Original Article

Efficacy and safety of microvascular decompression versus percutaneous balloon compression in the treatment of trigeminal neuralgia: a systematic review and meta-analysis

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Background: Trigeminal neuralgia (TN) is a type of transient and paroxysmal recurrent severe pain confined to the trigeminal nerve region. This study systematically evaluated the efficacy and safety of microvascular decompression (MVD) and percutaneous balloon compression (PBC) in the treatment of TN.

Methods: PubMed, Embase, The Cochrane Library, China National Knowledge Infrastructure, Wanfang, and Weipu databases were searched for articles published on the use of MVD and PBC in the treatment of TN from the dates of inception of the databases to October 2019. Articles on MVD and PBC in the treatment of TN were selected, and a meta-analysis was performed using RevMan 5.2 software.

Results: Eighteen studies (comprising 1,932 patients) were included in the study. MVD and PBC had similar overall effective rates in treating TN [odds ratio (OR) =0.79, 95% confidence interval (CI): 0.55–1.13, P=0.19]. Patients treated with PBC had a higher recurrence rate of TN than those treated MVD (OR =3.50, 95% CI: 2.25–5.44; P<0.00001), and patients treated with PBC experienced more adverse reactions than those treated with MVD (OR =17.79, 95% CI: 10.17–31.11; P<0.00001).

Discussion: The overall effective rates of PBC and MVD in the treatment of TN ewer similar, but MVD was associated with better recurrence and a lower rate of adverse reactions. Thus, both MVD and PBC can be used to effectively treat TN patients.

Keywords: Trigeminal neuralgia; microvascular decompression; percutaneous balloon compression; overall effective rate; meta-analysis

Submitted Nov 30, 2021. Accepted for publication Apr 11, 2022.
doi: 10.21037/apm-21-3901
View this article at: https://dx.doi.org/10.21037/apm-21-3901

Introduction

Trigeminal neuralgia (TN) is a type of transient and recurrent paroxysmal severe pain confined to the trigeminal nerve region (1). Typical TN and atypical TN are the main types of TN. The onset of TN pain is spontaneous or triggered by talking, eating, or other non-noxious stimuli (2). TN is considered a rare disease, and reports on its incidence range from 4.3–27 new cases per 100,000 people per year (3). Studies on its prevalence indicate that the incidence of TN ranges from 0.03–0.3% in the general population (2,4). The initial treatment for TN is generally oral drugs (e.g., carbamazepine and obensiequine). However, such drugs may cause dizziness, nausea and lethargy (2,5). Moreover, after long-term use, the analgesic effect of these drugs of decrease significantly, and 50% of patients eventually need surgical management to relieve the pain (6).

Operative interventions for TN include MVD, PBC, percutaneous radiofrequency rhizotomy (PRR), percutaneous glycerol rhizotomy (PGR), and stereotactic radiosurgery (SRS)(7). Dandy's hypothesis that vascular compression is the cause of TN is currently accepted. Based on this hypothesis and due to its excellent ability to control pain, microvascular decompression (MVD) has long been considered a common and reasonable method for the treatment of primary TN (8). Kaye *et al.* (8) reviewed the risks and benefits of various surgeries and reported that the rate of initial pain control ranges from 80.3–96% for MVD surgery. However, as vascular compression does not occur in all TN patients, radiofrequency thermocoagulation and percutaneous balloon compression (PBC) are also used to treat TN. Among the surgical options, MVD has been proven to be the most successful and durable surgical approach for treating TN, but the utility of MVD is restricted by the risk of craniotomy and complications, especially in elderly patients (2,9). It is essential to select feasible, fast, effective and safe surgical methods to improve the quality of life of elderly patients. Under the guidance of X-ray, PBC expands the balloon to compress the semilunar ganglion, so that the abnormal neurons related to TN are destroyed (10,11). According to one report, pain was relieved in 90% of patients following these PBC procedures, but up to 50% of patients were estimated to experience pain recurrence after 5 years (7,12). Traditionally, PBC has been reserved for older patients or patients who might not be able to endure the craniotomy necessary for MVD. Compared to MVD, PBC is simple, minimally invasive, and safe.

Results on the curative effect of MVD versus PBC for TN are inconsistent. A study has shown that patients treated with MVD had a better curative effect than those treated with PBC (13). While other studies have shown that the curative efficiency of MVD is equal to that of PMC (14,15). A recent meta-analysis revealed that MCD for elderly patients with TN could be undergone safely (16). Additionally, another meta-analysis suggested that for patients without specific surgical contraindications, MVD is a better option as the surgical treatment for TN (17). To date, little research has been conducted to compare MVD and PMC, and determine the best procedure; thus, well-designed studies are urgently needed. Moreover, previous studies included small sample sizes and had low reliability.

In this study, clinical studies related to MVD and PBC in TN were collected by searching the Chinese and English databases, and the efficacy and safety of MVD and PBC were compared using evidence-based methods to determine the best choice for clinical workers and patients. We present the following article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3901/rc).

Methods

Search strategy

The study was conducted using Preferred Reporting Items for Systematic Reviews and MetaAnalyses statements (18). To find all the related articles, 2 investigators independently searched the PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Embase (http://www.embase.com), The Cochrane library (http://www.cochranelibrary.com), China National Knowledge Infrastructure(https://www.cnki.net), Wanfang (https://www.wanfangdata.com.cn), and Weipu (http://qikan.cqvip.com) databases for articles published from the dates of inception of the databases to October 9, 2021 using the following keywords: "trigeminal neuralgia", "micro-vascularde compression", "percutaneous micro balloon compression", "PMC", "PBC", "microvascular decompression" and "MVD". The reference lists of the retrieved articles were manually searched to identify additional eligible studies.

Inclusion and exclusion criteria

To be included in the meta-analysis, the studies had to meet the following criteria: (I) be a published clinical study examining the use of MVD and PMC in the treatment of TN; (II) include patients with primary TN or secondary recurrence after surgical treatment; (III) include patients who had received the MVD or PBC intervention measures; and (IV) include outcomes on the postoperative overall effective rate, recurrence rate, and rate of adverse reactions. Studies were excluded from the meta-analysis if they met any of the following exclusion criteria: (I) were not a clinical study (e.g., were reviews, case reports, or conference reports); (II) included patients with secondary TN; (III) included patients with organic lesions in the brain tissue; and (IV) examined non-human patients.

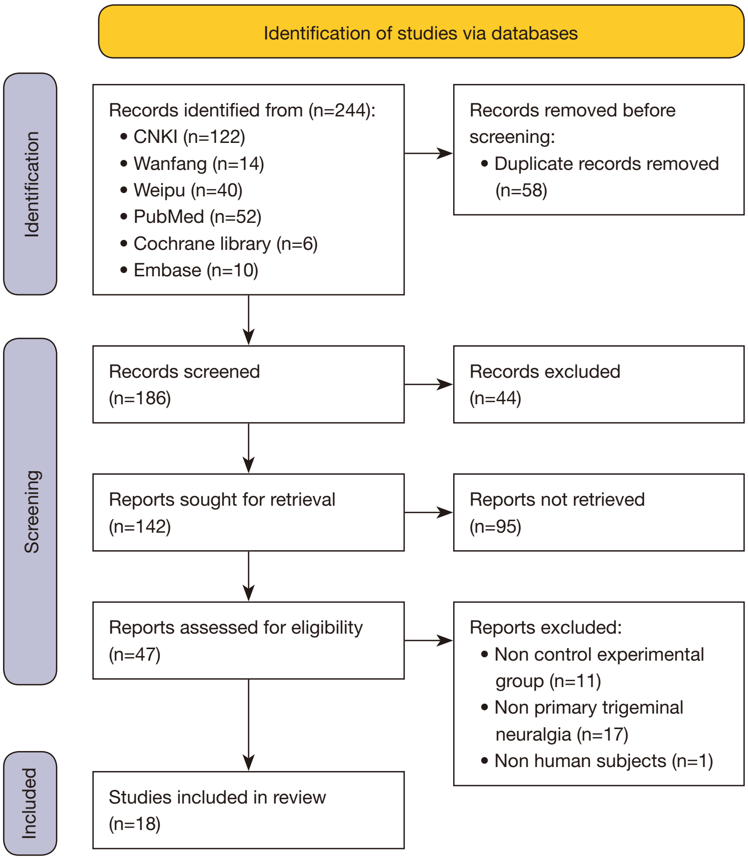

Figure 1 Flow chart of literature search and study selection process, CNKI, China National Knowledge Infrastructure.

Data extraction and risk of bias assessment

According to a pre-designed standardized form, 2 researchers independently extracted the relevant data from the eligible studies, including data on the first author, publication year, mean age of participants, number of study patients, and TN disease type. The methodological quality of the articles was independently evaluated by 2 researchers. Any disagreement were resolved through discussion between the 2 reviewers or by consulting a third party. Based on the Cochrane risk of bias tool for assessing the risk of bias (19), the following 7 items were used to evaluate the studies: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective outcome reporting, and other biases. The articles were classified as having a "low risk", "high risk", or "unclear risk".

Statistical analysis

The meta-analysis was conducted using RevMan5.2 software. The measures of effect for dichotomous data are expressed as odds ratios (ORs) with 95% confidence intervals (CIs). If the $I^2>50\%$ or the P value <0.05, a random-effects model was used; otherwise, a fixed-effects model was used (20). A P value <0.05 was considered statistically significant.

Results

Literature review and study characteristics

The search in this meta-analysis retrieved 244 articles from 2 types of language databases (Chinese databases =176, and English databases =68). After duplication check and initial exclusion, only 142 potentially suitable articles were further evaluated. Ultimately, 18 studies (13-15,21-35) met the selection criteria, and were included in the meta-analysis. A flow diagram of the meta-analysis is presented in *Figure 1*.

The basic information of the studies included in this meta-analysis is summarized in *Table 1*. The included studies were published in 2 different countries from 2013

Table 1 Basic characteristics of the included studies

First author, year	Type	PBC		MVD		Age		Outcome indicators
		Male	Female	Male	Female	PBC (mean ± SD)	MVD (mean ± SD)	
Ni *et al.*, 2020 (24)	PTN	12	18	13	17	71.13±11.42	71.13±11.42	①②③
Chen *et al.*, 2018 (21)	PTN	15	27	23	45	63.4[a]	59.3[a]	①②③
Bao, 2013 (29)	PTN	15	12	7	11	59.7±7.9	51.6±11	①②③
Dong, 2019 (30)	PTN	13	16	18	23	47.32±8.08	48.12±7.92	①③
Du, 2020 (13)	PTN	100	132	98	134	60.23±5.94	59.78±6.61	①③
Fu *et al.*, 2020 (35)	PTN	14	24	18	24	79.1±7.2	78.9±7.8	①②③
Hu *et al.*, 2018 (32)	PTN	35	32	13	12	52.5±10.6	50.7±11.1	①②③
Li *et al.*, 2021(26)	PTN	27	31	31	23	68.23±6.24	67.35±5.36	①③
Li *et al.*, 2016 (22)	PTN	22	40	20	42	66.5±2.9	66.8±2.7	①②③
Shang *et al.*, 2020 (34)	PTN	17	19	17	23	53.5±4.8	50.5±6.0	①②③
Wang *et al.*, 2014 (28)	PTN	–	–	–	–	–	–	①②③
Wang *et al.*, 2021 (27)	PTN	10	28	11	27	55.47±13.02	54.68±10.44	①②③
Xing *et al.*, 2020 (33)	PTN	23	23	20	26	59.82±4.75	58.51±3.13	①②③
Xu, 2021 (25)	PTN	13	19	12	20	53.94±21.75	54.32±21.17	①
Yao, 2015 (31)	PTN	73	51	12	17	58[a]	52[a]	①②③
Ye *et al.*, 2019 (23)	PTN	19	31	20	30	53.23±10.56	53.68±10.19	②③
Zhang *et al.*, 2020 (15)	PTN	27	18	25	20	54.5±6.1	53.6±7.2	①
Zhu *et al.*, 2021 (14)	PTN	16	17	14	17	58.14±6.72	57.09±6.53	①③

[a], The study did not report the standard deviation of patient age; ① total effective rate; ② recurrence rate; ③ incidence of adverse reactions; –, this value is not reported in the article. MVD, microvascular decompression; PBC, percutaneous balloon compression; PTN, primary trigeminal neuralgia.

to 2021, and most of them (n=16) were published in China. All patients suffered from primary TN. The sample size of the included studies were 12–100 male and 12–132 female patients after PBC treatment, and 7–98 male and 11–134 female patients after MVD treatment. The age of patients ranged from 47.32±8.08 to 71.13±11.42 years in the PBC group, and 48.12±7.92 to 78.9±7.8 years in the MVD group. The TN outcomes for all patients included the overall response rate, recurrence rate, and incidence of adverse reactions (see *Table 1*).

Meta-analysis of the outcomes

Overall effective rates after treatment with PBC versus MVD

Among the 18 studies, 17 (13-15,21,22,24-35) comprising 1,832 cases (863 MVD cases and 969 PBC cases) examined the overall effective rate of the treatments. As the heterogeneity test results were statistically insignificant (I^2=22%, P=0.20), the fixed-effects model was used to pool the data for the meta-analysis. The OR for the overall effective rate for PBC versus MVD treatment was 0.79 (95% CI: 0.55–1.13, P=0.19), and was not statistically significant. Thus, the overall effective rate of MVD treatment was similar to that of PBC treatment (see *Figure 2*).

Recurrence rates after treatment with PBC versus MVD

Twelve studies (14,21-24,27-29,31-33,35) comprising 1,068 cases (590 PBC cases, and 478 MVD cases) reported the recurrence rate of TN after treatment. The heterogeneity results were I^2=0% (P=0.61); thus, the OR for PBC versus MVD treatment was 3.50 (95% CI: 2.25–5.44; P<0.00001) using the fixed-effects model. The results

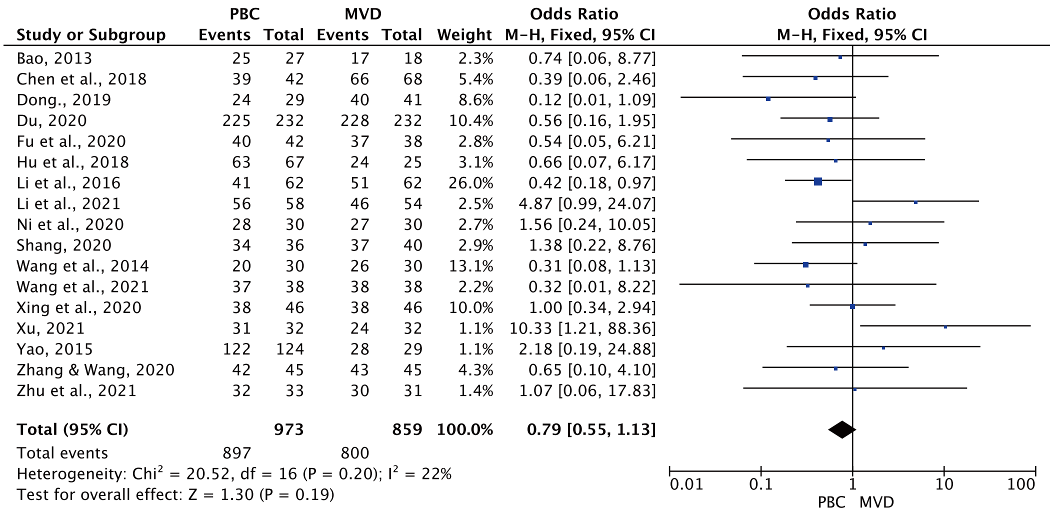

Figure 2 Forest plot of the pooled meta-analysis for the overall effective rates after treatment with PBC versus MVD. Each study was labeled with the author name and publication year. Larger squares indicate a larger weight of the study in the pooled estimate. The solid horizontal lines display the 95% CI of the point estimate. The dashed vertical line represents the pooled estimate. CI, confidence interval; MVD, microvascular decompression; PBC, percutaneous balloon compression.

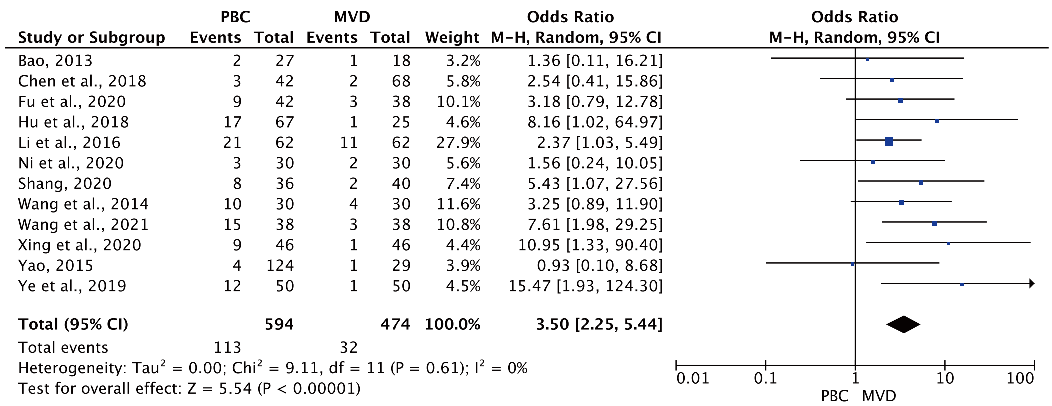

Figure 3 Forest plot of the pooled meta-analysis for the recurrence rates after treatment with PBC versus MVD. Each study was labeled with the author name and publication year. Larger squares indicate a larger weight of the study in the pooled estimate. The solid horizontal lines display the 95% CI of the point estimate. The dashed vertical line represents the pooled estimate. CI, confidence interval; MVD, microvascular decompression; PBC, percutaneous balloon compression.

showed that the MVD treatment level was statistically lower than the PMC treatment level (see *Figure 3*).

Adverse reaction rates after treatment with PBC versus MVD

Sixteen studies (13,21-35) compared the adverse reaction rates between MVD and PBC cases. The heterogeneity results were I^2=64% (P=0.0003); thus, the rate of adverse reaction for PBC versus MVD treatment was 17.79 (95% CI: 10.17–31.11; P<0.00001) using the random-effects model. The results showed that the rate of adverse reaction was significantly lower in MVD cases than PMC cases (see *Figure 4*).

Quality evaluation of the included studies

As *Figure 5* shows, the random-number table method was mentioned in 4 studies (13,22,23,27), and the free-

Study or Subgroup	PBC Events	PBC Total	MVD Events	MVD Total	Weight	Odds Ratio M-H, Random, 95% CI
Bao, 2013	27	27	4	18	2.6%	177.22 [8.91, 3524.83]
Chen et al., 2018	32	42	10	68	8.0%	18.56 [6.99, 49.31]
Dong., 2019	6	29	2	41	5.4%	5.09 [0.95, 27.33]
Du, 2020	11	232	3	232	6.7%	3.80 [1.05, 13.80]
Fu et al., 2020	34	42	5	38	7.0%	28.05 [8.32, 94.60]
Hu et al., 2018	62	67	8	25	6.9%	26.35 [7.63, 91.01]
Li et al., 2016	57	62	11	62	7.4%	52.85 [17.20, 162.41]
Li et al., 2021	48	58	11	54	8.1%	18.76 [7.26, 48.52]
Ni et al., 2020	24	30	0	30	2.7%	229.92 [12.34, 4285.19]
Shang, 2020	19	36	5	40	7.3%	7.82 [2.49, 24.53]
Wang et al., 2014	20	30	3	30	6.3%	18.00 [4.38, 74.01]
Wang et al., 2021	19	38	6	38	7.6%	5.33 [1.81, 15.69]
Xing et al., 2020	27	46	1	46	4.3%	63.95 [8.10, 505.11]
Yao, 2015	119	124	4	29	6.4%	148.75 [37.28, 593.45]
Ye et al., 2019	13	50	2	50	5.8%	8.43 [1.79, 39.70]
Zhu et al., 2021	17	33	6	31	7.4%	4.43 [1.44, 13.60]
Total (95% CI)		**946**		**832**	**100.0%**	**17.79 [10.17, 31.11]**
Total events	535		81			

Heterogeneity: $Tau^2 = 0.77$; $Chi^2 = 41.15$, df = 15 (P = 0.0003); $I^2 = 64\%$
Test for overall effect: Z = 10.09 (P < 0.00001)

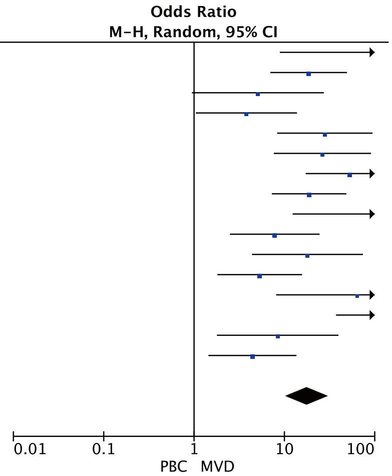

Figure 4 Forest plot of the pooled meta-analysis for adverse reaction rates after treatment with PBC versus MVD. Each study was labeled with the author name and publication year. Larger squares indicate a larger weight of the study in the pooled estimate. The solid horizontal lines display the 95% CI of the point estimate. The dashed vertical line represents the pooled estimate. CI, confidence interval; MVD, microvascular decompression; PBC, percutaneous balloon compression.

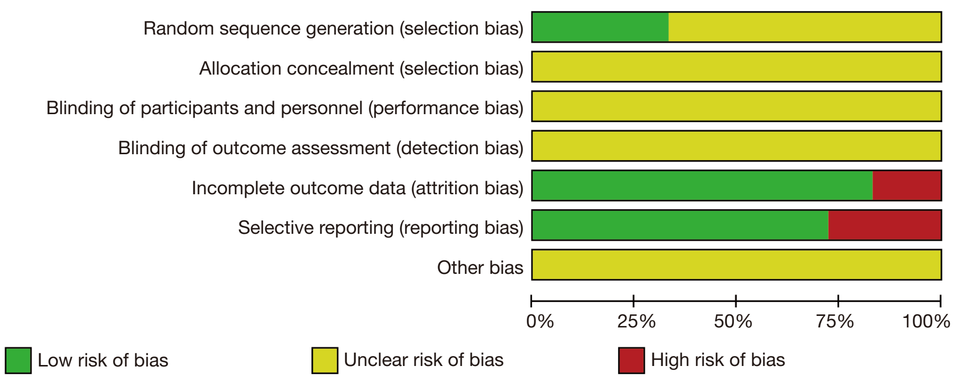

Figure 5 Bar graph of bias risk.

combination method was mentioned in 2 studies (11,15), which indicated a low risk of bias; the remaining studies failed to mention any method. None of the studies mentioned distribution concealment or implementation of blindness. The data of 4 studies (13,15,23,25) were insufficient, but not enough to affect the effect value. As for the selective reporting result, 2 studies (15,25) did not report on the number of adverse reactions, and 5 studies (13,15,23,25,30) did not report on the number of recurrences, and thus could not be included in the meta-analysis. No other source of bias was found in any of the studies.

Discussion

A primary risk factor for TN is age, and the incidence of TN gradually increases with age (1). TN is most common in middle-aged and elderly people, and the average age of onset is between 45 and 65 years (36). With a male to female ratio of 3:2, the disease is more common in women than men (6). The main cause for TN is the compression of the 5th cranial nerve, which contains 3 major branches that control the motor functions of the face (37). However, the pathogenesis of TN is not completely clear (38,39). Due to the severe pain, TN often has a catastrophic effect on patients, and seriously affects their quality of life (40). In this meta-analysis, we compared the efficacies of MVD and PBC in the treatment of TN. The main finding of the present study is that there was no significant difference in the total response rate between the PBC and MVD groups (OR =0.79, 95% CI: 0.55–1.13, P=0.19); however, the recurrence rate of the PBC group was significantly higher than that of the MVD group (OR =3.89, 95% CI: 2.53–5.98; P<0.00001), and the incidence of adverse reactions in the PBC group was significantly higher than that of the MVD group (OR =17.79, 95% CI: 10.17–31.11; P<0.00001).

In relation to the overall effective rates, Zhang *et al.* found that there was no significant difference between MVD (93.3%) and PBC groups (95.6%) (P>0.05) (15). Similarly, Zhu *et al.* reported overall effective rates of 96.97% and 96.77% for PBC and MVD, respectively, and found no statistically significant difference between the 2 surgical methods (P>0.05) (14). Thus, the 2 surgical methods have similar treatment efficiency. Both MVD and PBC surgery obviously relieve the pain symptoms of TN patients. The accurate localization and correct treatment of the responsible vessels are key to the success of MVD, which is an effective method with a good curative effect. MVD and PBC use different principles to treat TN, but the concepts and technologies behind both MVD and PBC have been greatly improved after years of development. Notably, Xu *et al.* found that PBS had significantly better effective rates than MVD in the treatment of TN (P<0.05) (25), while the effective rates of MVD was better than PBS (MVD 97.56%: PBS 82.75%; P<0.05). However, Xu *et al.*'s results may be ascribed to the small sample size of the study, different follow-up time, and different patient selection criteria.

Recurrence and complications following treatments for TN, specifically those following PBC, remain problems. A previous study indicated that the recurrence rate of TN following MVD was as high as 10.00%, and often occurs 2 years after operation (41). Similarly, another study reported that the recurrence rate of TN following PBC was 10.70% (42). Patients in the PBC group were more likely to experience recurrent TN than those in the MVD group (21). These results are consisted with the finding of the present study. The data also suggested that patients treated with MVD had a lower recurrence rate for TN than those treated with PBC. MVD requires a craniotomy, but provides direct vision of the vascular loops that lead to compression and thus is better able to treat lesions. Conversely, while PBC can be used to physically damage the trigeminal semilunar ganglion in the patient's focal area, it cannot be used to thoroughly treat the cause (43,44). We also confirmed that the incidence of numbness and complications in the MVD group was significantly lower than that in the PBC group.

In a previous study, 3 patients (10.0%) and 2 patients (6.67%) had recurrent TN in the PBC and MVD groups, respectively, during the 6-month follow-up period, and facial numbness was the most common postoperative complication. In another study, 24 of 30 (80%) patients experienced facial numbness after PBC (24). In Li *et al.*'s study, complications in the PMC group (82.67%) were higher than those in the MVD group (20.37%) (26). Complications of MVD include facial palsy or weakness, loss of hearing, cerebellum injury, infection, death, and spinal fluid leakage (45). Postoperative facial numbness is related to excessive intraoperative traction, so trigeminal nerve should be handled gently to avoid excessive traction during surgery. PBC is a kind of neuro-destructive surgery, which may lead to sequential histological changes of nerve ganglia, and postoperative complications, such as facial numbness and masseter weakness (46). Most patients (90%) experienced postoperative facial numbness when the balloon was pressed for 1–1.5 minutes (47) A previous study found that facial numbness was the most common complication after PBC (50.0%) (27). This may be due to the surgical approach (i.e., balloon compression causes a compression injury to the nerve tissue, and can cause the same partial or total loss of trigeminal nerve function as radiofrequency ablation) (48). These results were consistent with the findings of our study, and suggested that MVD is superior to PBC in terms of adverse reactions, such as facial numbness and masseter weakness, in the treatment of TN patients. Operative interventions for TN include MVD, PBC, percutaneous radiofrequency rhizotomy (PRR), percutaneous glycerol rhizotomy (PGR), and stereotactic radiosurgery (SRS) (7). MVD is generally considered to have the best long-term efficacy, highest first postoperative remission rate with lowest incidence of sensory loss complication. and the lowest recurrence rate (7). In addition, PBC operation is completely fast. Due to the operation under general anesthesia, so the patient pain is small and high safety, especially suitable for the elderly patients who could not tolerate craniotomy (49,50).

The effective rate of long-term postoperative pain relief was 94.37% in MVD group and 91.67% in PMC group, with no statistical significance between the two groups (P>0.05), suggesting that both surgical methods could relieve TN for a long time and stably. The pain relief rate was 90.00% and 86.67% after PBC and MVD surgery, respectively (P>0.05). The levels of IL-1b, TNF-a, and IL-6 were significantly decreased at post-operative 3 days and 5 days compared with pre-operation in the 2 groups (P<0.05) (24).

With regard to treatment, carbamazepine is the first choice for TN drug. And baclofen, clonazepam and ocazepam could be used. A study by Stomal-Słowińska *et al.* (51) suggests that oxazepine has a low incidence of adverse reactions and a better therapeutic effect. In addition, studies have shown that combination medication is safer and more reasonable than single medication(52), which can not only improve the degree of pain relief, but also reduce the side effects of medication. However, at present, many patients are still treated with single drug(53). Therefore, it is suggested to use combined drugs as far as possible in clinical practice. With the development and progress of endoscopy technology, endoscopic MVD will be widely used in the future due to its smaller trauma, shorter operation time and lower recurrence rate. The etiology and pathogenesis of PTN are still unclear, so it is necessary to develop new drugs to treat TN in the future.

This study had several advantages. First, the statistical heterogeneity of the included studies was small. Second, the proposed methodologies in the literature were high quality. Third, there was no significant publication bias in any of the outcome indicators, and the combined results had high credibility. However, this study also had a number of limitations. First, most of the included studies were published by Chinese scholars, and the lack of high-quality clinical studies in foreign countries may lead to selection bias. Second, the included studies were retrospective or non-randomized controlled trials with a low level of evidence. Third, the corresponding follow-up time was inconsistent and the failure to perform subgroup analyses across different age groups may have resulted in biased reporting.

Conclusions

Our meta-analysis demonstrated that MVD and PBC are both viable alternatives in the treatment of TN. Notably, MVD resulted in lower recurrence rate and a lower rate of adverse reactions in the treatment of TN than PBC. The purpose of generating high-quality evidence is to provide guidance on the application of MVD or PBC in clinical practice. Thus, further randomized controlled trials with large samples sizes, scientific designs, and strict implementations need to be conducted to study the efficacy and safety of MVD or PBC in the treatment of TN.

Acknowledgments

Funding: The study was supported by Hainan Province Medical and Health Research (Project No. 18A200176), and Hainan Province Medical and Health Research (Project No. 19A200131).

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3901/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3901/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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(English Language Editor: L. Huleatt)

Cite this article as: Wu J, Xiao Y, Chen B, Zhang R, Dai M, Zhang Y. Efficacy and safety of microvascular decompression versus percutaneous balloon compression in the treatment of trigeminal neuralgia: a systematic review and meta-analysis. Ann Palliat Med 2022;11(4):1391-1400. doi: 10.21037/apm-21-3901

