	8.3	6.0	8.0	3.5 (3.1)
40-49	17.7	18.8	17.4	17.0	16.5	14.8	16.9	15.1	17.0	6.9 (5.1)
50-59	23.2	24.6	26.5	26.0	25.4	26.2	25.0	25.4	25.2	12.2 (8.7)
60-69	27.1	25.4	24.7	24.4	23.4	25.2	22.4	23.9	24.8	23.3 (16.4)
70-79	17.7	16.5	17.4	17.7	19.1	18.8	19.4	21.1	18.1	21.7 (16.1)
≥80	3.4	3.6	3.5	3.6	4.1	4.7	5.3	5.7	4.0	6.8 (2.7)

TN, trigeminal neuralgia.
Values are presented as percent or number (%).
[a]Mean from 2008-2015.
[b]Age-adjusted incidence rate. Adjusted to the world standard population (WHO 2000-2025) [21].