



# Factors that may delay disappearance of trigeminal neuralgia after percutaneous balloon compression

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## ABSTRACT

**Introduction.** We set out to explore the factors that may affect delayed disappearance (DD) of trigeminal neuralgia (TN) after percutaneous balloon compression (PBC).

**Material and methods.** PBC was undergone by 221 patients with TN (95 male, 126 female) aged 33–89 years (mean 65). Delayed disappearance after surgery occurred in 59 patients. Follow-up continued until pain disappeared.

**Results.** A total of 221 patients, with an overall effective rate of 98.19%, including 59 patients with DD (26.70%), 158 patients with non-DD (71.49%), and four patients without relief, were included in this study. The time of delayed disappearance ranged from two to 30 days after surgery, with an average of c.9 days. Factors related to delayed disappearance included symptom duration ( $\geq 8$  years), history of radiofrequency thermocoagulation, diabetes mellitus, herpes zoster, pain involving V2, and non-pear-shaped balloon. These were independent influencing factors ( $p < 0.05$ ).

**Conclusions.** PBC is a safe and effective surgical method for treating TN. Delayed disappearance is a common phenomenon after surgery, and is influenced by many factors.

**Key words:** percutaneous balloon compression, trigeminal neuralgia, delayed disappearance, symptom duration  
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## Introduction

At present, the treatment methods for trigeminal neuralgia (TN) mainly include drug therapy, microvascular decompression (MVD), radiofrequency thermocoagulation (RFT), and percutaneous balloon compression (PBC). PBC is mainly suitable for elderly patients with ineffective oral drugs, multi-branch pain, and poor surgical tolerance. It has the advantages of minimal trauma, high safety, and rapid effect.

However, pain may not disappear immediately after PBC surgery. Clinically, the phenomenon where pain does not disappear immediately after surgery, but gradually disappears during observation after surgery, is known as 'delayed disappearance' (DD). Nerve tissue undergoes sequential

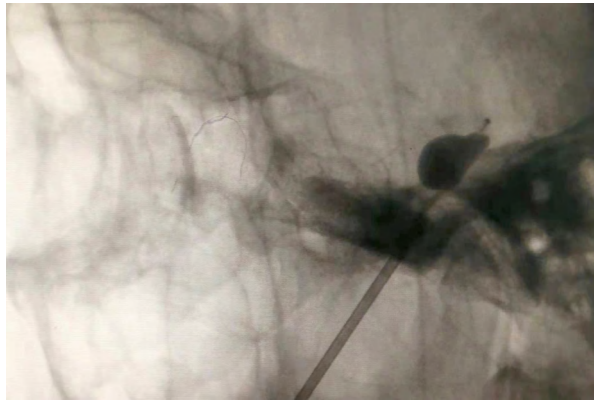
pathological changes after the ganglion is compressed by the balloon. When the filling pressure in the balloon is maintained for a period of time, most nerve cells are mechanically damaged. However, pathological changes do not occur, which may be the pathological basis of delayed disappearance. To date, no studies have reported on delayed disappearance in patients with TN who underwent PBC surgery.

Therefore, our study examined 59 patients with delayed disappearance of TN treated using PBC in our department. For the first time in this study we have examined related factors such as symptom duration, concomitant diseases, and balloon shape, to further explore the influencing factors of delayed disappearance, thus inferring the prognoses for patients and so guiding clinical work.

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**Figure 1.** Pear-shaped balloon in situ. Pear-shaped balloon formed in Meckel's cave during percutaneous balloon compression (PBC) surgery

## Material and methods

### Material

A total of 221 patients who underwent PBC in our department from January 2018 to June 2021, and who were willing to be followed up after their surgery, were recruited as research participants. This study was approved and implemented by the Hospital Ethics Committee, and all patients who participated provided signed informed consent.

The inclusion criteria were: (1) medical history, symptoms and signs, and brain computed tomography and magnetic resonance imaging results that all met the International Headache Society (IHS)-II (2008) and IHS-III (2013) diagnostic criteria for TN [1, 2]; and (2) oral carbamazepine invalid or serious adverse reactions.

Patients were excluded if: (1) they could not tolerate general anaesthesia, had dysfunction of the heart, lungs, liver, kidneys, or other vital organs, or had an obvious neurological impairment; or (2) had secondary TN; or (3) their medical records or follow-up information were incomplete.

### Methods

Patients were placed in a supine position, and Hartel's puncture technique was performed after successful induction of general anaesthesia [3]. Under the fluoroscopic guidance of a C-arm machine (Ziehm 8000, Germany), the needle was inserted 3 cm outside the angle of incidence, and a No. 14 needle was inserted into the opening of the foramen ovale. A 4-F Fogarty catheter, connected to the T-joint, was slowly introduced into Meckel's cave along the puncture path. Next, 0.4–0.8 mL gadolinium diamine was injected to inflate the balloon to achieve a pear-like shape (Fig. 1). The compression continued for 3–5 min (average: 4 min, Tab. 1). The contrast agent in the balloon was evacuated, and then the catheter and puncture needle were pulled out. The puncture port was compressed for 10 min before a sterile dressing was applied. Patients were followed up postoperatively via telephone or

**Table 1.** Compression time

Time (min)	Number of patients (%)
3	39 (17.65)
4	143 (64.70)
5	39 (17.65)

Variables are presented as n (%) for nominal data; mean  $\pm$  SD or continuous data (average: 4 min); SD — standard deviation

**Table 2.** Barrow Neurological Institute (BNI) pain intensity scale score

Score	Definition
I	No pain, no medication
II	Occasional pain, not requiring medication
III	Some pain, adequately controlled with medication
IV	Some pain, not adequately controlled with medication
V	Severe pain/no pain relief

outpatient visits. This follow-up continued until the pain disappeared.

### Observation indices and effect evaluation

(1) The time taken for pain symptoms to disappear, to be relieved, or to recur was recorded. The Barrow Neurological Institute (BNI) pain score was used to create an efficacy score (Tab. 2). "Immediate disappearance of pain" after surgery referred to a pain score of Grade I after the patient awoke from anaesthesia. "Delayed disappearance" (DD) was defined as when the patient's BNI score gradually changed to Grade I from the first postoperative day. "Non-improvement of postoperative pain" meant that the pain did not change, or was even aggravated, in the period between recovery from anaesthesia and the follow-up visit.

(2) The number of cases of intraoperative and postoperative complications (inhibitory reactions of the trigeminal nerve, facial numbness, facial hypoesthesia, masticatory-muscle weakness, tinnitus, diplopia, keratitis, herpes labialis, headache, cerebral haemorrhage, and blindness) was recorded.

(3) Any factors possibly related to delayed disappearance (including age, symptom duration, sex, side, history of RFT, MVD, concomitant disease, pain involving V2, balloon volume, compression time [ $\leq 4$  min], and shape) were evaluated.

### Statistical analysis

Statistical Package for the Social Sciences (SPSS) 26.0 software was used for analysis, and the enumeration data was analysed using a  $\chi^2$  test. Multivariate logistic regression analysis was performed on the basis of single-factor analysis to screen for independent risk factors and  $p < 0.05$  was considered statistically significant.

## Results

### Demographic data and clinical characteristics

A total of 221 patients with TN underwent PBC, performed by the same neurosurgeon in the Neurosurgery Department of Qilu Hospital, from January 2018 to June 2021. Table 3 shows the demographic data and clinical characteristics of the patients.

### Overall effect and complications of PBC for TN

A total of 221 patients were analysed with an overall effective rate of 98.19%, including 59 patients with delayed disappearance (26.70%), 158 patients with non-delayed disappearance (71.49%), and four patients without relief (1.81%) (Tab. 4). There were many complications during and after PBC. The incidence of inhibitory reaction of the trigeminal nerve during surgery was 97.3%. The most common postoperative complications were: facial numbness, masticatory-muscle weakness, tinnitus, diplopia, and keratitis, which occurred at rates of 76.9%, 28.1%, 14.5%, 11.8%, and 10.4%, respectively (Tab. 5).

### Analysis of delayed disappearance time and influencing factors

The duration of postoperative pain in the delayed disappearance group ranged from two to 30 days (Tab. 6), and the average duration of delayed disappearance was c.9 days. In univariate logistic regression analysis, symptom duration ( $\geq 8$  years), MVD, RFT, hypertension, diabetes mellitus, herpes zoster, pain involving V2, and non-pear-shaped balloon were all statistically significant ( $p < 0.05$ ) as set out in Tab. 7. Multivariate logistic regression analysis showed that symptom duration ( $\geq 8$  years), RFT, diabetes mellitus, herpes zoster, pain involving V2, and non-pear-shaped balloon were independent factors for recurrence ( $p < 0.05$ ) as set out in Tab. 8.

## Discussion

PBC surgery, an effective treatment for TN, is mainly suitable for elderly patients with ineffective oral drugs, multi-branch pain, and poor surgical tolerance. Percutaneous balloon compression (PBC) is based on the principle that the balloon selectively compresses the damaged myelinated nerve fibres that conduct pain in Meckel's cave, preserving the motor branches of the trigeminal nerve [4], and closing the trigger switch of the pain conduction pathway of the trigeminal nerve to eliminate pain. The statistical rates of immediate disappearance after PBC surgery in China and abroad vary significantly, ranging from approximately 74% to 100% [5–8]. The incidence of delayed disappearance has been described as 9.31–19%, which was different from our findings in the present study. However, the average duration of delayed disappearance was approximately nine days, which was consistent with the research by Li Zaiyu et al. [9] in China [5, 9, 10].

**Table 3.** Demographic characteristics of 221 patients

<b>Sex</b>	
M	95
F	126
<b>Age (range; years)</b>	
< 40	2 (0.9%)
41–50	12 (5.4%)
51–60	35 (15.9%)
61–70	65 (29.4%)
71–80	80 (36.2%)
> 80	27 (12.2%)
<b>Symptom duration (range; years)</b>	
	8 (0.04–50)
<b>Distribution by side</b>	
Left	79 (35.7%)
Right	142 (64.3%)
<b>Trigeminal division</b>	
V <sub>1</sub>	4 (1.8%)
V <sub>2</sub>	76 (34.4%)
V <sub>3</sub>	12 (5.4%)
V <sub>1+2</sub>	57 (25.8%)
V <sub>1+3</sub>	2 (0.9%)
V <sub>2+3</sub>	40 (18.1%)
V <sub>1+2+3</sub>	30 (13.6%)
<b>Previous failed procedures</b>	
Microvascular decompression	74
Radiofrequency thermocoagulation	60
Percutaneous balloon compression	3
Glycerol gangliolysis	2
<b>Therapeutic effect of drugs</b>	
No response to medical treatment	110
Multiple side effects of drugs	75
<b>Concomitant disease</b>	
Hypertension	79
Diabetes mellitus	43
Coronary heart disease	25
Cerebral infarction	23
Herpes zoster	116
Chronic bronchitis	5
Sequelae of cerebral haemorrhage	2
Others (MS etc.)	9

Variables are presented as n (%) for nominal data, M — male; F — female; MS — multiple sclerosis

Percutaneous balloon compression (PBC) is prone to causing complications such as inhibition of the trigeminal nerve reaction during surgery, postoperative facial numbness,

**Table 4.** Barrow Neurological Institute (BNI) pain grades of 221 patients after percutaneous balloon compression (PBC)

BNI pain grade	Preoperatively of PBC, number of patients (%)	Immediately after PBC, number of patients (%)	During postoperative period, number of patients (%)
I	0	158 (71.5)	217 (98.2)
II	0	27 (12.2)	0
III	21 (9.5)	28 (12.7)	1 (0.4)
IV	65 (29.4)	8 (3.6)	3 (1.4)
V	135 (61.1)	0	0
<b>Total</b>	221 (100)	221 (100)	221 (100)

This table reflects changes in numbers and percentages of pain in different grades before and after PBC. Variables are presented as n (%) for nominal data

**Table 5.** Complications of 221 patients during/after percutaneous balloon compression (PBC) (n/%)

Complication	Number of patients (%)
Inhibitory reactions of trigeminal nerve	215 (97.3)
Cardiac arrest	15 (6.8)
Facial numbness	17 (76.9)
Severe facial hypoesthesia	26 (11.8)
Paresthesia	14 (6.3)
Masticatory-muscle weakness	62 (28.1)
Tinnitus	32 (14.5)
Diplopia	26 (11.8)
Keratitis	23 (10.4)
Labial herpes	18 (8.1)
Headache	2 (0.9)

Number and percentage of complications during or after PBC, variables are presented as n (%) for nominal data

paresthesia, and masticatory-muscle weakness. Because Meckel's cave, where the semilunar segment of the trigeminal nerve is located, is adjacent to the oculomotor, trochlear, abducens, and vestibular nerves and other structures, it is common for patients to experience diplopia, keratitis, tinnitus, and other complications due to excessive balloon filling. Most inhibitory reactions of the trigeminal nerve are transient, with an incidence as high as 97.3% in this study. The incidences of postoperative complications, such as facial numbness, paresthesia, and masticatory-muscle weakness, and their recovery times, which have been reported in many articles both in China and abroad, may be related to factors such as the size of Meckel's cave, the volume and shape of the balloon, and the compression time of the balloon [11, 12].

At present, there is a lack of research on factors influencing delayed disappearance after PBC surgery in China and abroad. Therefore, the focus of this study was to include many factors affecting delayed disappearance. Our study has confirmed for the first time in the world that symptom duration ( $\geq 8$  years), RFT, diabetes mellitus, herpes zoster, pain involving V2, and

non-pear-shaped balloon are factors affecting delayed disappearance after PBC surgery.

It is surprising that symptom duration ( $\geq 8$  years) was a significant factor in our results. We believe that the longer the course of TN, the more obvious the nerve compression. After mechanical damage is caused by PBC, it will take a period of time for the trigeminal nerve to adapt to the damage and for the neuroelectrophysiology to return to normal [5]. Yadav et al. [6] confirmed that the delay to cure in patients with facial spasm after surgery positively correlated with the length of the course of the disease, and even reported a formula to calculate that delay to cure. This would seem to demonstrate the delayed repair of cranial nerves after mechanical injury.

Radiofrequency thermocoagulation (RFT) utilises a difference in temperature tolerance between different nerve fibres of the trigeminal nerve to selectively destroy fine fibres that transmit pain while preserving the coarse fibres for transmitting touch, which have relatively high thermal resistance. Observation of nerve injury under the microscope after radiofrequency thermocoagulation is characterised by thermosetting degeneration, necrosis, fracture of the adventitia and nerve fibres, complete destruction of the myelin sheath and axonal structure of nerve fibres, and charring to varying degrees of connective tissues such as blood vessels [13, 14]. At present, there is a lack of basic research on nerve fibre repair after treatment of TN with RFT. We speculate that the 'scar' after the repair of the adventitia and nerve fibres delays the conduction of electrical signals.

Diabetic peripheral nerve disease occurs in approximately two-thirds of patients with diabetes, and neuropathic pain is induced by sensory hyperalgesia due to increased intracellular glycated end products, increased activities of inflammatory cytokines and aldose reductase, oxidative stress, and other factors [15, 16].

Urban et al. conducted research on the involvement of the trigeminal nerve and facial nerve in patients with diabetes. They found that 60% of cases had distal symmetrical sensory nerve multiple lesions; using electrophysiological examination, they also found that a high-glucose environment would affect the function of the trigeminal nerve [17, 18]. This indicates

**Table 6.** Timetable of delayed pain disappearance (days)

Number	Duration of DD	Number	Duration of DD	Number	Duration of DD
1	5	21	10	41	30
2	9	22	7	42	2
3	3	23	5	43	5
4	13	24	21	44	5
5	12	25	2	45	12
6	20	26	5	46	21
7	3	27	7	47	3
8	7	28	7	48	6
9	5	29	4	49	7
10	3	30	10	50	7
11	10	31	7	51	7
12	12	32	21	52	10
13	7	33	30	53	4
14	30	34	10	54	12
15	10	35	5	55	7
16	3	36	6	56	2
17	8	37	30	57	2
18	5	38	3	58	14
19	2	39	2	59	3
20	3	40	21	-	-

DD — delayed disappearance

**Table 7.** Univariate logistic regression analysis for delayed pain disappearance (DD)

Variable	DD (n/%)	No DD (n/%)	P
Age (≥ 65years)	40 (27.0)	108 (73.0)	0.938
Sex: M	27 (29.3)	65 (70.7)	0.542
Symptom duration (≥ 8 years)	33 (40.2)	49 (59.8)	<b>0.001</b>
Microvascular decompression	28 (37.8)	46 (62.2)	<b>0.006</b>
Radiofrequency thermocoagulation	39 (65.0)	21 (35.0)	<b>0.000</b>
<b>Concomitant disease</b>			
Hypertension	32 (40.5)	47 (59.5)	<b>0.001</b>
Diabetes mellitus	19 (44.2)	24 (55.8)	<b>0.000</b>
Cerebral infarction	10 (43.5)	13 (56.5)	0.064
Coronary heart disease	8 (22.9)	27 (77.1)	0.568
Herpes zoster	58 (50.0)	58 (50.0)	<b>0.000</b>
Left side	19 (24.1)	60 (75.9)	0.434
Involvement of V2	58 (29.1)	141 (70.9)	<b>0.002</b>
Balloon volume (≤ 0.4ml)	26 (28.0)	67 (72.0)	0.827
Compression time (≤ 4min)	26 (28.3)	66 (71.7)	0.501
'Non-pear-shaped' balloon	36 (72.0)	14 (28.0)	<b>0.000</b>

Statistically significant values are given in bold, and p < 0.05 was considered a statistically significant difference

**Table 8.** Multivariate logistic regression analysis for delayed pain disappearance

Variable	OR	95% CI	P
Symptom duration (≥ 8 years)	5.092	1.527-16.975	<b>0.008</b>
Microvascular decompression	0.220	0.051-1.760	<b>0.179</b>
Radiofrequency thermocoagulation	32.500	3.239-326.064	<b>0.003</b>
Hypertension	3.244	0.901-11.684	<b>0.072</b>
Diabetes mellitus	4.012	1.758-13.645	<b>0.048</b>
Herpes zoster	125.302	11.716-1,340.075	<b>0.000</b>
Involvement of V2	29.069	2.112-400.058	<b>0.012</b>
'Non-pear-shaped' balloon	5.174	1.493-17.931	<b>0.010</b>

Statistically significant values are given in bold, and p < 0.05 was considered a statistically significant difference; OR — odds ratio; CI — confidence interval; P — probability; V2 — maxillary nerve (the 2nd branch of trigeminal nerve)

that continuous cytokine stimulation in patients with diabetes is likely to be the influencing factor for the occurrence, aggravation, delayed disappearance, and recurrence of TN. At the same time, another result of our study (which has been received by 'World Neurosurgery') confirmed that there was a correlation between postoperative recurrence of TN and

delayed disappearance, and that diabetes was a non-independent factor for recurrence.

Herpes zoster is neurotropic and can hide in the neurons of the posterior roots or ganglia of the nerves for years, or even decades. The reasons for delayed disappearance caused by the reactivation of herpes virus after PBC may be related to the following factors [19]: 1) the trigeminal nerve was damaged during surgery, and the irritation led to virus propagation; 2) the resistance and immunity of the patient decreased due to surgery, and the herpes virus in the semilunar ganglion of the trigeminal nerve was induced and activated; 3) the herpes zoster membrane ruptured to form an erosion or secondary suppurative infection, or even cause herpes zoster meningitis; and 4) surgical stimulation caused dissolution of chromatin in the trigeminal nerve ganglion cells, exudation of serous fluid under the stratum corneum, and generation of facial blisters. After antiviral treatment the pain symptoms of the patient resolve, along with the disappearance of herpes.

The expanded sacculle directly and mechanically damaged the myelinated nerve fibres and nerves, and blocked the blood supply to the semilunar ganglion of the trigeminal nerve by pulling and pressing Meckel's cave, thus promoting fibre demyelination and pain conduction inhibition. There are more independent branches and anastomotic branches in the blood supply system of the maxillary branch (V2) of the trigeminal nerve than there are in V1 and V3 [20]. Therefore, in theory, patients with TN involving V2 are more likely to have delayed disappearance during PBC treatment.

A balloon that is pear-shaped is considered to be the key to the effectiveness and reduction of complications after PBC surgery [21, 22]. The shape of the balloon is closely related to its location and insertion process. Poor location of a balloon can lead to a non-pear-shaped balloon morphology during surgery and influence the postoperative effect [23]. The compression effect of the non-pear-shaped balloon on the semilunar segment of the trigeminal nerve was worse than that of the pear-shaped balloon, and more recovery time was needed. This might be because of the insufficient effective contact area of balloon compression or the delay of vascular injury caused by mechanical traction.

### Future directions

We have confirmed, for the first time, that symptom duration ( $\geq 8$  years), history of RFT, diabetes mellitus, herpes zoster, pain involving V2, and a non-pear-shaped balloon are independent influencing factors. This allows us to better judge the recovery time of patients after PBC surgery to verify the effect of the surgery and give patients a reasonable explanation of their condition.

### Limitations

The sample size of this study was small, and other possible contributory factors (e.g. intra-balloon pressure, Meckel's cave size) were not analysed. There is a lack of basic research

on delayed disappearance after PBC, and there was a lack of evidence to support hypotheses in our discussion.

## Conclusion

Influenced by many factors, delayed disappearance is a common phenomenon after surgery. Because of the existence of delayed disappearance, we suggest waiting at least one month after surgery before judging whether PBC is invalid.

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