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ORIGINAL RESEARCH

Microvascular decompression and radiofrequency for the treatment of trigeminal neuralgia: a meta-analysis

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Purpose: Surgical treatments are used for trigeminal neuralgia (TN) when drug treatment fails. Surgical options can be divided into two categories: ablation (destructive) or non-ablation. Microvascular decompression (MVD) is primarily a non-ablation option, while radiofrequency thermocoagulation/rhizotomy (RF) is an ablation option. The aim of this study was to compare outcomes of MVD versus RF in the treatment of TN.

Materials and methods: This article evaluates the clinical results and economic effectiveness of trigeminal nerve RF and MVD for the treatment of TN. This review was conducted according to the methodological standards described in the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement. The PubMed, Embase and Cochrane libraries were searched in January 2018. We have registered our review at the Review Registry.

Results: Nine studies were included in this review. The sample size was 2163 participants. The results showed that compared with RF, MVD had a lower risk of requiring a secondary procedure. The MVD group also had a lower risk of facial numbness. There was no significant difference in postoperative medication use between the two groups. Compared to RF, MVD was more likely to increase the risk of hypacusis and hypesthesia and to decrease the risk of facial pain and dysesthesia. The total cost of MVD, including the operation, hospital stay and additional procedures, was much higher than that of RF.

Conclusion: MVD had a lower risk of requiring a secondary procedure and facial numbness after surgery. RF could be considered in patients who are unfit for MVD or refused invasive treatment.

Keywords: meta-analysis, facial pain, surgical treatment

Plain language summary

Microvascular decompression (MVD) and radiofrequency thermocoagulation/rhizotomy (RF) are the two main surgical treatments for trigeminal neuralgia. In this article, we compared the efficacy and safety of these two methods. We found that MVD was associated with better efficacy, but greater postoperative complications and total costs compared to RF.

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Introduction

Trigeminal neuralgia (TN) is defined as "sudden, usually unilateral, severe, brief, stabbing recurrent pains in the distribution of one or more branches of the fifth cranial nerve" by the International Association for the Study of Pain (IASP).[1] Although drug therapy is the first-line treatment for TN, surgical intervention is an important

alternative treatment in patients with refractory TN or intolerable side effects. Surgical intervention for the treatment of TN falls into two categories: non-ablation and ablation.[2]

The classic non-ablation technique for the treatment of TN is microvascular decompression (MVD), which is based on the neurovascular compression hypothesis first described by Dandy. MVD was first performed by Gardner in 1959 and then popularized by Janetta, and it has been considered the gold standard for TN treatment for nearly 60 years.[3] MVD requires the separation of the trigeminal nerve from the adjacent vessels through a craniotomy under general anesthesia. Although MVD is considered a classic procedure for the treatment of TN, complications such as postoperative facial numbness, intracranial hemorrhage, cerebrospinal fluid leakage, and deafness may occur due to possible trauma resulting from the craniotomy. And some long term observational studies noticed that the recurrence rate increases significantly 5 years after MVD.[4] Ablation refers to palliative destructive procedures involving controlled damage to the trigeminal gasserian ganglion or the peripheral branch of the trigeminal nerve with the aim of relieving pain. They can be performed for TN arising from any cause, including non-vascular decompression.[5] Several methods of ablation have been developed over the past few decades. Radiofrequency thermocoagulation (RF) for TN involves puncturing the semilunar ganglion or trigeminal nerve branch with a CT- or X-ray-guided a RF ablation needle. Sensory and motor stimulation are used to replicate the patient's pain and locate and destroy the responsible nerve. Recurrence is possible after RF ablation; some patients need to continue medication treatment, while others may require reoperation, and postoperative facial numbness is a notable problem. Glycerol and balloon compression can also be used for trigeminal gasserian ganglion ablation, however, they have poorer selectivity compared with RF.[2] Gamma Knife is another ablation strategy aimed to selectively destroy the afferent fibers of trigeminal nerve, although it takes nearly a month for the completely work. In this meta-analysis, we chose the two widely used procedures, MVD and RF, to compare the efficacy and economic effectiveness of them for the treatment of TN.

Materials and methods

This review was conducted according to the methodological standards described in the Cochrane Handbook for Systematic Reviews of Interventions[6] and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.[7] This work has been reported in line with AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines. We have registered our research at https://www.researchregistry.com.

The study name is Microvascular Decompression and Radiofrequency for the Treatment of Trigeminal Neuralgia: A Meta-Analysis.

Literature search

Studies were searched in three electronic databases (PubMed, Embase and Cochrane Library) in January 2018. Keywords were determined through expert opinion, Medical Subject Headings and Excerpta Medica Trees, and reviews of the primary search results. The search strategies were developed by information specialists and are presented in Supplement 1.

Selection criteria

We defined the inclusion criteria as follows: (1) Population (P): all patients who were diagnosed with TN; (2) Intervention (I) and comparisons (C): MVD versus RF thermocoagulation or rhizotomy; (3) Outcomes (O): the need for additional procedures after surgery, facial numbness, postoperative use of medication, incidence of any adverse events and specific adverse events, and total costs of intervention. (4) Study design (S): controlled studies.

Data extraction and risk of bias assessment

The data extraction form was developed and adapted by a pilot data extraction. The following items were extracted: first author, year of publication, total number of participants, length of follow up, patient characteristics (treated/newly diagnosed, age, gender distribution, pain score at baseline, side affected by TN), comparisons, numeric data for pre-defined outcomes and information relevant to risk of bias. Two authors extracted the data independently. Disagreements were resolved by consensus between the two authors or by consulting a third author when necessary.

The risk of bias of the included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale Cohort Studies.[8] Three domains of risk of bias were assessed: selection bias, comparability of exposure and non-exposure groups and detection/attrition bias relevant to outcomes.

Statistical analysis

RevMan 5.3 was used for statistical analysis. For dichotomous data, we used relative risk (RR) and 95% confidence intervals (CI) as the measurements of the pooled effect; for continuous data, the mean difference (MD) and 95% CI were used. The statistical heterogeneity of the studies' measured effects was evaluated using *P*-values derived from the chi square test and I^2 statistic. We considered heterogeneity statistically significant when the *P*-value was <0.1 and I^2 was ≥50%. We used a random effects model for all meta-analyses. When significant heterogeneity was present, a sensitivity analysis was carried out to explore the sources of heterogeneity. A subgroup analysis was conducted if the source was identified. "Leave-one-out" sensitivity analyses were conducted to detect the influence of a single study on the overall estimate.

Results

Study selection and study characteristics

The initial search identified 426 references; after duplicates were removed, 374 references were screened by viewing their titles and abstracts. After the first-level screening, 34 full texts were inspected for eligibility. Finally, 25 studies were excluded, and the 9 remaining studies[9–17] were included in this review. (Figure 1)

For the 9 included studies,[9–17] the sample sizes ranged from 50 to 759, and a total of 2163 participants were included. All the participants were diagnosed with TN. The ages of the included participants ranged from 20 to 90 years, and the average age of the participants in each study varied from 50 to 76.2 years. There were 2 studies only noted the outcome events while not mentioned the follow up period. The follow-up of the other 7 studies ranged from 16 months to 14 years. All studies compared MVD (835 participants) with RF rhizotomy or thermocoagulation (1328 participants). Table 1 lists the study characteristics in detail.

Risk of bias assessment

The included studies were assigned ratings of 3 to 7 stars. Overall, the representativeness of the exposed and non-exposed cohorts and the ascertainment of exposure were good in all the included studies. However, the comparability between groups was not good as the studies were non-randomized. The baseline characteristics of the participants were not balanced between groups. The attrition rates of the included studies were not high. The details of the risk of bias assessment are presented in Supplement 2.

Meta-analysis results

Number of patients requiring additional procedures after surgery

Eight studies[9–16] with 1640 participants reported this outcome. The results indicated that MVD reduced the risk of requiring a secondary procedure after surgery compared with RF (RR 0.33, 95% CI 0.19 to 0.56, I^2=67%, Figure 2). We explored the sources of heterogeneity but failed to identify an explanation. However, we tested the influence of each study with a sensitivity analysis. The results showed that the pooled effect was robust and did not differ considerably after each study was removed.

Facial numbness

Four studies[10,11,14,15] with 599 participants contributed data for this analysis. The participants in the MVD group had a lower risk of facial numbness than those in the RF group (RR 0.27, 95% CI 0.19 to 0.39, I^2=0%, Figure 3). We did not identify significant statistical heterogeneity. When each study was removed individually from the meta-analysis, the results still favor the MVD group with a lower risk of facial numbness.

Postoperative use of medication

Only two studies[14,15] with 350 participants reported this outcome. There was no significant difference between the two groups (RR 0.34, 95%CI 0.06 to 1.86, I^2=82%, Figure 4). The statistical heterogeneity was significant, but the source of the heterogeneity was unclear. The sensitivity analysis also showed an unstable pooled effect; when either study was removed, the result became statistically significant in favor of MVD, with fewer events of postoperative medication use.

Incidence of any adverse events and specific adverse events

Four studies[9,10,13,14] with 1048 participants reported the incidence of any adverse events. A higher risk of adverse events was observed in the MVD group than in the RF group (RR 2.25, 95%CI 1.13 to 4.48, I^2=0%, Figure 5). We did not identify significant statistical heterogeneity. The sensitivity analysis did not show a robust result. When either Holland et al.[10] or Koopman et al.[13] was removed, the meta-analysis showed no difference between the groups.

Other specific adverse events included spinal fluid leakage from the incision, meningitis, headache and nausea, pulmonary embolism, keratitis, ipsilateral numbness, hearing loss, facial nerve palsy, facial pain, hypacusis, hypesthesia, herpes labialis and so on. MVD showed an

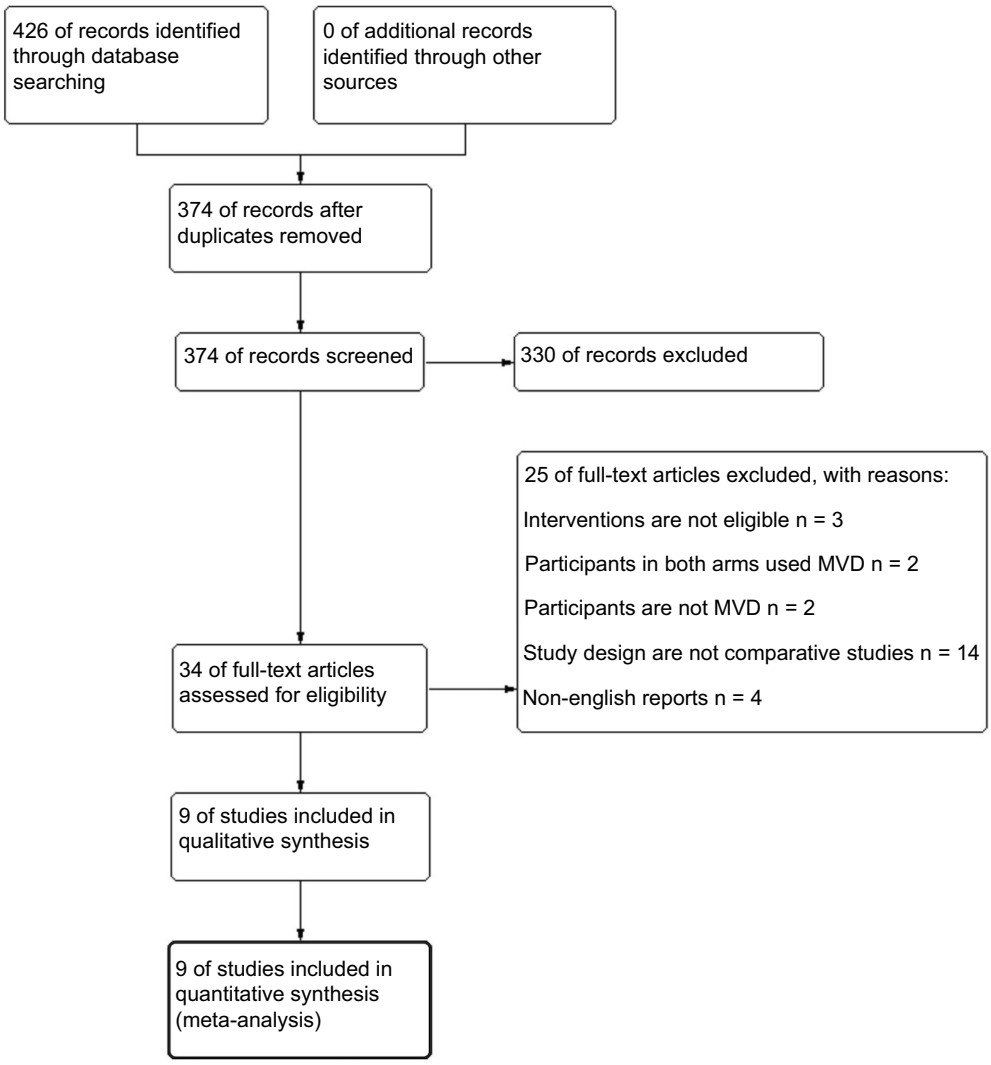

Figure 1 Study screening flow diagram.

increased risk of hypacusis but a decreased risk of hypesthesia compared to RF.

Total cost of intervention

Two studies[10,14] with 218 participants reported this outcome. Holland just calculated the total cost of the initial index treatment including physician charges and hospital charges. However, in Hitchon's study, the cost of additional procedures was also summated into total charges with the follow-up of 32±46 months. The total cost of MVD was much higher than that of RF (MD $37,190, 95% CI $19,900 to $54,470, I^2=91%, Figure 6).

Discussion

Summary of main findings

In this study, we performed a meta-analysis to compare the clinical outcomes of MVD and RF used as the first surgery for TN. Overall, MVD was associated with a greater rate of freedom from pain and lower incidences of facial numbness, but greater postoperative complications and total costs compared to RF.

Epidemiology and pathophysiology of TN

TN is characterized by paroxysms of unilateral, severe electric shock-like pain along the trigeminal nerve divisions. It can be triggered by common activities, such as eating, talking, brushing teeth, and so on.[18] It is estimated that approximately 1 per 5,500 people worldwide suffer from TN; the morbidity is higher among females than males, and it increases with age.[19,20] At present, the cause of TN is still controversial. The most common view is that vascular compression is involved in the pathogenesis of TN.[21,22]

Table 1 Study characteristics

Study	Diagnosis	Treated/ untreated	Age (mean)	Male/female	Current pain score	Right/left side	No. of participants (MVD/ RF)	Follow up	Outcomes
Hitchon 2016[16]	TN	Untreated	MVD: 57 RF: 75	MVD: 33/46 RF: 13/23	MVD: 1±2 RF: 2±3	MVD: 49/30 RF: 19/17	115 (79/36)	MVD: 16/22 months RF: 65/57 months	Patient required additional procedures Facial numbness, Postoperative use of medication, Other complications.
Marshall 2015[10]	TN	Untreated	MVD: 53.9 RF: 76.2	MVD: 10/17 RF: 11/12	NR	MVD: 15/12 RF: 12/11	50 (27/23)	NR	Patient required additional procedures, Facial numbness, Other complications.
Koopman 2011[13]	TN	Untreated	PRT: 67.3 MVD: 57.8	MVD: 43/44 RF: 288/384	NR	NR	759 (87/672)	Until the earliest of one of the following events: admission for a complication, repeat procedure or end of a 1-year follow-up period	Patient required additional procedures, Other complications.
Laghmari 2007[9]	TN	Medical treatment	MVD: 50 RF: 53	MVD: 32/19 RF: 31/42	NR	MVD: 29/21 RF: 35/38	124 (51/73)	95 months	Pain relief, Patient required additional procedures, Other complications.
Sanches-mejia 2006[16]	TN	Untreated	MVD: 58.1 RF: 72.8	MVD: 34/59 RF: 3/9	NR	NR	105 (93/12)	MVD: 70.1 months RF: 86.1 months	Patient required additional procedures
Tronnier 2001[17]	TN	NR	NR	NR	NR	NR	431 (225/206)	MVD: 10.9 years RF: 14 years	Patient required additional procedures, Other complications.
Zakrzewska 1993[15]	TN	NR	54	191/285	NR	NR	330 (65/265)	45 months	Patient required additional procedures, Postoperative use of medication, Numbness, Other complications.
Meglio 1989[12]	TN	NR	NR	NR	NR	NR	53 (20/33)	24 months	Patient required additional procedures, Other complications.
Bederson 1989[11]	TN	Treated	59.9	76/176	NR	NR	196 (166/30)	5.1 years	Patient required additional procedures, Facial numbness, Other complications.

Abbreviations: TN, trigeminal neuralgia, NR, not reported, MVD, microvascular decompression; RF, radiofrequency rhizotomy.

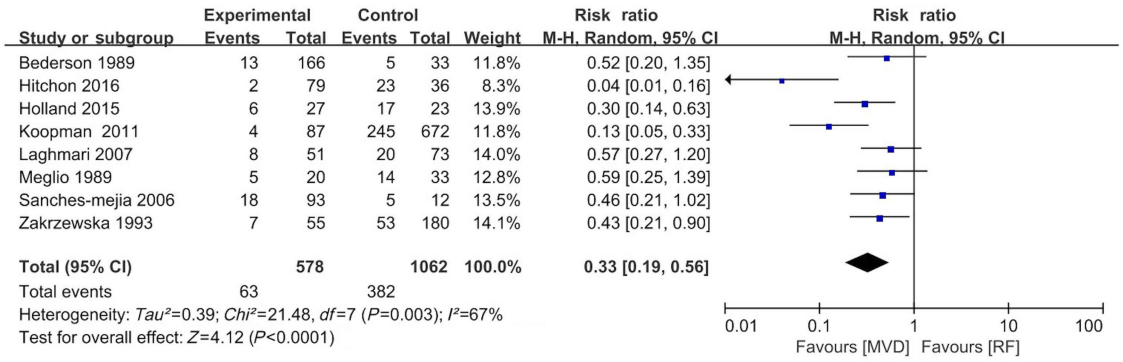

Figure 2 Forest plot of the number of patients requiring additional procedures after surgery.
Abbreviations: MVD, microvascular decompression; RF, radiofrequency thermocoagulation and rhizotomy; RR, risk ratio; CI, confidence interval.

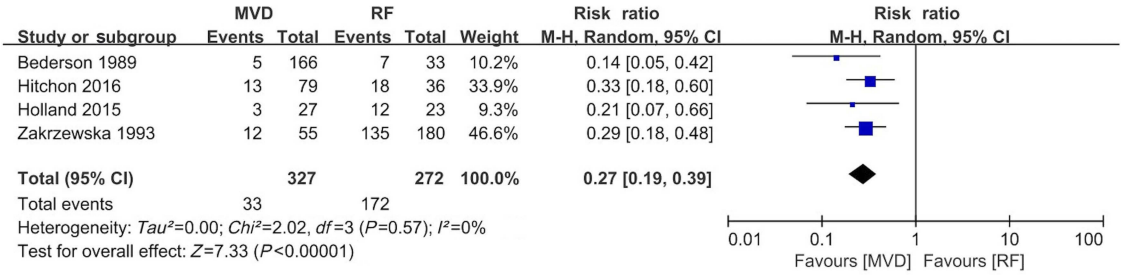

Figure 3 Forest plot of facial numbness.
Abbreviations: MVD, microvascular decompression; RF, radiofrequency thermocoagulation and rhizotomy; RR, risk ratio; CI, confidence interval.

Figure 4 Forest plot of postoperative use of medication.
Abbreviations: MVD, microvascular decompression; RF, radiofrequency thermocoagulation and rhizotomy; RR, risk ratio; CI, confidence interval.

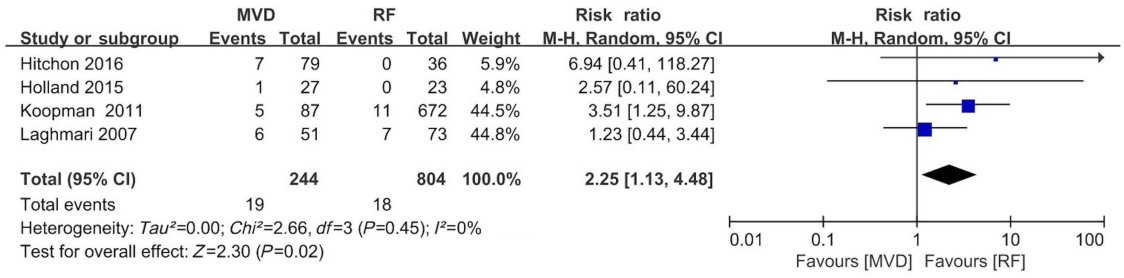

Figure 5 Forest plot of the incidence of any adverse events and specific adverse events.
Abbreviations: MVD, microvascular decompression; RF, radiofrequency thermocoagulation and rhizotomy; RR, risk ratio; CI, confidence interval.

Efficacy analysis

In the studies that we included, most investigators reported the need for additional procedures as an outcome. We found that MVD reduced the risk of needing a secondary procedure after surgery compared with RF (RR 0.33, 95% CI 0.19 to 0.56, I^2=67%), indicating that MVD is superior

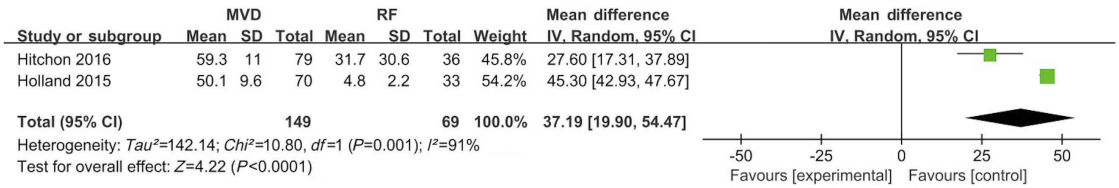

Figure 6 Forest plot of the total cost of intervention.
Abbreviations: MVD, microvascular decompression; RF, radiofrequency thermocoagulation and rhizotomy; RR, risk ratio; CI, confidence interval.

to RF in terms of pain recurrence.[23] These results are not dissimilar to those in the literature showing that MVD provides an approximately 80% chance of being pain-free, with a recurrence rate of approximately 10% over 10–20 years,[24,25] whereas RF patients report pain-free results of 80% at 1 year after treatment, 75% at 3 years, and 73% at 5 years.[26]

Although the postoperative medication usage analysis did not show any significant difference between the two procedures, it is unlikely that MVD and RF are equally efficient. Because only two studies (n=350) were included in these analyses, we cannot draw firm conclusions. Given that the most common origin of TN pain is nerve compression, it stands to reason that the pain will be more effectively treated directly, with open MVD, than with minimally invasive RF.[9,27] However, surgical interventions are selected via discussions between the patient and the surgeon on a case-by-case basis. Patients who undergo MVD are often younger, healthier, and have fewer comorbidities.[28,29] These patient characteristics may also affect the outcomes of these two procedures. Consider that, this evidence drawn out based on limited studies was uncertain and further investigation of efficacy analysis was needed.

Facial numbness

This study found that RF had a greater association with facial numbness than MVD did, which is consistent with Tatli's findings.[30] Compared with MVD, RF carries a specific risk of facial numbness as an extension of its therapeutic mechanism; additionally, there seems to be a correlation between pain relief and the intensity of facial numbness. The sensory branches of the trigeminal nerve are composed of different types of sensory nerve fibers, including unmyelinated c fibers, which transmit nociceptive signals, and myelinated Aα and Aβ fibers, which conduct tactile sensations.[31,32] In clinical practice, it is difficult to realize the highly selective ablation of pain conduction c fibers without damaging Aα and Aβ fibers, which are the main cause of postoperative facial numbness. However, although the permanent facial numbness (mainly hypesthesia, although paresthesias have also been described) is common, it seems to be tolerable to most patients.[33,34] Moreover, clinicians have found choosing an appropriate thermocoagulation temperature, can balance the intensity of RF-related facial numbness and pain relief.[35] Therefore, we considered that the cause of facial numbness is not the most important factor in the choice of preferred treatment.

Other complications

As an invasive procedure, MVD has been widely reported to have greater surgical risks than RF, including cerebrospinal fluid leak, wound infection, cranial venous sinus thrombosis, hearing loss, pneumonia, facial paresis, and stroke.[30,36–38] In our study, a higher risk of adverse events was also observed in the MVD group, but with the exceptions of hypacusis and hypesthesia, we could not find significant differences of any other complications between MVD and RF. Possible complications may not have been reported either because they did not occur or because the investigators did not classify them as side effects. Moreover, we could not analyze the temporal evolution of side effects because many studies did not report the time course (transient or permanent) of the complications. Given the safety and fair success rate of RF, many surgeons prefer this procedure for their elderly patients.[34,39–41] While the results are overwhelmingly promising, the protocol of same-day discharge and follow-up by external clinicians after RF may lead to an underreporting of its complications.

Two of the included studies provided cost-effectiveness analyses. The results showed that these two procedures may differ in total cost by a large degree. Holland described a savings of $27,000 to $42,000 per patient for patients who underwent RF compared with MVD.[10] Hitchon performed an in-depth, decision-based cost-effectiveness analysis, which concluded that although the total charges for subsequent procedures in the RF group increased over time but remained lower than the cost of MVD.[14]

Strengths and limitations of the review

The current study has several strengths. We followed the Cochrane standards to conduct this review. Bias was well controlled during the process of conducting the review. Our search strategy was developed by an information specialist, which allowed us to identify as many relevant studies as possible. The study selection, data extraction and risk of bias assessment were performed by two independent reviewers.

However, the poor comparability between groups may limit the reliability of the meta-analysis. Because this analysis is based on previously reported data, it may have imported bias from the studies that were included. The number of patients was not balanced between the MVD and RF groups. In addition, the patients in our study were not matched according to age, gender, affected trigeminal branch, or the specific vessel involved. Most articles used their own scales to measure treatment success and pain relief, thus leaving the results open to interpretation and causing stratification problems during the analytic process. Furthermore, with the development of intraoperative electrophysiological monitoring in recent years, the associated complications can be theoretically reduced in these two therapies.[42,43] Consequently, the present analysis shows the need for improved study protocols to increase the current level of evidence.

Conclusion

MVD yields better pain relief efficacy than RF. The risks and side effects of the 2 treatment modalities should be carefully weighed. Although the surgical complications associated with MVD are not negligible and total costs of MVD are much more than RF, facial numbness after RF may also compromise the patient's quality of life. For patients without specific surgical contraindications, MVD is a better option as the surgical treatment for TN; otherwise, RF could be used as an alternative therapy.

Disclaimer

The poor comparability between groups and limited studies may diminish the reliability of the meta-analysis. Further investigations should be done in order to increase the current level of evidence.

Acknowledgments

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Disclosure

The authors report no conflicts of interest in this work.

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