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Review Article

The Effectiveness of Cervical Medial Branch Thermal Radiofrequency Neurotomy Stratified by Selection Criteria: A Systematic Review of the Literature

Andrew Engel, MD,* Wade King, MMedSc, MMed(Pain),† Byron J. Schneider, MD,‡ Belinda Duszynski,§ and Nikolai Bogduk, MD, PhD¶

*Affordable Pain Management, Chicago, Illinois, USA; †Mayo Multidisciplinary Pain Clinic, Mayo Private Hospital, Taree, NSW, Australia; ‡Department of Physical Medicine and Rehabilitation, Vanderbilt University, Nashville, Tennessee; §Spine Intervention Society, Hinsdale, Illinois, USA; ¶University of Newcastle, Faculty of Health and Medicine, Newcastle, Australia

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Correspondence to: Andrew J. Engel, MD, Affordable Pain Management, 5327 N Sheridan Road, Suite B, Chicago, IL 60640, USA. Tel: 773-944-0365; Fax: 773-944-0470; E-mail: engel.andrew@gmail.com.

Abstract

Objective. To determine the effectiveness of cervical medial branch thermal radiofrequency neurotomy in the treatment of neck pain or cervicogenic headache based on different selection criteria. **Design**. Comprehensive systematic review. **Methods**. A comprehensive literature search was conducted, and the authors screened and evaluated the studies. The Grades of Recommendation, Assessment, Development, and Evaluation system was used to assess all eligible studies. **Outcome Measures**. The primary outcome measure assessed was the success rate of the procedure, defined by varying degrees of pain relief following neurotomy. Data are stratified by number of diagnostic blocks and degree of pain relief. **Results**. Results varied by selection criteria, which included triple placebo-controlled medial branch blocks, dual comparative medial branch blocks, single medial branch blocks, intra-articular blocks, physical examination findings, and symptoms alone. Outcome data showed a greater degree of pain relief more often when patients were selected by triple placebo-controlled medial branch blocks or dual comparative medial branch blocks, producing 100% relief of the index pain. The degree of pain relief was similar when triple or dual comparative blocks were used. **Conclusions**. Higher degrees of relief from cervical medial branch thermal radiofrequency neurotomy are more often achieved, to a statistically significant extent, if patients are selected on the basis of complete relief of index pain following comparative diagnostic blocks. If selected based on lesser degrees of relief, patients are less likely to obtain complete relief.

Key words: Radiofrequency Neurotomy; Neck Pain; Headache; Cervical; Zygapophysial Joint

Introduction

When defined in the strictest terms, cervical medial branch thermal radiofrequency neurotomy (CMBTRFN) is a minimally invasive procedure for the treatment of pain mediated by one or more of the medial branches of the cervical dorsal rami. In practical terms, it is a treatment for pain stemming from one or more of the cervical zygapophysial joints, as, of all the structures innervated by the cervical medial branches, the zygapophysial joints are the only ones that theoretically might harbor a source of chronic pain. There are no known causes of chronic pain that discretely affect the muscles that are segmentally innervated by individual medial branches [1]. Although myofascial pain or trigger points might seem to be a competing cause of pain, the diagnosis of these entities in the cervical spine has not been validated and lacks reliability [2]; they cannot be distinguished from tender

zygapophysial joints [3]. Moreover, the diagnostic criteria for trigger points do not stipulate discrete myotomal innervation, which would allow them to be selectively anesthetized by cervical medial branch blocks.

The procedure involves coagulating the target medial branches with a thermal radiofrequency electrode placed parallel to each nerve. In this regard, CMBTRFN is a distinctive procedure. It differs from pulsed radiofrequency neurotomy, which operates by a different electrophysiological mechanism; which does not coagulate the target nerve; and for which a different evidence base applies [4, 5].

The paradigm of CMBTRFN is that if pain can be relieved temporarily by controlled diagnostic blocks, then longer-lasting relief should be achieved by coagulating the nerves that mediate the pain. In broader terms, the procedure is used to treat either chronic neck pain or cervicogenic headache that is mediated by cervical medial branches.

A previous systematic review [6] addressed the studies that described the outcomes of CMBTRFN when performed according to the practice guidelines of the Spine Intervention Society [7]. Those guidelines prescribe that the procedure is indicated only if pain can be completely relieved by controlled diagnostic blocks of one or more cervical medial branches. Under those conditions, provided that an accurate procedural technique is used, the number needed to treat for achieving complete relief of pain is 2 [6].

However, some practitioners may not necessarily implement these guidelines. They may not perform diagnostic blocks to select patients for treatment. They may not require complete relief of pain when blocks are used, or they may not perform controlled blocks.

Theoretically, such deviations from practice guidelines run the risk of selecting patients inappropriate for the procedure, because they do not have pain mediated by cervical medial branches. In other reviews on this topic, these theoretical concerns are often disregarded, and therefore, the authors indiscriminately group all studies to determine their representative effectiveness [8–10].

The present study was, therefore, undertaken to explore if differences in selection criteria are associated with differences in outcome. Explicitly, the null hypothesis tested was that differences in selection criteria would not result in differences in success rates from subsequent treatment.

Methods

Two investigators, both formally trained in evidence-based medicine, independently searched the scientific literature for publications on the outcomes of fluoroscopically guided, thermal radiofrequency treatment for neck pain and/or cervicogenic headache using the same criteria as a previously published review on CMBTRFN [6]. Initially they each conducted digital searches using the search engine Ovid to explore the databases Embase, Medline, and EBM Reviews using the key words cervical, zygapophysial, facet, medial, branch, radiofrequency, and neurotomy. The searches encompassed all scientific papers published through May 2019. Excluded were nonhuman studies, conference abstracts, and case reports. When suitable papers were retrieved, the references of each were consulted for relevant citations that might not have been identified by the database searches.

Each investigator independently appraised each publication, using an evidence table developed by the Standards Division of the Spine Intervention Society to facilitate assessment of studies of therapeutic effectiveness. The investigators then discussed the studies with each other to determine the value of each paper's contribution to the published evidence of the outcomes of CMBTRFN.

In that regard, the investigators were guided by the following questions on matters of outcome.

- Does the study provide evidence that the treatment relieves pain?
- If so, to what extent is the pain relieved?
- In what proportion of patients treated does this relief occur?
- For how long does that relief last?
- Is relief of pain corroborated by other outcome measures?

For these questions to be answered, studies needed to provide categorical data. Categorical data were considered essential because, although group data (e.g., changes in mean pain scores) might reflect whether a treatment is effective on average, they do not reveal how many patients benefit or to what extent. In contrast, categorical data explicitly reveal how many patients achieved a particular outcome from which success rates can be derived [11–13].

The outcomes of interest were $\geq$50% relief of pain, $\geq$75% relief of pain, and complete relief of pain, on the grounds that whereas patients can accept $<$50% relief as a worthwhile degree of improvement, 80% is the median degree of desired relief, with complete relief being the optimal outcome [14]. Additionally, outcomes were sought for improvement in function and reduction in use of health care for the index condition.

For duration of outcome, data were required for at least at six months, on the grounds that duration of relief less than six months is not acceptable for a neuroablative procedure. Success rates at one year were noted if reported but were not considered essential, because CMBTRFN is a procedure that can be repeated in order to reinstate relief if and when pain recurs.

A second set of guiding questions pertained to quality.

- Do methodological flaws compromise the credibility of the data?
- Do potential biases compromise the data?

Answers to these questions were incorporated into the assessment of the body of literature according to the

Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system of appraisal for determining the quality of a body of evidence [15, 16]. In the context of the present study, the principles of GRADE stipulate that randomized controlled trials initially should be rated as high-quality evidence and observational studies be rated as low quality. Subsequently, evidence should be downgraded if it is at risk of bias (for lack of concealment or blinding of assessors or for loss to follow-up), if it lacks consistency, or if there are imprecisions in the measurement of effect size. Evidence can be upgraded if the effect is large or if there are no important threats to validity.

For each study, success rates were calculated as the number of patients who obtained a particular degree of relief, divided by the number of patients treated. For this calculation, a worst-case analysis was applied, such that the denominator of the proportion included all patients treated, not just those followed. As a result of this adjustment, in some instances, the success rates so calculated differed from those reported in the original publication. When studies within a particular category were homogeneous, their outcomes were pooled in order to allow comparisons between groups of studies.

Success rates between different studies were compared using the 95% confidence intervals of the respective proportions. In the first instance, success rates were considered to be significantly different if their 95% confidence intervals did not overlap. When confidence intervals overlapped slightly, statistical significance was tested using the 95% confidence intervals of the difference between proportions (http://vassarstats.net/prop2_ind.html).

Excluded from the review were publications that were essays with only cursory descriptions of outcomes [17], studies in which different treatments were used but the outcomes were not stratified by treatment [18], and studies whose data duplicated those of previous studies by the same authors [19]. Other studies that were excluded due to methodological flaws compromising the credibility of the data are cited below, in the context of the selection criteria that they used.

Four studies by two separate authors [20–23] were not included because they used a technique and electrodes no longer in use. Moreover, some of their studies did not actually describe or illustrate the technique used [20, 23] or gave incomplete or ambiguous descriptions of technique [21, 22]. All the publications did not sufficiently describe the criteria for selection of patients, how responses to treatment were evaluated, or the duration of follow-up of each patient [20–23].

Results

The included studies were stratified according to their selection criteria. They were also segregated according to whether they pertained to the treatment of neck pain or to cervicogenic headache. Table 1 summarizes all the included studies.

Neck Pain, Complete Relief, Placebo-Controlled Blocks

The earliest study that used placebo-controlled blocks was a randomized controlled study of CMBTRFN [24]. The sample size was small, in order to minimize the number of patients who underwent sham treatment, which is reflected by the wide confidence intervals of the success rate. Success was defined as complete relief of pain, accompanied by restoration of activities of daily living, and

Table 1. The sample sizes and six-month success rates (with 95% confidence intervals) for various grades of success, matched to the criteria used to select patients with neck pain for treatment with cervical medial branch thermal radiofrequency neurotomy

Selection Criteria	Study	N	Outcome						Comments
			Complete Relief		>80% Relief		>50% Relief		
			Success Rate, %	95% CI, %	Success Rate, %	95% CI, %	Success Rate, %	95% CI, %	
Complete relief, placebo-controlled blocks	Lord [24]	12	58	30–86					Success = complete relief of pain, restoration of ADLs, no other health care.
	McDonald [25]	17	59	36–82					
	Barnsley [26]	35	46	29–63					
	Pooled	64	52	40–64					
Complete relief, comparative blocks	Lord [27]	10	70	42–90					Success = complete relief of pain, restoration of ADLs, no other health care.
	McDonald [25]	11	55	26–84					
	MacVicar [28]	104	61	52–70					
	Pooled	125	61	52–70					
75% relief, comparative blocks	Sapir [29]	50	12	3–21					
	Shin [32]	22	32	13–51	45	24–66	73	54–92	
	Speldewinde [30]	151	39	31–47	45	37–53	56	48–64	
	Park [31]	11			28	1–55	64	36–92	
	Pooled	234	31	25–37	44	37–51	59	52–66	
50% relief, comparative blocks	Shin [32]	6	17	0–47	34	0–72	50	10–90	

no need for other health care (for neck pain). The success rate at six months was 58% (95% CI = 30–86%).

A later study [25] constitutes a long-term follow-up of the randomized controlled trial [24] but included new patients and patients who had undergone sham treatment in the controlled trial and underwent rescue treatment. The subset of 17 patients who were diagnosed with placebo-controlled blocks includes the 12 who were so diagnosed in the controlled trial. In these patients, the success rate for complete relief of pain at six months was 59% (95% CI = 36–82%).

The third study was an independent replication study [26]. For the 35 patients treated, the success rate for complete relief of pain was 46% (95% CI = 29–63%) at six months.

By definition, this body of evidence constitutes high-quality evidence according to the rules of GRADE [15, 16]. Moreover, the studies were homogeneous. They used the same diagnostic protocol and the same procedural technique. The studies were prospective without loss to follow-up. Each study used an independent observer to assess outcomes. Success was defined as complete relief of index pain plus restoration of activities of daily living with no need for other health care. There was consistency in the effect, with a pooled success rate of 52% (95% CI = 40–64%) at six months. For these reasons, there are no grounds for downgrading the rating of high quality.

Two of these studies [24, 26] compared outcomes between patients with litigation and those with no litigation. Although those with litigation tended to have lower success rates, the differences were not statistically significant.

Neck Pain, Comparative Blocks, Complete Relief

The first study to select patients using comparative blocks [27] was a pilot study undertaken to plan a controlled trial [24]. At six months after treatment, seven of 10 patients (70%, 95% CI = 42–98%) were pain-free.

A subsequent prospective observational study included 11 patients selected after comparative blocks [25] and not reported in other studies. Six of these patients (55%, 95% CI = 26–84%) had complete relief at six months after CMBTRFN.

A larger observational study corroborated and extended these data [28]. This study reported success in 68 of 104 patients who had complete relief after comparative blocks. However, in the original publication, five of these patients obtained only 80% relief of pain after treatment but were considered to have had successful outcomes because they had restored their activities of daily living and had no further need for health care. For the present purposes, these patients can be censored, leaving 63 patients for whom success was defined as complete relief of pain at six months, together with restoration of activities of daily living and no need for further health care. This constitutes a success rate of 61% (95% CI = 52–70%).

This body of evidence constitutes low-quality evidence according to the rules of GRADE [15, 16] because it lacks a controlled trial. However, the studies were homogeneous, having used the same diagnostic protocols and the same procedural technique. Each was prospective without loss to follow-up. Each used an independent observer to assess outcomes. Success was defined as complete relief of index pain at six months with restoration of activities of daily living and no need for other health care. There was consistency of effect. Therefore, there are no grounds for downgrading the quality. However, in the context of treating chronic neck pain, the pooled success rate of 61% with narrow confidence intervals (95% CI = 52–70%) amounts to a large magnitude of effect, there being no other treatment that has been shown to be capable of providing complete relief of pain. For this reason, it could be argued that the evidence warrants upgrading to moderate quality.

Neck Pain, Comparative Blocks, 75% Relief

A prospective observational study compared the outcomes of patients according to whether they were subject to litigation concerning their neck pain after whiplash [29]. At six months, three of 32 litigants and three of 18 nonlitigants were pain-free, for a combined success rate of six of 50 (12%, 95% CI = 3–21%).

A larger observational study reported outcomes encountered in a specialist pain practice in a community setting [30]. Of 151 patients, at six months after treatment, 39% (95% CI = 31–47%) had complete relief of pain, 45% (95% CI = 37–53%) had at least 80% relief, and 56% (95% CI = 48–64%) had at least 50% relief. There was a loss to follow-up of nearly 28%. Using worst-case analysis, these patients were considered treatment failures. These figures represent cumulative success rates, in that the success rates for lower grades of relief include those patients who had higher grades of relief. These outcomes were associated with improvements in function and reduction of health care, but data were not provided for the combined outcome of pain relief together with improvement in function and reduction of health care.

A third but smaller observational study of 11 patients had no patients with complete relief of pain at six months, but 28% (95% CI = 1–55%) had at least 80% relief and 64% (95% CI = 36–92%) had at least 50% relief [31]. As above, these success rates are cumulative.

A fourth observational study [32] enrolled patients who variously had either 75% or 50% relief from comparative blocks. Of the 22 patients who had 75% relief, the success rate for achieving complete relief after CMBTRFN was 32% (95% CI = 13–51%). For achieving 80% relief, the success rate was 45% (95% CI = 24–66%), and for 50%

relief, it was 73% (95% CI = 54–92%). As above, these success rates are cumulative.

Consisting only of observational studies, this body of evidence is notionally of low quality. However, consistency between studies is poor, with success rates ranging from 0% to 12% to 32% and 39% for complete relief of index pain, compounded by wide confidence intervals for some studies because of small sample sizes. This invites downgrading the evidence to very low quality.

Neck Pain, Comparative Blocks, 50% Relief

Data on outcomes in patients who had 50% relief from comparative blocks could be found in only one study [32]. Although most of the patients in this study had 75% relief from comparative blocks, there were six who had only 50%. Three reported at least 50% relief, of whom two had at least 80% relief and one had complete relief.

By the rules of GRADE, a single study does not constitute a body of evidence and, therefore, should not be graded. Consequently, there is no gradable body of evidence for the outcome of CMBTRFN in patients selected by comparative blocks with 50% relief of index pain.

As an isolated study, this study is reasonably well reported. It provides detailed data on responses to blocks and responses to CMBTRFN, but the sample size that it had, for 50% relief from blocks, is too small to draw sensible conclusions for clinical practice.

Neck Pain, Single Blocks, Complete Relief

Only one study could be found that reported selecting patients on the basis of complete relief following single diagnostic blocks [33]. Although this study claimed that 74% of 46 patients had complete relief of pain at six months and 64% at 12 months after treatment, several irregularities call into question the validity of these figures, for which reason this study was not included in the comparative analysis.

The study was presented as a retrospective chart review that did not involve an independent observer but relied on review of charts completed by the treating physician. The retrospective design raises the risk of incomplete retrieval of cases. Indeed, the authors reported that records were not available for two of the patients in their study and that some other patients were lost to follow-up [33]. Failure to include all patients treated, particularly those with poorer outcomes who did not return for review, risks overstating the estimate of effect. Not having an independent assessor incurs the risk of reporting bias by the patients and observer bias by the treating physician.

By the rules of GRADE, a single study does not constitute a body of evidence and, therefore, should not be graded. Consequently, it must be held that there is no body of evidence for outcomes from CMBTRFN in patients selected by complete relief of index pain from a single block.

Neck Pain, Miscellaneous

The seminal study on CMBTRFN [34] selected patients on the basis of a single diagnostic block being "positive," but it did not elaborate on what constituted a positive block. The study claimed that 37% of patients had 70–100% relief of pain following treatment, but no information was provided as to how these data were collected or how long after treatment patients were assessed. In a similar report [35], patients were selected on the basis of a block that was "successful." Outcomes were described under the compound classification of "entire or significant" relief. Patients were "observed" for a period between three months and 2.5 years. No other or more detailed data were provided. Both studies were performed decades ago, before more sophisticated conventional study parameters were in place. Although the reported findings are important historically, their incorporation into a rigorous modern data review is problematic.

Several other studies used a variety of criteria to select patients for treatment with CMBTRFN, such as single medial branch blocks with less than complete relief of pain [36, 37] or an intra-articular block followed by a medial branch block [38–41]. However, none of these studies provided categorical data on outcomes or had follow-up for at least six months.

Although these studies purport to show that CMBTRFN is effective, individually and collectively they did not report sufficient quantitative data upon which to judge how effective CMBTRFN was or for how long it was effective. Therefore, these studies could not be admitted into the present review, either as standalone evidence or for comparison with the outcomes of other studies.

One study selected patients on the basis of 75% relief from a medial branch block using local anesthetic and steroid followed by a conventional medial branch block, but the patients had neck pain following major cervical spine surgery [42]. At six months after CMBTRFN, 16% of 32 patients had complete relief of pain, and 50% had $\geq$50% relief. For the present purposes, these data are noted but have not been included in the analysis because the sample was unlike that of any other study.

Neck Pain, Clinical Features Alone

Several studies performed CMBTRFN in patients with neck pain who were selected on the basis of clinical features alone. One treated patients with back pain and patients with neck pain but did not separate the outcomes according to region treated [43]. A second study reported that 55% of patients achieved an improvement in pain scores by at least 16/100 but provided no data on success rates for greater degrees of improvement [44].

In a third study [45], 65 patients were treated with CMBTRFN at various levels: C3-C5, C4-C6, and C5-C7. The authors did not provide data on pain scores; they measured success only on the basis of perceived global impression of change. At six months, only 11% of patients considered themselves "very much improved," and 57% rated the treatment as unsuccessful.

Consisting of only observational studies, this body of evidence must be rated as low quality. Moreover, it does not show that CMBTRFN is successful when patients are selected on the basis of clinical features. Quite the opposite, it shows that when used in patients selected on the basis of clinical features alone, CMBTRFN achieves only small, clinically insignificant improvements in index pain or has a very small success rate for more meaningful improvements.

Cervicogenic Headache

The literature on the treatment of cervicogenic headache is divided essentially into studies in which the authors believed that cervicogenic headache could be diagnosed from clinical features alone and studies in which diagnostic blocks were used to establish the diagnosis.

Four studies addressed the efficacy of RFN of the C3 to C6 medial branches in patients selected solely on the basis of clinical features. The first study [46] briefly reported that 80% of 15 patients had good relief of pain at eight weeks but reported no outcomes beyond that time. In what appears to be an extended report of these same patients [47], the authors reported that four of 15 patients had complete relief of pain between four and 14 months. Another eight had "good relief," but this outcome was not defined. The authors concluded that a randomized controlled trial was warranted.

In the trial that followed [48], 15 patients were treated with C3-C6 RFN, and seven had what was called a positive pain response at eight weeks. However, four of 14 control patients treated with a greater occipital nerve block also had that same response. These two success rates are not significantly different statistically. In another small randomized controlled trial [49], success rates were not reported, but group data showed no difference in outcome at six months between patients who underwent active RFN at C3-C6 and patients who underwent sham RFN at these levels.

Collectively, these latter data show that RFN at C3-C6 is no more effective than sham treatment in patients with cervicogenic headache, selected on the basis of clinical features alone.

A different picture emerges when patients are selected on the basis of response to diagnostic blocks. Table 2 summarizes the included studies.

In a study that used a variety of inclusion criteria and subsequent interventions, the authors included eight patients who had 50% relief following third occipital nerve (the superficial medial branch of the C3 dorsal ramus) blocks and underwent third occipital RFN [50]. Of these eight, 13% (95% CI = 0–36%) had complete relief at six months after treatment, 38% (≥4–72%) had >80% relief, and 50% (95% CI = 15–85%) had 50% relief.

In a retrospective study, the authors reported their experience with patients suspected of having cervicogenic headache on clinical grounds but who also underwent single diagnostic blocks of the C3 and C4 medial branches [51]. Thirty patients who obtained at least 50% relief from blocks underwent C3-C4 RFN. At six months after treatment, 77% (95% CI = 62–92%) reported at least 75% relief of their pain.

In a prospective observational study [52], patients were selected for treatment if they had complete relief of headache following comparative blocks of the third occipital nerve. The 49 patients who had positive responses to these blocks underwent third occipital RFN. At six months after treatment, 67% (95% CI = 54–80%) experienced complete relief of headache, as assessed by an independent observer.

To some extent, the results of the preceding study [52] were corroborated in principle by another study [53]. In that study, 31 patients were treated with CMBTRFN for headache arising from a C2-3 joint or a C3-4 joint, or combinations thereof. Of those patients, 21 had

Table 2. The sample sizes and success rates (with 95% confidence intervals) for various grades of success, matched to the criteria used to select patients with cervicogenic headache for treatment with cervical medial branch thermal radiofrequency neurotomy

Selection Criteria	Study	N	Outcome						Comments
			Complete Relief		>75% Relief		>50% Relief		
			Success Rate, %	95% CI, %	Success Rate, %	95% CI, %	Success Rate, %	95% CI, %	
Complete relief, comparative blocks	Govind [52]	49	67	54–80					Success = complete relief of pain, restoration of ADLs, no other health care.
50% relief, single block	Hamer [50]	8	13	0–36	38	4–72	50	15–85	
	Lee [51]	30			77	62–92			
	Pooled	38			66	51–81			

previously undergone cervical fusion, four had a cervical fracture, and six had arthritis of the cervical spine. Many of these patients had repeat treatment for a total of 61 procedures. The outcomes were reported in an unusual way, which prevents direct comparison with other studies. Success was reported per procedure, not per patient. So, conventional success rates (such as the proportion of patients with complete relief for six months, after a first RFN) could not be extracted from the data published. Nonetheless, the authors reported that, in patients who had a fusion, complete relief occurred in 33/37 procedures. The median duration of relief (until return of 50% of preprocedural pain) was 176 days. In patients with a fracture, complete relief occurred in five of eight procedures, with a mean duration of 121 days. In the six patients with arthritis, no procedure provided complete relief of headache; relief of at least 70% occurred after all 16 procedures, but for a mean duration of only 10 days.

In terms of GRADE, the literature on CMBTRFN for cervicogenic headache attracts a twofold grading. For selecting patients on clinical grounds alone, the evidence is high quality because it includes two randomized controlled trials, but that evidence shows that CMBTRFN in such patients is no more effective than sham treatment. For the selection of patients with diagnostic blocks, the evidence consists of three disparate studies and, therefore, must be rated as low quality. No study had a sufficiently large sample size to produce narrow confidence intervals of the magnitude of effect. This precludes possible upgrading.

Repeat RFN

CMBTRFN does not permanently destroy its target nerves; it only coagulates their peripheral axons. The dorsal root ganglia of these nerves remain intact, and the nerves slowly recover from coagulation over a period of months. As the nerves recover, pain can recur. Consequently, CMBTRFN is not a permanent cure for neck pain or cervicogenic headache. However, when pain recurs, relief can be reinstated by repeat neurotomy.

Some authors have advocated repeat neurotomy, but on the basis of modest data, such as defining success as a reduction in pain by at least 3/10 [54]. Others have provided more compelling data, such as 39/41 patients being able to regain at least 50% relief of index pain following repeat RFN [55].

Stronger data appear in those studies that used complete relief of pain following comparative blocks or placebo-controlled blocks to select patients for treatment [25, 26, 28, 52, 56]. Two of these studies shared the same data and reported successfully reinstating complete relief of pain in 11/12 patients on one or more occasions, thereby preserving relief of pain for a period of two to five years [25, 56]. In the third study, complete relief was reinstated in 10 of 11 patients after repeat RFN. In the fourth study [52], complete relief of headache was reinstated in 12 of 14 patients who underwent repeat treatment, thereby extending the duration of complete relief for a median duration of 217 days.

The most detailed data come from a study in which CMBTRFN was performed separately in two practices [28]. In the first practice, complete relief was reinstated at least once in 10 of 11 patients, and CMBTRFN extended the period of continuing complete relief to between 20 and 70 months. The median duration of complete relief was 15 months for each RFN, with an interquartile range of 12–24 months. In the second practice, complete relief was reinstated in 12 of 12 patients, also extending the period of total relief to between 20 and 70 months. The median duration of relief (range) was 15 (11–26) months per RFN.

Statistical Analysis

Figure 1 summarizes graphically the data from Table 1. It depicts a matrix showing the relationship between the outcomes achieved from CMBTRFN and the selection criteria used, in terms of whether placebo blocks, comparative blocks, or single blocks were used and whether complete relief, >75% relief, or >50% relief of index pain from blocks was required. In the figure, the diamonds represent the six-month success rate and 95% confidence intervals reported by each study. Filled diamonds represent the randomized controlled trial. Bold diamonds reflect a body of literature that is graded as moderate quality or high quality. Dotted diamonds represent studies of low quality. Those studies whose objective was to achieve complete relief of pain after CMBTRFN did not measure or report patients who achieved lesser degrees of relief. Therefore, in order to allow comparisons with other studies, the success rates for complete relief of pain were used to back-fill lesser grades of relief in Figure 1, on the grounds that, by definition, patients who had complete relief would also have had at least 80% relief and 50% relief.

Figure 1 reveals several salient features in several dimensions. These emerge upon comparing columns and comparing rows within columns.

In the first instance, across the third row, Figure 1 shows that the success rates for achieving 50% relief of pain with CMBTRFN are essentially the same regardless of which selection criterion is used. In the second instance, however, the rows of the third and fourth columns show that, for comparative blocks with 75% or 50% relief, the success rates decrease as the grades of relief increase from 50% to complete relief of pain after CMBTRFN.

Comparing columns 1 and 2 shows that the success rates after CMBTRFN are not significantly different statistically between studies that used comparative blocks with 100% relief of pain to select patients and those that

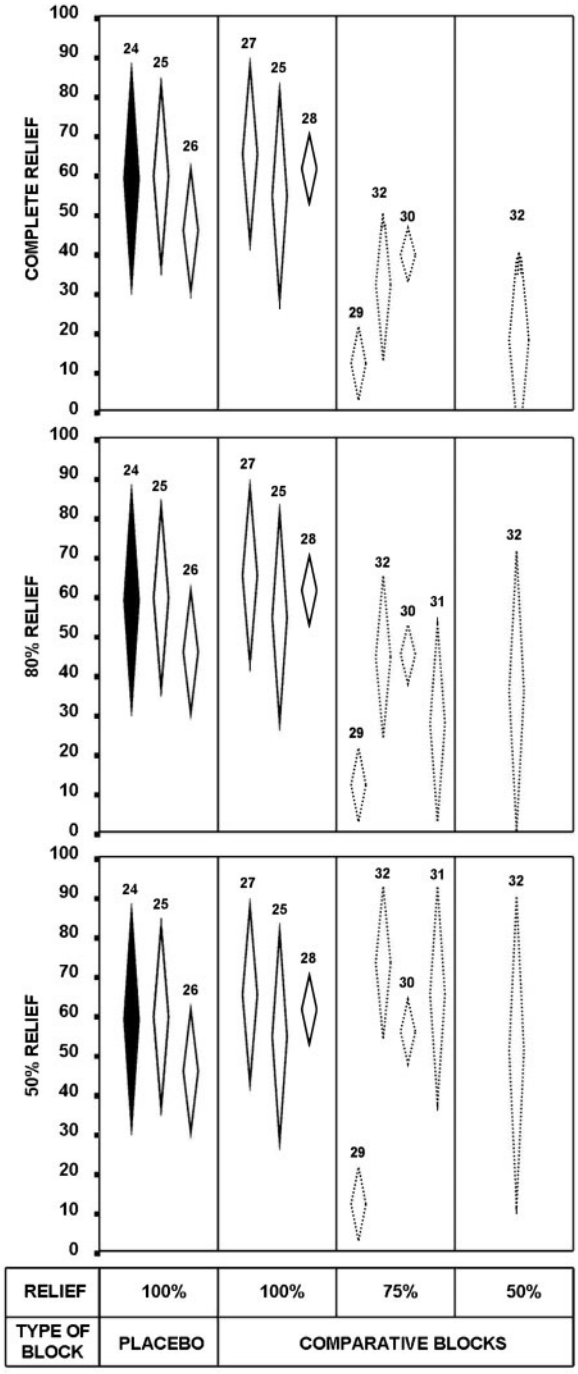

Figure 1. Six-month success rates (with 95% confidence intervals) for various grades of success, matched to the criteria used to select patients with neck pain for treatment with cervical medial branch thermal radiofrequency neurotomy.

used complete relief of pain following placebo-controlled blocks for achieving complete relief of pain after treatment. However, if columns 2, 3, and 4 are compared, differences arise.

Whereas the success rates are the same for achieving 50% relief of pain, differences arise for progressively higher grades of outcome. For achieving complete relief of pain or 80% relief, the success rates of comparative blocks with 75% relief are not significantly different from those of comparative blocks with 50% relief. In contrast, comparative blocks with 100% relief of pain produce significantly greater success rates than do comparative blocks with 75% or 50% relief for achieving either 80% relief or complete relief of pain after CMBTRFN, because their confidence intervals do not overlap.

An added dimension to this distinction is that in all the studies that achieved complete relief of pain after CMBTRFN, the definition of success included restoration of activities of daily living and no need for other health care. This was a feature of only one of the three studies whose selection criteria were comparative blocks with either 75% or 50% relief.

In essence, Figure 1 shows that differences in selection criteria have no bearing on the success rate for achieving at least 50% pain relief. However, using more stringent diagnostic criteria achieves greater success rates for higher grades of relief, to a statistically significant extent.

Figure 2 provides for a similar analysis in the context of cervicogenic headache. For achieving 50% or 75% relief of headache, success rates are either similar or dissimilar. For achieving complete relief of headache, the success rate of 67% after comparative blocks with 100% relief is obviously greater than the success rate after single blocks with 50% relief and is significantly greater statistically. Moreover, that greater success rate applies not only to achieving complete relief of pain but complete relief accompanied by restoration of activities of daily living and no need for other health care for headache. In essence, selecting patients with comparative blocks yields both greater success rates and a higher grade of relief.

Discussion

The cardinal feature that emerged in the present review is that the success rate of CMBTRFN is related to how patients are selected for treatment. Success rates are distinctly lower when selection criteria are limited to clinical features alone. Success rates are greater when diagnostic blocks are used. Higher grades of relief are achieved when controlled blocks are used, and when higher grades of relief are required from those blocks. This pattern of difference is evident for the treatment of cervicogenic headache and more strongly so for the treatment of neck pain.

For the treatment of cervicogenic headache, the evidence shows that there is no attributable effect when patients are selected by clinical features alone. This is not surprising because clinical features have been shown not to be valid for the diagnosis of cervicogenic headache [57, 58]. For that reason, the diagnostic criteria for cervicogenic headache prescribed by the International Headache Society include response to diagnostic blocks in order to show that the headache actually does have a cervical source [59].

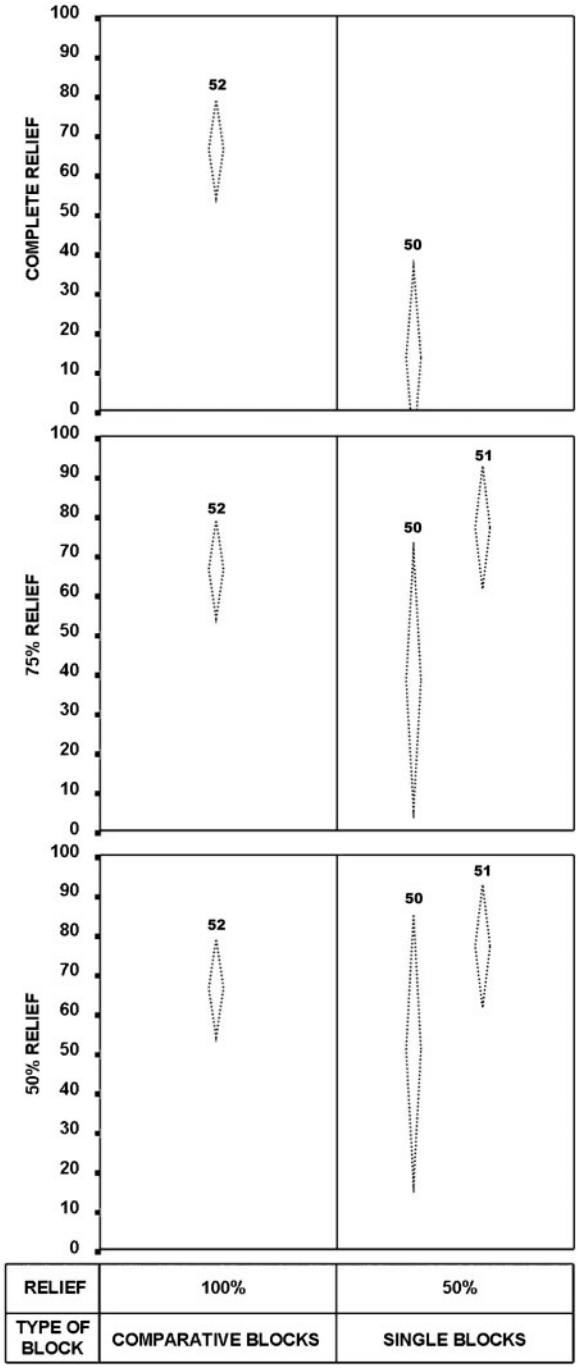

Figure 2. Six-month success rates (with 95% confidence intervals) for various grades of success, matched to the criteria used to select patients with cervicogenic headache for treatment with cervical medial branch thermal radiofrequency neurotomy.

In that regard, a single study [52] has shown that in patients with third occipital headache diagnosed by controlled blocks of the third occipital nerve, complete relief can be achieved in some 67%. The median duration of relief was 297 days, with a success rate of 86% for reinstating relief if and when pain recurred. Although this success may be appealing, especially for a condition for which there is no other proven treatment [58], physicians should understand that a single study constitutes very low-quality evidence under GRADE. That grade will not change unless and until additional studies establish the true magnitude of effect.

For the treatment of neck pain by CMBTRFN, there is a larger and richer collection of evidence. The present review reveals features of that evidence that are relevant to physicians and the patients they treat, to insurers, and to authors of systematic reviews.

The cardinal feature is that outcomes differ according to selection criteria. For some outcomes, the differences are not statistically significant, but for the higher grades of outcome, particularly complete relief of pain, they are statistically significant. Consequently, in that context, the results of the present review refute its null hypothesis. Outcomes are not the same for different selection criteria.

The implication for authors of reviews, and for insurers who choose to review the literature, is that not all interventions that are called CMBTRFN are the same. Their outcomes cannot be lumped together. Studies must be stratified for selection criteria, as these determine outcomes. Negative studies cannot be used to negate positive studies if their selection criteria are different.

For physicians and their patients, and for those who pay for the treatment, the results of the present review, summarized in Figures 1 and 2 and in Tables 1 and 2, allow informed choices to be made.

There is high-quality evidence that CMBTRFN is ineffective if and when patients are selected on the basis of clinical features alone. This resonates with the fact that no clinical feature has been shown to be valid for the diagnosis of neck pain, and especially not for the diagnosis of zygapophysial joint pain at a particular segment or segments, which might be treated with CMBTRFN. Diagnostic blocks must be performed in order to establish and pinpoint the source of pain.

Although many practitioners use a variety of diagnostic blocks to select patients for treatment, many of these have not been validated. There is no admissible evidence that patients selected based on response to intra-articular blocks or single medial branch blocks will achieve good outcomes after CMBTRFN.

There is low-quality evidence that if patients are selected using comparative blocks with 50% relief of index pain, they might have a 68% chance of achieving 50% relief of pain, a 43% chance of achieving 80% relief, and only a 29% chance of achieving complete relief. Changing the selection criteria to 75% relief after comparative blocks does not significantly improve the chances of achieving 50%, 80%, or complete relief of pain. Physicians might elect to offer their patients these chances, but other protocols offer different outcomes.

There is moderate-quality to high-quality evidence that using comparative blocks with 100% relief of index pain offers patients a 61% chance of achieving complete relief of pain—which is the outcome that patients most

desire. Moreover, the published evidence shows that this relief is accompanied by restoration of activities of daily living and no need for other health care for neck pain. This standard of outcome is unparalleled by any other intervention for the treatment of neck pain, but it does not apply to nonspecific neck pain. It applies only, and strictly, to neck pain that is completely relieved by comparative local anesthetic blocks.

Of interest to consumers—be they patients, physicians, or insurers—is the duration of effect of treatments that they undergo, perform, or pay for. Accordingly, they look for or demand long-term data on outcome. This idiom, however, is misplaced in the context of CMBTRFN. This intervention is not designed to achieve a permanent "cure." Although the treatment can provide high degrees of relief, the treated nerves can recover and pain can recur. However, in that event, it has been shown in multiple studies that relief can be reinstated by repeat treatment.

In that regard, the placebo-controlled trial of CMBTRFN [24] was not designed to test long-term duration of effect. It was specifically designed to test for attributable effect and was terminated as soon as the study had enough statistical power to refute a placebo effect. Long-term benefits have been demonstrated by subsequent observational studies [25, 28, 56], the equivalent of so-called phase 4 studies in drug trials. These have shown that the durations of effect after a single CMBTRFN vary between individuals, but when treatment is repeated, complete relief can be reinstated and preserved for years [25, 28, 56].

This evidence informs physicians and their patients that different grades of relief can be expected after treatment with CMBTRFN, with different chances of success. Critical to those differences, however, is how patients are selected for treatment. For patients to be fully informed about their options, discussions need to be undertaken before and during the diagnostic phase, not before treatment.

Conclusions

A review of all the published evidence on cervical medial branch thermal radiofrequency neurotomy shows that different grades of outcome can be achieved depending on the number of diagnostic blocks performed and the relief obtained from those blocks. Higher degrees of relief are more often achieved, to a statistically significant extent, if patients are selected on the basis of complete relief of index pain following comparative diagnostic blocks.

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