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ORIGINAL RESEARCH

Percutaneous balloon compression versus radiofrequency thermocoagulation in patients with trigeminal neuralgia

Longji Cui[1], Xianbin Ning[2,*], Zhongjie Zhang[3]

[1]Department of Pain Management, Affiliated Hospital of Beihua University, 132011 Jilin, Jilin, China
[2]Department of Neurosurgery, Affiliated Hospital of Beihua University, 132011 Jilin, Jilin, China
[3]Department of Anesthesiology, Affiliated Hospital of Beihua University, 132011 Jilin, Jilin, China

***Correspondence**
nxianbin_dr@163.com
(Xianbin Ning)

Abstract

Background: Percutaneous balloon compression (PBC) and radiofrequency thermocoagulation (RFT) are widely used minimally invasive treatments for trigeminal neuralgia (TN). However, controversies persist regarding their comparative long-term efficacy, recurrence rates, postoperative physiological stress and inflammatory responses. This study is to analyze the efficacy of PBC and RFT in the treatment of patients with TN. **Methods**: This retrospective, single center, cohort study included 165 patients with primary TN, treated from January 2017 to December 2022, after failure or intolerance to medical therapy. The PBC group (n = 85), underwent percutaneous microballoon compression of the Gasserian ganglion, and the RFT group (n = 80) underwent radiofrequency thermocoagulation. The primary outcomes were pain relief, assessed using the Barrow Neurological Institute (BNI) pain intensity score, and pain recurrence rates at one and three years postoperatively. Secondary outcomes comprised pain relief rate at 24 hours post-surgery, serum inflammatory markers (Tumor Necrosis Factor-alpha (TNF-α), Interleukin-1β (IL-1β), and Interleukin-6 (IL-6)) at 7 days post-surgery, and levels of stress hormones (norepinephrine (NE) and cortisol (Cor)) at 1- and 2-days post-surgery. **Results**: At 24 hours postoperatively, no significant difference was observed in the pain relief effect between the two groups ($p > 0.05$). However, at 7 days post-operation, TNF-α, IL-1β, and IL-6 levels were significantly lower in the PBC group compared to the RFT group ($p < 0.05$). Similarly, at 1- and 2-day post-operation, norepinephrine and cortisol levels were significantly lower in the PBC group ($p < 0.05$). At 1, 3 years post-operation, the PBC group demonstrated significantly better pain relief and lower recurrence rates than the RFT group ($p < 0.05$). **Conclusions**: For the treatment of trigeminal neuralgia, PBC of the trigeminal ganglion provides effective pain relief with reduced postoperative inflammatory and stress responses. Compared with radiofrequency thermocoagulation, PBC might offer superior long-term efficacy and lower recurrence rates.

Keywords

Trigeminal neuralgia; Rhizotomy; Electrocoagulation

1. Introduction

Trigeminal neuralgia (TN) is a prevalent neuropathic pain disorder characterized by recurrent, severe, and typically unilateral facial pain within the distribution of the trigeminal nerve. Although most prevalent among middle-aged and elderly populations, its incidence in younger individuals has been increasing in recent years. TN imposes a substantial physiological and psychological burden on affected individuals, severely impairing quality of life [1, 2]. The management of TN generally involves pharmacological and non-pharmacological approaches. Medication remains the first-line treatment; however, surgical intervention should be actively considered when pharmacological treatment fails to provide adequate relief or when long-term use leads to drug tolerance and adverse effects, such as dizziness and nausea. Common surgical options include trigeminal ganglion block, microvascular decompression, percutaneous balloon compression (PBC), and radiofrequency thermocoagulation (RFT) [3, 4]. Previous studies have reported that both PBC and RFT achieve efficacy rates exceeding 90% in the treatment of primary TN [5]. Nevertheless, the two techniques differ fundamentally in their mechanisms of action: PBC utilizes mechanical compression to selectively damage pain-transmitting nerve fibers, whereas RFT employs thermal energy to induce non-selective thermal coagulation and destruction of nerve tissue. The underlying

hypothesis of this study is that these distinct mechanisms of injury may lead to different degrees of postoperative tissue inflammation and systemic stress responses, which in turn may influence long-term pain relief and recurrence rates. Over time, RFT has been associated with a higher incidence of postoperative complications and pain recurrence [6]. Although both treatment modalities have been studied, their comparative efficacy and safety remain subjects of debate, and much of the existing research has notable methodological limitations and short follow-up durations.

While previous studies have compared these two procedures, most have focused primarily on short-term pain relief and complication rates. There is a notable lack of systematic and dynamic comparative research on long-term recurrence rates, as well as on the corresponding postoperative physiological stress and inflammatory responses. Specifically, few studies have explored the correlation between postoperative changes in inflammatory cytokines (*e.g.*, TNF-α, IL-1β, IL-6) and stress hormones (*e.g.*, norepinephrine (NE), cortisol (Cor)) with long-term treatment outcome.

The novelty of the present study lies in two key aspects. First, it involves a follow-up of up to three years to systematically compare the long-term pain relief and recurrence rates of PBC and RFT. Second, it is the first to conduct an in-depth investigation into the differential effects of the two surgical methods on the body's early postoperative inflammatory and stress response indicators. Through this multidimensional, long-term comparative analysis, the study aims to bridge a critical gap in the current literature regarding how these two minimally invasive procedures affect long-term patient prognosis through distinct pathophysiological pathways. Ultimately, this work seeks to provide evidence-based medical guidance for clinical decision-making. Aiding the selection of optimal minimally invasive treatment strategies for trigeminal neuralgia based on both clinical efficacy and biological impact.

2. Materials and methods

2.1 General information

This retrospective cohort study includes 165 patients with TN who were treated in Affiliated Hospital of Beihua University between January 2017 and December 2022 based on the medical records. Patients were categorized according to their treatment method into a PBC group (85 cases) and an RFT group (80 cases). It must be emphasized that due to the retrospective and non-randomized nature of the study, grouping was based on clinical decision-making rather than random allocation. Therefore, selection bias and unmeasured confounding factors may have influenced the results. This study was approved by the Ethics Committee of Affiliated Hospital of Beihua University (Approval no. 20250085). The requirement for individual patient written informed consent was waived.

Inclusion Criteria: (1) Patients met the diagnostic criteria for classical or idiopathic TN as defined by the International Classification of Headache Disorders, 3rd edition (ICHD-3) [7], and had secondary TN caused by clear etiologies such as tumors or multiple sclerosis excluded through cranial MRI or other imaging studies. (2) Patients experienced inadequate pain relief despite undergoing a full course of treatment with sufficient doses of systemic medications (*e.g.*, carbamazepine, oxcarbazepine) or sought surgical treatment due to intolerance of adverse drug reactions. (3) First surgical intervention for TN. (4) Complete medical records, including preoperative, intraoperative, and follow-up data.

Exclusion Criteria: (1) Secondary TN due to identifiable etiologies (*e.g.*, tumor, multiple sclerosis). (2) History of ipsilateral TN surgery, such as microvascular decompression or Gamma Knife radiosurgery. (3) Contraindications to anesthesia or puncture, including severe cardiopulmonary dysfunction, coagulopathy, or local infection. (4) Patients with comorbid severe psychiatric disorders or cognitive impairment who were unable to accurately describe their pain levels or cooperate with follow-up. (5) Patients with incomplete clinical records, or those whose key long-term efficacy data were missing due to being lost to follow-up, death, or other reasons, rendering them unable to complete the required 1-year, 3-year follow-up assessments for this study.

2.2 Methods

RFT group (Radiofrequency Thermocoagulation): Patients were positioned supine with a shoulder pad, and continuous electrocardiogram (ECG) monitoring was used throughout the procedure. Local anesthetic infiltration with lidocaine was administered. Following sterile draping, digital subtraction angiography (DSA) was used to mark the puncture point medial to the mandibular angle. Under DSA guidance, a puncture needle was advanced towards the foramen ovale, and a radiofrequency electrode was subsequently inserted. Sensory and motor stimulation were performed to confirm correct electrode placement by replicating the patient's typical pain distribution. The temperature was set to 70–75 °C (or $<$65 °C for the ophthalmic branch) and maintained for 2–3 minutes, depending on patient tolerance. after lesion creation, facial sensory testing was performed. Complete disappearance of pain sensation and dullness of tactile sensation indicated nerve destruction. The puncture needle was then withdrawn, and the puncture site was compressed for 5 minutes to ensure hemostasis, followed by disinfection and application of a sterile dressing. Patients were prescribed 24 hours of bed rest and prophylactic antibiotics postoperatively.

PBC group (Percutaneous Balloon Compression): Patients received 0.5 mg intramuscular atropine preoperatively to prevent the trigemino-cardiac reflex. The procedure was performed under general anesthesia with endotracheal intubation or, when permissible, a laryngeal mask airway to minimize postoperative discomfort. The head was positioned naturally in the midline. Patient positioning was verified using anteroposterior and lateral fluoroscopy to ensure the superposition of the bilateral bony external auditory canals. The Hartel anterior approach was utilized, with a needle inserted 2–3 cm lateral to the oral commissure on the affected side. Under anteroposterior and lateral fluoroscopic guidance, a 14-gauge puncture needle was used to puncture the foramen ovale. After confirming the needle tip's position within the foramen ovale, the stylet was removed. A 4-French Fogarty balloon catheter,

pre-loaded with a guidewire, was inserted through the needle, and advanced into Meckel's cave. The guidewire was then withdrawn. The balloon was inflated gradually with 0.3–0.8 mL (average 0.5 mL) of non-ionic contrast (iopamidol) until a "pear-shaped" outline was seen on fluoroscopy. The balloon remained inflated for 90–180 seconds, then was deflated and withdrawn together with the needle. The puncture site was compressed for 5–10 minutes to achieve hemostasis and covered with a sterile dressing. The patient was then gradually recovered from anesthesia.

2.3 Explanation of differences in anesthesia methods

The anesthesia protocols differ due to the specific procedural needs and safety considerations of each technique.

Local anesthesia for RFT: The success of RFT is critically dependent on intraoperative patient feedback for precise neurophysiological localization of the target nerve fibers. Following the insertion of the puncture needle, the proceduralist must perform sensory stimulation with a microcurrent to elicit a response from the conscious patient. The patient is asked to confirm whether the evoked sensation precisely replicates the location and character of their typical trigeminal pain. Thermocoagulation is initiated only after the patient confirms a concordant response. This interactive process is essential for maximizing therapeutic efficacy while minimizing the risk of injury to adjacent, non-target nerve branches (*e.g.*, those mediating corneal sensation or masticatory muscle function). Therefore, maintaining patient consciousness and cooperation is a core requirement for the precision and safety of RFT, rendering general anesthesia unsuitable for this procedure.

General anesthesia for PBC: In contrast to RFT, the PBC procedure relies exclusively on anatomical landmarks, identified via fluoroscopic guidance, and does not require intraoperative patient feedback. The primary therapeutic action involves the inflation of a balloon catheter within Meckel's cave to apply intense mechanical compression to the Gasserian ganglion. This maneuver induces a profound nociceptive stimulus that would be intolerable for a conscious patient. Furthermore, potent stimulation of the trigeminal ganglion poses a significant risk of inducing the trigemino-cardiac reflex, a physiological response that can lead to severe bradycardia, hypotension, or, in rare cases, cardiac arrest. Performing the procedure under general anesthesia with a secure airway (*e.g.*, endotracheal intubation) allows for the effective prevention and management of this reflex, thereby ensuring patient safety and physiological stability. Consequently, general anesthesia is a prerequisite for performing PBC safely and humanely.

Acknowledgment of potential confounding factors: The different anesthesia protocols introduce a potential confounding factor in evaluating stress hormone levels (NE, Cor). Patients in the RFT group were awake and experienced both the psychological stress of the procedure and the deliberate replication of their neuropathic pain. Conversely, patients in the PBC group remained unconscious and had no intraoperative awareness. As a result, the observed differences in early postoperative stress hormone levels likely reflect a composite of surgical trauma, the inflammatory response, and the distinct intraoperative anesthetic experiences. This systematic bias must be given full consideration when interpreting the data related to the physiological stress response.

2.4 Observation indicators

(1) Postoperative pain relief efficacy: Pain was evaluated at 24 hours, 1 year, 3 years postoperatively using the Barrow Neurological Institute (BNI) pain intensity scale [8]. For the evaluation, the data was not dichotomized; instead, the distribution of patients across the various BNI grades was directly compared between the two groups. The BNI grading criteria are as follows:

BNI I: No TN pain, no medication required.

BNI II: Occasional pain, no medication required.

BNI III: Some pain, adequately controlled with medication.

BNI IV: Pain not adequately controlled with medication.

BNI V: Severe, unrelieved pain.

(2) Inflammatory response indicators: Tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) levels were measured and compared between the two groups before surgery and at 7 days post-operation. 3 mL of fasting venous blood was collected from all patients in the early morning before surgery and at 7 days post-operation. Serum levels of TNF-α, IL-1β, and IL-6 were measured using an enzyme-linked immunosorbent assay (ELISA).

(3) Stress response indicators: Norepinephrine (NE) and cortisol (Cor) levels were measured and compared between the two groups before surgery and at 1- and 2-days post-operation. 3 mL of fasting venous blood was collected from all patients in the early morning before surgery and at 1- and 2-days post-operation. Serum NE and Cor levels were measured using ELISA.

(4) Assessment of long-term efficacy and pain recurrence. Patients were followed up at 1, 3 years postoperatively through either outpatient visits or telephone calls to assess long-term efficacy and pain recurrence.

Pain recurrence was defined as follows: after achieving satisfactory postoperative pain relief (*i.e.*, BNI pain grade I or II), any subsequent worsening of pain during follow-up that required the resumption of regular analgesic medication (*i.e.*, an increase in BNI grade to III) was considered a recurrence. Similarly, if the pain worsened to a level that could no longer be effectively controlled by medication (*i.e.*, an increase in BNI grade to IV or V), it was also classified as recurrence.

In simple terms, a transition from a state manageable without medication (BNI Grade I/II) to one requiring medication for pain control (BNI $\geq$ III) was considered a recurrence. Cases with incomplete data, such as those resulting from death or loss to follow-up, were excluded during the initial screening phase and not included in the recurrence rate calculation.

2.5 Follow-up methods

All patients were followed up through outpatient reviews and telephone interviews at 1 month, 6 months, 1 year, and annually thereafter until 3 years or study completion (31 December 2023).

All 165 patients completed at least 12 months of follow-up. The follow-up period ranged from 12 to 84 months, with

a median of 51 months and a mean of 50.5 ± 18.2 months. During follow-up, pain relief, complications, and recurrences were meticulously documented.

2.6 Statistical methods

Data were analyzed using SPSS 26.0 (IBM, Armonk, NY, USA). The Shapiro-Wilk test was used to test the normality of the data. Homogeneity of variances was assessed using Bartlett's test. Normally distributed continuous variables were expressed as mean ± standard deviation ($\bar{x} \pm s$). For comparisons, analysis of variance (ANOVA) and *t*-tests were employed. Specifically, independent-sample *t*-tests were used for between-group comparisons and paired-sample *t*-tests for within-group comparisons. categorical variables were expressed as number of cases and percentage (%), and comparisons between groups were performed using the chi-squared (χ^2) test. A p-value < 0.05 was considered statistically significant. BNI grades were treated as an ordinal categorical variable. For pain relief outcomes at 1, 3 years postoperatively, an ordinal logistic regression model was used to evaluate the effect of different treatment methods on pain outcomes.

For long-term pain recurrence, a time-to-event analysis was performed. Kaplan-Meier curves were plotted to display the recurrence-free survival probability of the two groups over the three-year follow-up period. The log-rank test was used to compare the survival curves between the two groups. To quantify the magnitude of the efficacy difference, a Cox proportional hazards model was employed to calculate the hazard ratio (HR) and its 95% confidence interval (CI) for recurrence in the PBC group relative to the RFT group. For all statistical tests, a p-value < 0.05 was considered significant.

3. Results

3.1 General information

The Baseline characteristics of the two groups are shown in Table 1. The data were comparable between the two groups ($p > 0.05$).

3.2 Postoperative pain relief

At 24 hours post-operation, there was no significant difference in the pain relief effect between the two groups ($p = 0.380 > 0.05$, Table 2).

3.3 Inflammatory response indicators

At 7 days post-operation, the levels of TNF-α, IL-1β, and IL-6 in the PBC group were significantly lower than those in the RFT group ($p < 0.001$, Table 3, Fig. 1).

3.4 Stress response indicators

At 1 and 2 days post-operation, the levels of NE and Cor in the PBC group were significantly lower than those in the RFT group ($p < 0.001$, Table 4, Figs. 2,3).

3.5 Follow-up

The distribution of long-term pain relief outcomes (BNI grade) for patients in both groups is presented in Table 5. To more precisely quantify the difference in efficacy between the two groups, an ordinal logistic regression analysis was performed (Table 5).

After controlling for baseline variables, the analysis revealed that the PBC group demonstrated significantly superior pain relief outcomes compared to the RFT group at all follow-up time points. At 1-year post-surgery, the odds of the PBC group achieving a better BNI grade were 2.37 times higher than those of the RFT group (OR = 2.37, 95% CI: 1.25–4.49, $p = 0.008$). This advantage became more pronounced over time, with the OR increasing to 3.38 ($p = 0.047$) at 3 years post-surgery. These findings suggest that PBC not only offers better short-term efficacy but also demonstrates more significant long-term stability and superiority. Concurrently, the pain recurrence rate in the percutaneous balloon compression group was significantly lower than that in the radiofrequency thermocoagulation group ($p < 0.05$).

3.6 Long-term recurrence

The follow-up period was 12–84 months due to varied enrollment times. Since only 110 patients completed the 3-year follow-up, Kaplan-Meier survival analysis was the primary method for evaluating long-term efficacy. The long-term recurrence patterns of the two groups were assessed using Kaplan-Meier survival analysis, with the results shown in Fig. 4. The log-rank test revealed a highly significant statistical difference between the recurrence-free survival curves of the two groups over the follow-up period ($p = 0.001$).

As shown in Fig. 4, the survival curve for the PBC group consistently lies above that of the RFT group, indicating that patients in the PBC group maintained a higher probability of remaining recurrence-free at throughout the observation period.

To further quantify this difference, a Cox proportional hazards model analysis was performed. The results demonstrated that patients in the PBC group had a significantly lower risk of pain recurrence, with a hazard ratio (HR) of 0.30 (95% CI: 0.15–0.59, $p < 0.001$) compared to the RFT group. This finding indicates that treatment with PBC reduces the long-term risk of recurrence by 70% relative to RFT.

4. Discussion

This retrospective cohort study systematically compared the clinical efficacy and biological response associated with PBC and RFT for the treatment of TN over three years. The principal findings indicate that while both minimally invasive techniques achieved comparable immediate postoperative pain relief at 24 hours, their long-term outcomes diverged significantly. Throughout the one- to three-year follow-up, PBC demonstrated superior pain control and a lower long-term recurrence rate than RFT. Furthermore, early postoperative systemic inflammatory response and physiological stress levels were significantly lower in the PBC group compared to the RFT group. The following discussion interprets these

TABLE 1. Comparison of baseline characteristics between two groups.

Demographic and clinical parameters	PBC group (n = 85)	RFT group (n = 80)	χ^2/t	p
Age (yr) (mean ± SD)	59.26 ± 3.41	60.25 ± 3.56	1.838	0.068
Disease duration (yr) (mean ± SD)	4.15 ± 2.13	4.32 ± 2.07	0.496	0.620
Gender (male/female)	31/54	29/51	0.001	0.977
Pain area (left/right)	36/49	38/42	0.441	0.506
TN branch distribution (n (%))				
Ophthalmic nerve, V1	45 (52.94)	38 (47.50)		
Maxillary nerve, V2	19 (22.35)	20 (25.00)	0.488	0.783
Mandibular nerve, V3	21 (24.71)	22 (27.50)		
Comorbidities (n (%))				
Hypertension	20 (23.53)	17 (21.25)	0.123	0.726
Diabetes	15 (17.65)	16 (20.00)	0.150	0.699
Cervical spondylosis	25 (29.41)	23 (28.75)	0.009	0.925
ENT diseases	15 (17.65)	12 (15.00)	0.211	0.646
ASA classification system (n (%))				
Stage I	46 (54.12)	38 (47.50)	0.722	0.395
Stage II	39 (45.88)	42 (52.50)		

ENT: Ear, Nose, and Throat; ASA: American Society of Anesthesiologists; PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation; TN: trigeminal neuralgia; SD: standard deviation.

TABLE 2. Comparison of pain relief effects 24 hours after surgery (n (%)).

BNI grading	PBC group	RFT group	OR	95% CI	p
BNI I	75 (88.24)	68 (85.00)			
BNI II	5 (5.88)	4 (5.00)			
BNI III	3 (3.53)	5 (6.25)	1.42	(0.650, 3.110)	0.380
BNI IV	2 (2.35)	3 (3.75)			
BNI V	0	0			

OR: Odds ratio; CI: Confidence Interval; BNI: Barrow Neurological Institute; PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation.

TABLE 3. Comparison of serum inflammatory cytokine levels before and after operation in the PBC and RFT groups ($\bar{x} \pm s$).

Group	n	Before operation	7 days after operation	t	p	95% CI	
						Lower limit	Upper limit
TNF-α (ng/L)							
PBC group	85	45.21 ± 6.35	27.16 ± 6.32	17.792	<0.001	16.0320	20.0668
RFT group	80	44.68 ± 6.48	33.63 ± 6.84	12.085	<0.001	9.2300	12.8700
t		0.530	6.319				
p		0.597	<0.001				
IL-1β (ng/L)							
PBC group	85	47.24 ± 7.28	32.53 ± 6.08	15.061	<0.001	12.7673	16.6516
RFT group	80	47.35 ± 7.35	38.76 ± 6.58	8.523	<0.001	6.5839	10.5961
t		0.104	6.333				
p		0.917	<0.001				
IL-6 (ng/L)							
PBC group	85	25.93 ± 6.32	12.05 ± 3.12	16.971	<0.001	12.2536	15.5064
RFT group	80	26.30 ± 6.60	15.53 ± 3.69	12.121	<0.001	9.0025	12.5400
t		0.368	6.520				
p		0.713	<0.001				

TNF-α: Tumor Necrosis Factor-alpha; IL-1β: Interleukin-1β; CI: confidence interval; PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation; IL-6: Interleukin-6.

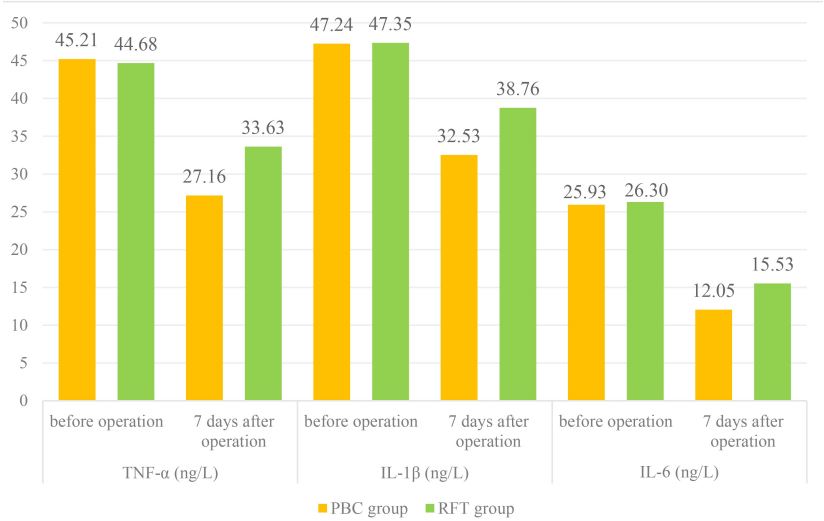

FIGURE 1. Comparison of inflammatory response indicators. TNF-α: Tumor necrosis factor-alpha; IL-1β: Interleukin-1β; IL-6: interleukin-6; PBC: Percutaneous balloon compression; RFT: Radiofrequency thermocoagulation.

TABLE 4. Comparison of stress response indicators (norepinephrine and cortisol levels) before and after operation in the PBC and RFT groups ($\bar{x} \pm s$).

Group	n	Indicator	Before operation	1 day after operation	2 days after operation	*F*	*p*-value
PBC group	85	NE (ng/L)	258.95 ± 40.35	301.30 ± 44.50	330.27 ± 50.10	53.601	<0.001
		Cor (μg/L)	102.50 ± 13.75	160.05 ± 23.39	190.15 ± 30.20	306.893	<0.001
RFT group	80	NE (ng/L)	260.47 ± 42.56	338.36 ± 50.37	370.25 ± 56.28	101.849	<0.001
		Cor (μg/L)	103.37 ± 15.10	186.63 ± 28.54	215.21 ± 35.31	354.077	<0.001
t (NE)			0.234	5.015	4.826		
p-value (NE)			0.815	<0.001	<0.001		
t (Cor)			0.387	6.521	4.908		
p-value (Cor)			0.699	<0.001	<0.001		

PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation; NE: norepinephrine; Cor: cortisol.

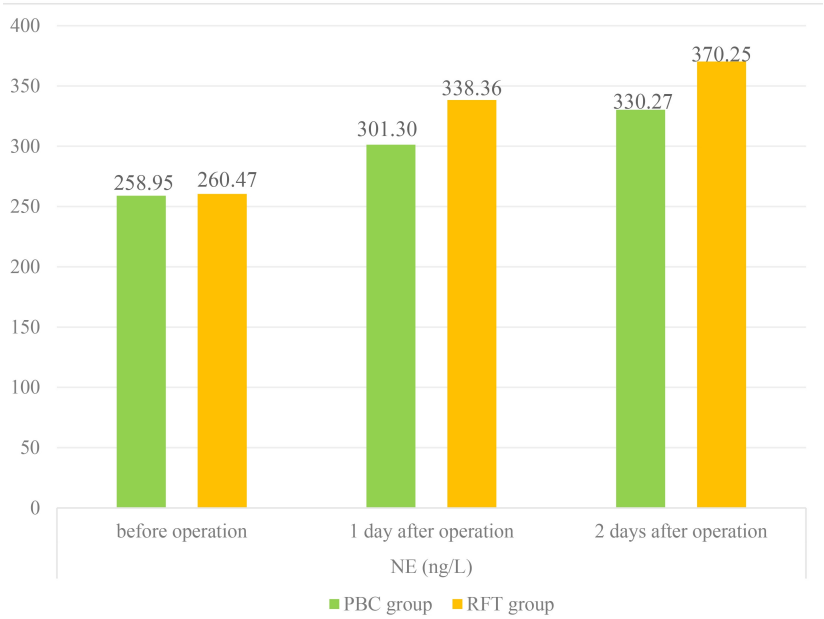

FIGURE 2. Comparison of stress response indicators (1). NE: norepinephrine; PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation.

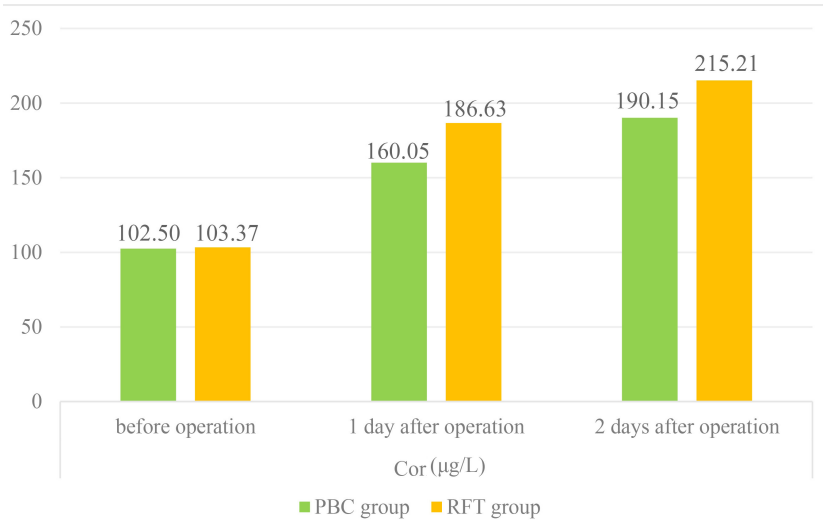

FIGURE 3. Comparison of stress response indicators (2). Cor: cortisol; PBC: percutaneous balloon compression; RFT: radiofrequency thermocoagulation.

TABLE 5. Comparison of long-term pain relief outcomes between the PBC and RFT groups (n, %).

Group	n	Follow-up time	BNI I	BNI II	BNI III	BNI IV	BNI V	OR	95% CI	*p*-value
PBC group	85	1 yr	62 (72.94)	20 (23.53)	2 (2.35)	1 (1.18)	0	2.37	1.25–4.49	0.008
RFT group	80		45 (56.25)	25 (31.25)	7 (8.75)	3 (3.75)	0			
PBC group	57	3 yr	42 (73.68)	10 (17.54)	2 (3.51)	3 (5.26)	0	3.38	1.11–10.31	0.047
RFT group	53		30 (56.60)	10 (18.87)	7 (13.21)	4 (7.54)	2 (3.77)			

OR: odds ratio; CI: Confidence Interval; PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation; BNI: Barrow Neurological Institute.

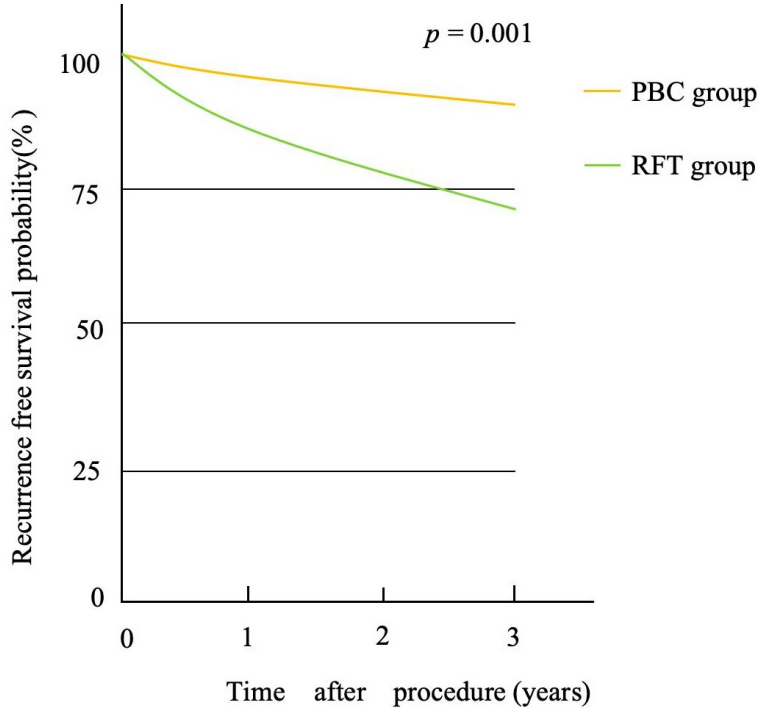

FIGURE 4. Kaplan-Meier curve for recurrence-free survival. The curve displays the probability of patients remaining free from pain recurrence during the 3-year follow-up period. The recurrence-free survival rate of the PBC group was significantly higher than that of the RFT group (p = 0.001, log-rank test). PBC: Percutaneous balloon compression; RFT: radiofrequency thermocoagulation.

results, explores potential biological mechanisms underlying the observed differences, situates them within the existing literature, and acknowledges the study's inherent limitations while suggesting directions for future research.

4.1 Interpretation of differences in early biological responses

In the early postoperative phase, serum levels of inflammatory markers (TNF-α, IL-1β, IL-6) and stress hormones (norepinephrine, cortisol) were significantly lower in the PBC group than in the RFT group. This finding suggests that the two surgical procedures impart distinct immediate physiological impacts.

The differing inflammatory response result from the distinct mechanisms of tissue injury. RFT relies on high temperatures (typically 70–75 °C) to produce thermal coagulation and ablation of nerve tissue. This non-selective thermal insult induces rapid coagulative necrosis in both target and surrounding tissues [9–11]. The resulting massive and acute cellular rupture releases a large volume of damage-associated molecular patterns (DAMPs), potent activators of the innate immune system that trigger an intense, cascade-like inflammatory response [12, 13]. PBC achieves its therapeutic effect primarily through mechanical compression. Balloon inflation exerts significant pressure on the Gasserian ganglion, disrupting pain transmission by inducing nerve fiber ischemia and mechanical injury [14]. This mechanical injury is more likely to trigger programmed cell death (apoptosis) rather than widespread necrosis [15]. Apoptosis is a comparatively orderly and controlled cellular clearance process that generates a significantly weaker inflammatory signal than necrosis [16]. Consequently, the downstream inflammatory cascade and the overall systemic inflammatory burden are reduced [17]. Thus, the observed lower inflammatory marker levels in the PBC group likely reflect its more biologically "gentle" mechanism of action.

Regarding the physiological stress response, although the PBC group also showed a statistically significant advantage, this must be interpreted cautiously due to the confounding effect of anesthesia. RFT is necessarily performed under local anesthesia, requiring the patient to remain conscious throughout the procedure. To precisely localize the target nerve, intraoperative electrical stimulation is used to replicate the patient's specific pain symptoms [18]. This process inherently constitutes a potent physiological and psychological stressor, sufficient to activate the sympathetic-adrenal medullary axis and the hypothalamic-pituitary-adrenal (HPA) axis [19, 20]. In contrast, PBC is performed under general anesthesia, rendering the patient unconscious and insensate to pain, thereby obviating the fear, anxiety, and nociceptive stimuli associated with the surgical operation [21]. Therefore, the observed differences in stress hormone levels likely result from a combination of surgical trauma, inflammatory intensity, and anesthetic modality, rather than the surgical technique alone. This represents a key limitation in interpreting these findings.

4.2 Potential mechanisms underlying differences in long-term efficacy and recurrence

A key observation of this study is that PBC's superior long-term efficacy becomes increasingly evident over time, as reflected by its significantly lower three-year recurrence rate. Although the precise mechanisms remain to be elucidated, differences in nerve injury and regeneration dynamics are likely contributing factors. It is important to emphasize that the following discussion is based on existing theoretical frameworks and does not represent a causal relationship directly confirmed by this retrospective analysis.

Pain recurrence following neurotomy is intrinsically linked to nerve repair and regeneration. The distinct injury patterns produced by RFT and PBC may promote two divergent pathways of neural repair. The intense thermal injury from RFT, which creates a highly inflammatory microenvironment, may predispose the nerve to a disordered or aberrant form of regeneration [22]. Thermal coagulation may not result in the uniform destruction of all target axons. Surviving, yet damaged, neurons, when stimulated by a plethora of local inflammatory factors, may undergo uncontrolled axonal sprouting [23]. This chaotic regenerative process is prone to the formation of aberrant neural connections or micro-neuromas, which are characterized by abnormal hyperexcitability and can function as ectopic pain generators, thus leading to the early recurrence of symptoms [24, 25].

In contrast, the mechanical compression injury associated with PBC, which favors apoptosis over necrosis, likely creates a more quiescent microenvironment for nerve repair. The attenuated postoperative inflammatory response may reduce aberrant axonal stimuli, facilitating a more orderly process of axonal recovery and remyelination [26]. This controlled repair could lower the likelihood of ectopic generation, contributing to more durable pain relief [27]. These findings align with prior meta-analytic evidence suggesting that apoptosis-dominant injury mechanisms underlie PBC's reduced recurrence rate. Collectively, the data support the view that PBC promotes a more stable, long-term modulation of pain transmission through a milder injury pattern and a more favorable microenvironment for nerve regeneration.

4.3 Contextualizing findings within the literature

The findings of this study largely corroborate and extend those of the recent literature, while also providing novel insights. For instance, a study by Zhao Bo *et al.* [28] confirmed PBC's superior long-term outcomes, emphasizing refinements in balloon pressure and compression duration to minimize recurrence, underscoring that PBC remains amenable to procedural optimization. Similarly, Yuwei Shi *et al.* [29] compared PBC with microvascular decompression (MVD), the current gold standard, and found comparable efficacy at two years, with PBC offering shorter operative times, reduced hospitalization, and fewer complications. This study expands on previous work by directly comparing PBC and RFT, two mainstream minimally invasive techniques, and extending the follow-up to three years. Our findings not only reaffirm

PBC's effectiveness but also demonstrate its superiority in sustained pain control. This provides clinically relevant, long-term evidence supporting PBC as the preferred minimally invasive strategy for TN, especially in managing postoperative recurrence.

Additionally, Liang Hui [30] Reported that combining ultrasound with C-arm guidance improved procedural precision, reduced radiation exposure, and minimized complications during foramen ovale puncture for RFT. These findings highlight the growing emphasis on technological refinements to enhance procedural safety and efficacy—an approach complementary to the current study's focus on biological and mechanistic outcomes.

4.4 Limitations and future directions

Despite its valuable insights, this study is subject to several inherent limitations, primarily due to its retrospective, single-center design.

Inherent bias of a retrospective design: This study's most significant limitation is its retrospective nature. The data were collected from existing medical records, which introduces the potential for selection bias and information bias. Selection bias may exist because patients who received PBC or RFT could have had systematic differences in unmeasured baseline characteristics. The choice of surgical procedure was not randomized but was determined by the attending physician's clinical experience and technical preference, as well as specific patient factors (such as the affected trigeminal branch, overall physical condition, and financial considerations). Information bias is also a concern, as the quality and completeness of medical records may have affected data accuracy. Although our analysis of baseline characteristics (Table 1) revealed no statistically significant differences between the two groups, this does not entirely preclude the potential influence of unmeasured or unrecorded confounding variables on the final efficacy assessment.

Lack of randomization and operator variability: The absence of a randomized design means that the comparability of baseline characteristics between the two groups, despite showing no statistical difference, cannot be fully assured. Furthermore, both PBC and RFT are highly operator-dependent procedures. The technical proficiency and experience of the surgeon can significantly influence clinical outcomes and complication rates. This study was unable to perform a stratified analysis or otherwise adjust for this potential operator variability, which may have introduced a source of unmeasured confounding.

Single-center design and generalizability: As all cases were sourced from a single medical institution, the external validity (generalizability) of our findings may be limited. The demographic characteristics of our patient population, local standards of medical practice, and the specific technical expertise of our surgical team may not be fully representative of other regions or different types of medical centers. Therefore, caution is warranted when extrapolating these findings to broader patient populations. Additionally, the accuracy of the data is entirely contingent upon the completeness and precision of the existing medical records, a common limitation in retrospective research.

Loss to follow-up and attrition bias: To maintain data integrity for long-term analysis, this study excluded patients who were lost to follow-up. This necessary step, however, may have introduced attrition bias. It is plausible that patients lost to follow-up systematically differed from those who completed the study, potentially in terms of treatment efficacy, complication rates, or socioeconomic status. Such a bias could lead to an overestimation of the observed therapeutic effects for both procedures.

Limitations in biomarker measurement: Our analysis of biomarkers was limited to specific postoperative time points and lacked preoperative baseline data or dynamic monitoring over a longer time series. This methodological limitation precludes a comprehensive analysis of the temporal dynamics of these biological responses and their relationship to the initial patient state.

Future directions: Given these limitations, future research should prioritize rigorously designed, multicenter, prospective, randomized controlled trials (RCTs). RCTs represent the gold standard for mitigating selection bias and confounding and are necessary to provide a higher level of evidence. Furthermore, future studies should aim to elucidate the biological mechanisms and predictive markers of postoperative recurrence. For instance, research could investigate the specific regulatory effects of mechanical compression on the expression profile of neuronal ion channels. Another avenue would be to explore whether a sustained upregulation of specific anti-inflammatory (*e.g.*, IL-10) or neuroprotective factors correlates with long-term, recurrence-free outcomes. Such studies would not only deepen the understanding of pain recurrence mechanisms but could also inform new strategies for patient stratification, prognostic prediction, and the development of novel therapeutic targets.

4.5 Biomarkers as potential predictors of recurrence

The observed differences in postoperative inflammatory profiles highlight the potential of biomarkers as predictors of long-term recurrence. While this study focused on pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), whose elevated levels correlated with higher recurrence in the RFT group, the inclusion of anti-inflammatory cytokines such as IL-10 may offer additional predictive power.

We hypothesize that a patient's endogenous IL-10 response following surgery may be a critical determinant of long-term pain recurrence. A robust postoperative IL-10 response could theoretically counteract the pro-inflammatory microenvironment induced by surgical trauma, particularly the thermal injury from RFT. By inhibiting the over-activation of macrophages and glial cells, IL-10 may foster a microenvironment more conducive to orderly nerve regeneration and remyelination, thereby mitigating the aberrant axonal sprouting and ectopic discharges implicated as a primary cause of pain recurrence.

Validation of this hypothesis would require prospective studies designed to serially collect serum samples at baseline and at key postoperative intervals (*e.g.*, 24 hours, 7 days, 1 month, 6 months). These samples could then be assayed for a panel of

pro- and anti-inflammatory cytokines, including IL-10. Longitudinal follow-up combined with statistical methods such as survival analysis could then determine whether early postoperative IL-10 levels, or the ratio of pro- to anti-inflammatory cytokines, serve as independent predictors of long-term pain recurrence.

Ultimately, the goal is to develop a clinically applicable predictive model capable of identifying patients with an "inflammatory phenotype" at high risk for recurrence. This high-risk subgroup could then be targeted for closer clinical follow-up or potentially even prophylactic, short-term anti-inflammatory or immunomodulatory therapies aimed at improving their long-term prognosis. Such a development would represent a significant step in advancing the treatment of TN, moving beyond a uniform surgical approach toward an era of precision medicine guided by individual patient biology. Furthermore, it could pave the way for novel perioperative interventions designed to optimize the nerve repair microenvironment.

5. Conclusions

In summary, this study found that both percutaneous balloon compression and radiofrequency thermocoagulation provide effective immediate pain relief for trigeminal neuralgia; PBC demonstrates superior long-term outcomes. Compared to RFT, PBC was associated with a significantly lower three-year recurrence rate and a more attenuated early postoperative inflammatory and physiological stress response. These findings suggest that the mechanism of nerve injury may be a critical determinant of long-term success in the minimally invasive treatment of this condition. Further prospective, mechanistic studies are warranted to validate these conclusions and guide the development of individualized, biology-based therapeutic strategies for trigeminal neuralgia.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

LJC, XBN—designed the study and carried them out; interpreted the data; prepared the manuscript for publication and reviewed the draft of the manuscript. LJC, XBN, ZJZ—supervised the data collection; analyzed the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Affiliated Hospital of Beihua University (Approval no. 20250085). The requirement for informed consent was waived by the Ethics Committee of Affiliated Hospital of Beihua University.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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