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Systematic Review

Systematic Review of the Therapeutic Effectiveness of Cervical Facet Joint Interventions: An Update

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Background: The prevalence of chronic, recurrent neck pain is approximately 15% of the adult general population. Controlled studies have supported the existence of cervical facet or zygapophysial joint pain in 36% to 67% of these patients, when disc herniation, radiculitis, and discogenic are not pathognomic. However, these studies also have shown false-positive results in 27% to 63% of the patients with a single diagnostic block. There is also a paucity of literature investigating therapeutic interventions of cervical facet joint pain.

Study Design: Systematic review of therapeutic cervical facet joint interventions.

Objective: To determine and update the clinical utility of therapeutic cervical facet joint interventions in the management of chronic neck pain.

Methods: The available literature for utility of facet joint interventions in therapeutic management of cervical facet joint pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria as utilized for interventional techniques for randomized trials and the criteria developed by the Newcastle-Ottawa Scale criteria for observational studies.

The level of evidence was classified as good, fair, and limited or poor based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF).
Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 to June 2012, and manual searches of the bibliographies of known primary and review articles.

Outcome Measures: The primary outcome measure was pain relief (short-term relief = up to 6 months and long-term > 6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and reduction in opioid intake.

Results: In this systematic review, 32 manuscripts were considered for inclusion. For final analysis, 4 randomized trials and 6 observational studies met the inclusion criteria and were included in the evidence synthesis. Based on one randomized, sham-controlled, double-blind trial and 5 observational studies, the indicated evidence for cervical radiofrequency neurotomy is fair. Based on one randomized, double-blind, active-controlled trial and one prospective evaluation, the indicated evidence for cervical medial branch blocks is fair. Based on 2 randomized controlled trials, the evidence for cervical intraarticular injections is limited.

Limitations: Paucity of the overall published literature and specifically lack of literature for intraarticular cervical facet joint injections.

Conclusions: The indicated evidence for cervical radiofrequency neurotomy is fair. The indicated evidence for cervical medial branch blocks is fair. The indicated evidence for cervical intraarticular injections with local anesthetic and steroids is limited.

Key words: Chronic neck pain, cervical facet or zygapophysial joint pain, cervical medial branch blocks, cervical radiofrequency neurotomy, cervical intraarticular facet joint injections

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Chronic neck pain is common in the adult general population (1-9), with a lifetime prevalence of 26% to 71% (2,4). Significant economic, societal, and health impact cannot be ignored as it is similar to the impact of low back pain and is recognized as a source of disability in the working population (10-25).

Cervical intervertebral discs, cervical facet joints, atlanto-axial and atlanto-occipital joints, ligaments, fascia, muscles, and nerve root dura have been shown to be capable of transmitting pain in the cervical spine with resulting symptoms of neck pain, upper extremity pain, and headache. However, very little is known about the causes of neck pain since the epidemiologic studies do not describe either the source or cause of the pain. Yin and Bogduk (26) estimated the prevalence of discogenic pain in 16%, zygapophysial joint pain in 55%, and lateral atlanto-axial joint pain in 9%, in 143 patients with chronic neck pain in a private practice pain clinic in the United States. However, diagnosis remained elusive in 32% of those patients who completed investigations. A significant proportion did not complete investigation. Based on controlled diagnostic blocks, cervical facet joints have been implicated as responsible for pain in the neck, head, and upper extremities in 36% to 67% of patients (27-37).

Systematic reviews (36,37) showed strong evidence for diagnostic accuracy of cervical facet joint blocks. In addition, Rubinstein and van Tulder (38) in a best-evidence review of diagnostic procedures for neck and low back pain concluded that there was strong evidence for the diagnostic accuracy of facet joint blocks in the diagnosis of neck pain. Even then, significant controversy surrounds various treatments utilized in the management of chronic neck pain arising from cervical facet joints (1,36,39-48). The evidence illustrated that long-term therapeutic benefits of intraarticular injection of facet joints was limited (36,40,49). The recent systematic review (36) showed the indicated evidence for therapeutic cervical medial branch blocks and radiofrequency neurotomy of medial branches in the cervical spine was moderate, or level II-1 (50-55). Cervical facet joint interventions for managing chronic neck pain are one of the most commonly performed interventions in the United States (56-67). With exploding medical costs and utilization, and repeated questions about the effectiveness of cervical facet joint interventions, it is essential to update the evidence periodically utilizing appropriate methodology (68). Thus, this systematic review was undertaken to evaluate and update the effectiveness of therapeutic cervical facet joint interventions (36).

Methods

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and meta-analysis of randomized trials and observational studies (1,17,69-79), Consolidated Standards of Reporting Trials (CONSORT) guidelines for the conduct of randomized trials (80-83), Standards for Reporting Observational Studies (STROBE) (84), Cochrane guidelines (74,75,85), Chou and Huffman's guidelines (86), and quality of reporting of analysis (71).

1.1 Criteria for Considering Studies for This Review

1.1.1 Types of Studies

Randomized controlled trials
Non-randomized observational studies
Case reports and reviews for adverse effects

1.1.2 Types of Participants

Participants of interest were adults aged at least 18 years with chronic upper and mid back pain of at least 3 months duration.

Participants must have failed previous pharmacotherapy, exercise therapy, etc., prior to starting interventional pain management techniques.

1.1.3 Types of Interventions

The interventions were therapeutic cervical facet joint blocks appropriately performed with proper technique under fluoroscopic or computed tomography (CT) guidance.

1.1.4 Types of Outcome Measures

- The primary outcome parameter was pain relief.
- The secondary outcome measures were functional improvement; change in psychological status; return to work; reduction or elimination of opioid use, other drugs, or other interventions; and complications.
- At least 2 of the review authors independently, in an unblinded standardized manner, assessed the outcomes measures. Any disagreements between reviewers were resolved by a third author and consensus.

1.2 Literature Search

Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed

2. EMBASE from 1980: www.embase.com
3. Cochrane Library www.thecochranelibrary.com/view/0/index.html
4. U.S. National Guideline Clearinghouse (NGC) www.guideline.gov
5. Previous systematic reviews and cross references
6. Clinical Trials: clinicaltrials.gov

The search period was from 1966 through June 2012.

1.3 Search Strategy

The search strategy emphasized chronic cervical pain of facet joint origin with a focus on all types of therapeutic interventions. Search terminology included cervical facet joint, cervical facet joint pain, cervical facet joint intraarticular injections, medial branch blocks, and radiofrequency neurotomy.

At least 2 of the review authors independently, in an unblinded standardized manner, performed each search. All searches were combined to obtain a unified search strategy. Any disagreements between reviewers were resolved by a third author and consensus.

1.4 Data Collection and Analysis

The review focused on randomized trials, observational studies, and reports of complications. The population of interest was patients suffering with chronic neck and upper extremity pain for at least 3 months. Only cervical facet joint interventions were evaluated. All of the studies providing appropriate management and with outcome evaluations of one month or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

1.4.1 Selection of Studies

- In an unblinded standardized manner, 2 review authors screened the abstracts of all identified studies against the inclusion criteria.
- All articles with possible relevance were then retrieved in full text for comprehensive assessment of internal validity, quality, and adherence to inclusion criteria.

1.4.2 Inclusion and Exclusion Criteria

Inclusion criteria were studies which documented the existence of cervical spinal pain of facet joint origin using controlled diagnostic facet joint injections or medial branches. Three types of facet joint interventions were included in this review: intraarticular facet joint injections, medial branch blocks, and medial branch radiofrequency neurotomy. All studies must provide appropriate management with outcome evaluations of at least 6 months and appropriate statistical analysis.

Reports without appropriate diagnosis and elimination of false-positive responses, abstracts beyond 2 years, non-systematic reviews, book chapters, and case reports were excluded.

1.4.3 Clinical Relevance

The clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (Table 1) (87). Each question was scored as positive (+) if the clinical relevance item was met, negative (–) if the item was not met, and unclear (?) if data were not available to answer the question.

1.4.4 Methodological Quality or Validity Assessment

The quality of each individual article used in this analysis was assessed by Cochrane review criteria (Table 2) (74) for randomized trials or the Newcastle-Ottawa Scale for observational studies (Tables 3 and 4) (88,89).

Each study was evaluated by at least 2 authors for

Table 1. *Clinical relevance questions.*

	P (+)	N (-)	U (unclear)
A) Are the patients described in detail so that one can decide whether they are comparable to those who are treated practice?			
B) Are the interventions and treatment settings described in sufficient detail to apply its use in clinical practice?			
C) Were clinically relevant outcomes measured and reported?			
D) Is the size of the effect clinically meaningful?			
E) Do the likely treatment benefits outweigh the potential harms?			

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (87).

Table 2. ***Randomized controlled trials quality rating system.***

A	1. Was the method of randomization adequate?	A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a die (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments. Examples of inadequate methods are: alternation, birth date, social insurance/ security number, date in which they are invited to participate in the study, and hospital registration number.	Yes/No/ Unsure
B	2. Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/ Unsure
C	Was knowledge of the allocated interventions adequately prevented during the study?		
	3. Was the patient blinded to the intervention?	This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.	Yes/No/ Unsure
	4. Was the care provider blinded to the intervention?	This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.	Yes/No/ Unsure
	5. Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or: –for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes" –for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination –for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome –for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "4" (caregivers) is scored "yes" –for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data.	Yes/No/ Unsure
D	Were incomplete outcome data adequately addressed?		
	6. Was the drop-out rate described and acceptable?	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored. (N.B. these percentages are arbitrary, not supported by literature).	Yes/No/ Unsure
	7. Were all randomized participants analyzed in the group to which they were allocated?	All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.	Yes/No/ Unsure
E	8. Are reports of the study free of suggestion of selective outcome reporting?	In order to receive a "yes," the review author determines if all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.	Yes/No/ Unsure
F	Other sources of potential bias:		
	9. Were the groups similar at baseline regarding the most important prognostic indicators?	In order to receive a "yes," groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).	Yes/No/ Unsure
	10. Were co-interventions avoided or similar?	This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.	Yes/No/ Unsure
	11. Was the compliance acceptable in all groups?	The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant.	Yes/No/ Unsure
	12. Was the timing of the outcome assessment similar in all groups?	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.	Yes/No/ Unsure

Adapted and modified from Furlan AD. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; 34:1929-1941 (74).

Table 3. *Newcastle-Ottawa quality assessment scale: Case control studies*.

Selection
1) Is the case definition adequate?
a) yes, with independent validation *
b) yes, e.g. record linkage or based on self reports
c) no description
2) Representativeness of the cases
a) consecutive or obviously representative series of cases *
b) potential for selection biases or not stated
3) Selection of Controls
a) community controls *
b) hospital controls
c) no description
4) Definition of Controls
a) no history of disease (endpoint) *
b) no description of source
Comparability
1) Comparability of cases and controls on the basis of the design or analysis
a) study controls for _____ (Select the most important factor.) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Exposure
1) Ascertainment of exposure
a) secure record (eg surgical records) *
b) structured interview where blind to case/control status *
c) interview not blinded to case/control status
d) written self report or medical record only
e) no description
2) Same method of ascertainment for cases and controls
a) yes *
b) no
3) Non-Response rate
a) same rate for both groups *
b) non respondents described
c) rate different and no designation

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (88).

stated criteria and any disagreements were discussed with a third reviewer. Authors with a perceived conflict of interest for any manuscript were recused from reviewing the manuscript.

For adverse effects, confounding factors, etc., it was not possible to use quality assessment criteria. Thus, these were considered based on interpretation of the reports published and critical analysis of the literature.

Only the randomized trials meeting the inclusion criteria with at least 50% of applicable criteria were utilized for analysis. However, studies scoring lower were described and provided with an opinion and critical analysis.

Table 4. *Newcastle-Ottawa quality assessment scale for cohort studies.*

Selection
1) Representativeness of the exposed cohort
a) truly representative of the average _____ (describe) in the community *
b) somewhat representative of the average _____ in the community *
c) selected group of users e.g. nurses, volunteers
d) no description of the derivation of the cohort
2) Selection of the non exposed cohort
a) drawn from the same community as the exposed cohort *
b) drawn from a different source
c) no description of the derivation of the non exposed cohort
3) Ascertainment of exposure
a) secure record (eg surgical records) *
b) structured interview *
c) written self report
d) no description
4) Demonstration that outcome of interest was not present at start of study
a) yes *
b) no
Comparability
1) Comparability of cohorts on the basis of the design or analysis
a) study controls for _____ (select the most important factor) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Outcome
1) Assessment of outcome
a) independent blind assessment *
b) record linkage *
c) self report
d) no description
2) Was follow-up long enough for outcomes to occur
a) yes (select an adequate follow up period for outcome of interest) *
b) no
3) Adequacy of follow up of cohorts
a) complete follow up - all subjects accounted for *
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) *
c) follow up rate < ____% (select an adequate %) and no description of those lost
d) no statement

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (88).

Observational studies had to meet a minimum of 50% of the utilized criteria for cohort and case-control studies. Studies scoring less were also described and provided with an opinion and a critical analysis.

If the literature search provided at least 5 randomized trials meeting the inclusion criteria and they were

Table 5. *Method for grading the overall strength of the evidence for an intervention.*

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality RCTs or studies of diagnostic test accuracy).
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher-quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws).
Limited or Poor	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Adapted and modified from methods developed by U.S. Preventive Services Task Force (86, 90-100).

homogenous for each modality (intraarticular injections, medial branch blocks, and radiofrequency neurotomy) evaluated, a meta-analysis was performed.

1.4.5 Data Extraction and Management

Two review authors independently, in an unblinded standardized manner, extracted the data from the included studies. Disagreements were resolved by discussion between the 2 reviewers; if no consensus could be reached, a third author was called in to break the impasse.

1.4.6 Assessment of Heterogeneity

Whenever meta-analyses were conducted, the I-squared (I2) statistic was used to identify heterogeneity (89). Combined results with I2 > 50% were considered substantially heterogenous.

Analysis of the evidence was based on the modality of treatment provided (i.e., intraarticular injections, medial branch blocks, and radiofreqency neurotomy).

1.4.7 Measurement of Treatment Effect in Data Synthesis (Meta-Analysis)

Data were summarized using meta-analysis when at least 5 studies per type of treatment were available that met the inclusion criteria.

1.5 Summary Measures

Summary measures included 50% or more reduction of pain in at least 40% of the patients, or at least a 3 point decrease in pain scores with improvement in functional status.

1.6 Analysis of Evidence

The analysis of the evidence was performed based on United States Preventive Services Task Force (USPSTF) criteria as illustrated in Table 5, criteria which has been utilized by multiple authors (86,90-100).

The analysis was conducted using 3 levels of evidence: good, fair, and limited or poor.

At least 2 of the review authors independently, in an unblinded standardized manner, analyzed the evidence. Any disagreements between reviewers were resolved by a third author and consensus. If there were any conflicts of interest (e.g., authorship), those reviewers were recused from assessment and analysis.

1.7 Outcome of the Studies

In the randomized trials, a study was judged to be positive if the therapeutic cervical facet joint intervention was clinically relevant and effective, either with a placebo control or active control. This indicates that the difference in effect for primary outcome measure is statistically significant on the conventional 5% level. In a negative study, no difference between the study treatments or no improvement from baseline is identified. Further, the outcomes were judged at the reference point with positive or negative results reported at one month, 3 months, 6 months, and one year.

For observational studies, a study was judged to be positive if the intervention was effective, with outcomes reported at the reference point with positive or negative results at one month, 3 months, 6 months, and one year.

The minimum amount of change in pain score to be clinically meaningful has been described as a 2-point change on a scale of 0 to 10 (or 20 percentage points), based on findings in trials studying general chronic pain (101), chronic musculoskeletal pain (102), and chronic low back pain (69,70,73,74,103,104), which have been commonly utilized. However, later descriptions of clinically meaningful improvement showed either pain relief

or functional status as 50% (52,105-124). Consequently, for this analysis, we utilize clinically meaningful pain relief of at least a 3-point change on an 11-point scale of 0 to 10, or 50% pain relief from the baseline, or functional status improvement of 40% as clinically significant.

2.0 Results

Figure 1 shows a flow diagram of study selection as recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (72). There were 32 studies considered for inclusion (49-55,125-149).

of the 32 studies identified, 19 were excluded (55,125,127,130-133,135-141,143,146-149). Table 6 shows the reasons for exclusion. of these, 6 were randomized trials and 13 were non-randomized studies.

Tables 7 to 9 illustrate characteristics of studies considered for inclusion. There were 6 randomized trials (49,51-53,126,145) with 3 duplicates (51,52,126) and 6 observational studies (50,54,128,129,142,144). There was one randomized trial evaluating radiofrequency neurotomy (53), one randomized trial evaluating cervical facet joint nerve blocks (51,52,126) with 3 duplicates (51,52,126), and 2 randomized trials evaluating intraarticular injections (49,145).

There were 5 observational studies evaluating radiofrequency neurotomy (54,128,129,142,144) and one observational study evaluating cervical facet joint nerve blocks (50).

There were no observational studies meeting inclusion criteria evaluating intraarticular injections.

2.1 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials meeting inclusion criteria was carried out utilizing Cochrane review criteria as shown in Table 10. Studies achieving Cochrane scores of 9 or higher were considered as high quality, 6 to 8 were considered as moderate quality, and studies scoring less than 6 were excluded.

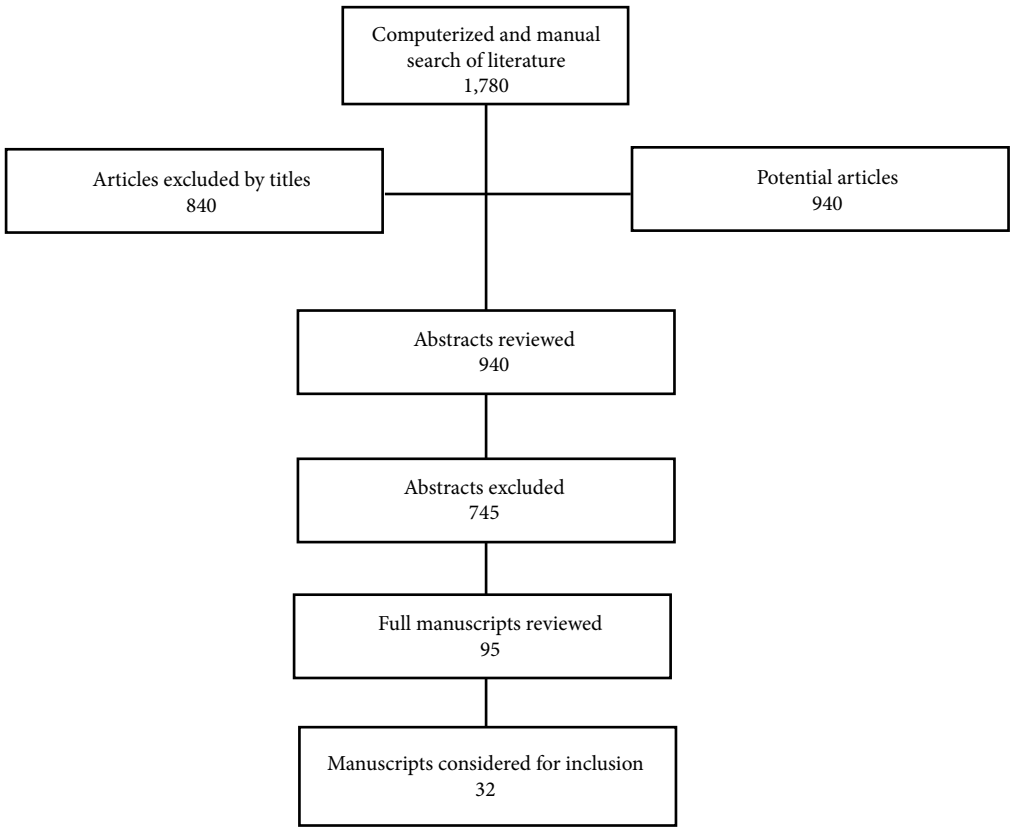

Fig. 1. *The flow diagram illustrating literature evaluating therapeutic cervical facet joint interventions*

Table 6. *List of excluded randomized trials and non-randomized studies evaluating cervical facet joint interventions.*

	Manuscript Author(s)	Comments
RANDOMIZED		
1	Manchikanti et al (130)	This was an evaluation of effect of sedation on diagnostic validity of cervical facet joint pain.
2	Manchikanti et al (131)	This was an evaluation of effect of sedation on diagnostic validity of cervical facet joint pain.
3	Slappendel et al (135)	The authors evaluated the efficacy of radiofrequency lesioning of the cervical dorsal root ganglion.
4	Haspeslagh et al (136)	In this study, 30 patients with cervicogenic headache were evaluated. This study was problematic, not only in the diagnosis but also in the application of technique. The authors claim that they developed a sequence of various cervical radiofrequency neurotomies that proved successful in a prospective pilot trial with 15 chronic headache patients. Their diagnosis was not established by controlled diagnostic blocks; and the treatments targeted toward different structures: cervical facet joints and dorsal root ganglion compared to occipital nerves.
5	Wallis et al (138)	The authors evaluated resolution of psychological distress of whiplash patients following treatment by radiofrequency neurotomy in a randomized, double-blind, placebo controlled trial; however, the follow-up was of short-term (3 months). The original manuscript is already included. The radiofrequency neurotomy outcomes are included.
6	Schaerer (140)	Number of patients receiving cervical radiofrequency not known.
OBSERVATIONAL		
1	McDonald et al (55)	The authors studied long-term effectiveness of percutaneous radiofrequency medial branch neurotomy in the treatment of chronic neck pain in 28 patients.
2	Manchikanti et al (125)	The authors evaluated the value of Sarapin with each patient acting as their own control without long-term follow-up.
3	Barnsley (127)	The authors evaluated in 35 patients the effectiveness of percutaneous radiofrequency neurotomy for chronic neck pain.
4	Shin et al (132)	Radiofrequency neurotomy of cervical medial branches for chronic neck pain was evaluated in 28 patients.
5	Mikeladze et al (133)	The study evaluated 114 patients retrospectively with chronic low back or neck pain from 2000 to 2001. The study included 31 patients with neck pain failing to meet the criteria for inclusion with pulsed radiofrequency neurotomy.
6	Siegenthaler et al (137)	Radiofrequency neurotomy was evaluated based on ultrasound localization of the nerves and 15 consecutive patients using a shortened radiofrequency procedure under fluoroscopic control.
7	Kim et al (139)	Authors evaluated 20 patients in each group with intraarticular injections with 20 patients diagnosed with myofascial pain syndrome, 20 patients with herniated nucleus pulposus, and another 20 patients with whiplash-associated disorders. There were 40 patients in myofascial pain syndrome and whiplash associated disorders, thus, it is not known how many of these patients were suffering with facet joint pain. There were no diagnostic blocks performed.
8	Tzaan & Tasker (141)	The authors evaluated only 13 patients for cervical facet joint neurolysis for chronic neck pain.
9	Lord et al (143)	Percutaneous radiofrequency neurotomy in the treatment of cervical zygapophysial joint pain was evaluated in 19 patients in an audit of results.
10	Park et al (146)	The authors evaluated in 11 patients the effect of radiofrequency neurotomy of lower cervical medial branches on cervicogenic headache.
11	Rambaransingh et al (147)	Twenty patients were evaluated to assess the effect of repeated zygapophysial joint radiofrequency neurotomy on pain disability and improvement duration.
12	Lang & Buchfelder (148)	The authors evaluated radiofrequency neurotomy for headache stemming from the zygapophysial joints C2/3 and C3/4 in an unknown number of patients. Full manuscript was not available.
13	Folman et al (149)	The authors evaluated 30 patients with intraarticular corticosteroids.

Table 7. *Study characteristics of randomized trials and observational studies of cervical radiofrequency neurotomy.*

Study/ Characteristics	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 months Long-term relief > 6 months
RANDOMIZED					
Lord et al, 1996 (53) Randomized, sham control, double-blind	24 patients selected in a specialty cervical spine research unit in Australia suffering with chronic pain of cervical facet joint origin after whiplash injury and have failed conservative management. The diagnosis was confirmed with the use of double-blind, placebo-controlled local anesthetics.	Radiofrequency group lesion 90 sec lesion at 80° C of medial branch; Control group received sham treatment with electrode insertion. Even though this is described as a placebo-control treatment, maybe it is better to be called sham control since each patient received local anesthetic block which has been shown to be effective in itself (51,52). Authors also produced multiple lesions at each level.	3, 6, and 12 month follow-up; 0 to 5 of 100 on visual analog scale; word count 3 or less on McGill Pain questionnaire.	Median time to return of pain in treatment group was 263 days; 8 days in control group; 10 patients underwent second procedures with varying results.	Positive even though the study has been criticized for small group size and variations with creative statistical analysis, this study continues to be the landmark evaluation to show efficacy of radiofrequency neurotomy in the cervical spine (150-152).
OBSERVATIONAL					
Sapir & Gorup, 2001 (54) Prospective	32 litigants and 18 non-litigants underwent radiofrequency neurotomy. 60 patients with cervical whiplash who remained symptomatic after 20 weeks of conservative management were considered for radiofrequency cervical medial neurotomy. Patients were classified as litigant or non-litigant based on whether the potential for monetary gain via litigation existed. Inclusion criteria was 80% reduction in pain with controlled comparative local anesthetic blocks. 50 patients underwent radiofrequency neurotomy and 46 patients completed the study.	The details for radiofreqency neurotomy were not provided.	Visual analog scale and self-report of improvement.	66% of the patients in the litigation group and 71% of the patients in the non-litigation group reported relief for more than one year. Time to recurrence defined as 50% return of pain was 8.0 ± 2.0 months. The frequency of recurrence of pain was similar in both groups.	The results were positive in this study in both litigants and non-litigants; however, there were only 32 litigants and 18 non-litigants undergoing radiofrequency neurotomy. Further, the difference between groups in the degree of symptomatology or response to treatment did not reach significance.
Cohen et al, 2007 (128) Retrospective	The data was gathered from 3 academic medical centers on 92 patients with chronic neck pain who underwent radiofrequency denervation after positive response to diagnostic local anesthetic blocks with bupivacaine 0.5%, 5 mL, per medial branch with a single block with a criterion standard of 50%	Radiofrequency denervation with insertion of the electrode parallel to the facet joints with confirmation of position at 50 Hz sensory stimulation achieved at 0.5 volts or less. 0.5 mL of lidocaine 1% was injected through each cannula to reduce thermal pain.	Radiofrequency was carried out for 90 seconds with an 80° C lesion.	55% of the patients who had at least 50%, but less than 80%, relief from diagnostic blocks had a successful procedure compared with 58% who experienced at least 80% relief from medial branch blocks.	Positive; however, conclusions may not be accurate since the only clinical variable associated with success was paraspinal tenderness, which is a non-specific finding. The sample was too small to differentiate between 80% and 50% relief (153).

Table 7 (cont.). *Study characteristics of randomized trials and observational studies of cervical radiofrequency neurotomy.*

Study/ Characteristics	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 months Long-term relief > 6 months
Macvicar et al, 2012 (129) Prospective	A total of 104 patients selected on the basis of complete relief of pain following controlled, diagnostic, medial branch blocks were treated with radiofrequency neurotomy. The study was performed at 2 centers in New Zealand. A heterogenous group of patients were included with suspicion of cervical zygapophysial joint pain. Patients were selected following the controlled comparative local anesthetic blocks with 100% pain relief concordant with duration of local anesthetic.	Radiofreqency neurotomy was performed by placing the needles parallel to medial branches, with creation of sufficient lesions in the sagittal and in an oblique plain, with 16-gauge 10 cm electrodes with 5 mm exposed tips. Radiofrequency was performed at 80° or 85° C for 90 seconds for each lesion.	Successful outcome was defined as complete relief of pain, or at least 80% relief, for at least 6 months, with complete restoration of activities of daily living, no need for any further health care, and return to work.	In the 2 practices, 74% and 61% of the patients achieved a successful outcome. Relief lasted 17 to 20 months from the first radiofrequency neurotomy and 15 months for repeat treatments. Patients maintained relief for a median duration of 20 to 26 months, with 60% still having relief at follow-up.	Positive This study was performed utilizing a rigorous criteria in a practical setting in New Zealand. Results are impressive.
Speldewinde, 2011 (142) Prospective	A total 151 procedures were performed in cervical spine on 130 patients. During the period from 2001 to 2010, patients were selected for radiofrequency thermal neurotomy in whom a diagnosis of cervical zygapophysial joint pain had been established with at least 2 fluoroscopically guided diagnostic medial branch nerve or intraarticular injections providing at least 80% relief in the index pain for the duration of the action of local anesthetic used.	Radiofrequency was performed at 80° for 90 seconds for medial branches.	Numeric Rating Scale, Functional Rating Index, Activities of Daily Living, General Health Questionnaire, psychiatric morbidity	Cervical radiofrequency neurotomy was successful in 76% of the patients. The outcomes were similar in all 3 regions. A significant proportion of patients had relief for longer than one year. Average pain relief was 12 months in the cervical spine with average of 88% pain relief.	Positive The study was performed in a community setting giving more of a practical setting in Australia. The study also utilized 80% pain relief with dual blocks as the criterion standard rather than 100% or 50%, which is an advantage.
Govind et al, 2003 (144) Prospective	Authors evaluated in a highly specialized center in Australia 49 patients diagnosed as suffering from third occipital headache on the basis on controlled diagnostic blocks of the third occipital nerve blocks.	Controlled diagnostic blocks with 2% lignocaine and 0.5% bupivacaine. Radiofrequency lesioning was performed at 80° for 90 seconds with multiple lesions at each level.	The criteria for successful outcome were complete relief of pain for least 90 days associated with restoration of normal activities of daily living, and no use of drug treatment for the headache.	88% achieved a successful outcome with a median duration of relief of 297 days. 14 of 49 patients (29%) underwent a repeat neurotomy to reinstate relief, with 12 (86%) achieving a successful outcome.	The study shows positive results without side effects with a revised technique of percutaneous radiofrequency neurotomy of third occipital headache; however, this study was performed in a highly specialized and sophisticated setting producing multiple lesions.

Table 8. *Study characteristics of randomized trials and observational studies of cervical facet joint nerve blocks.*

Study/ Characteristics	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 months Long-term relief > 6 months
RANDOMIZED					
Manchikanti et al, 2006, 2008, 2010 (51,52,126) Randomized, double-blind, active-control	120 patients were recruited from consecutive new patients presenting to an interventional pain management practice with neck pain without suspected disc herniation or radiculitis. All the patients have conservative management and were judged to be positive for facet joint pain utilizing controlled comparative local anesthetic blocks with 80% pain relief and ability to perform previously painful movements. Sixty patients received local anesthetic with steroid and another 60 patients received local anesthetics alone. 30 patients in each group also received Sarapin with local anesthetic and steroids.	Cervical medial branch nerve blocks with fluoroscopy were performed utilizing local anesthetic with or without Sarapin or steroid.	Measured numeric pain scores, Neck Pain index, opioid intake, and employment status at baseline, 3, 6, and 12 months. The procedures were repeated upon the return of pain and deterioration in functional status to less than 50%.	85% of the patients with local anesthetic only and 92% of the patients with steroid reported significant pain relief at 12 months, whereas the statistics were 85% and 93% for Group I and Group II at the end of 2 years. Functional status improvement of 50% or more by Neck Disability Index was seen in 63% and 68% at 12 months and 70% and 75% at 24 months in Group I and Group II.	Positive This is the first study conducted evaluating therapeutic medial branch blocks in a randomized double-blind fashion.
OBSERVATIONAL					
Manchikanti et al, 2004 (50) Prospective	100 consecutive patients meeting the diagnostic criteria of facet joint pain by means of comparative, controlled diagnostic blocks, with disabling chronic neck pain of various origins of at least 6 months duration and have failed conservative management were included.	Medial branch blocks with fluoroscopy with bupivacaine with or without methylprednisolone. Patients had repeat blocks as clinically indicated.	Pain relief, Oswestry Disability Index, psychological status, work status Timing: 3 months, 6 months, and 12 months	Significant pain relief at 3, 6, and 12 months, compared to baseline measurements. There was also significant improvement in disability status, psychological status, and return to work. Significant pain relief was observed at 92% at 3 months, 82% at 6 months, and 56% at 12 months.	Positive This was the first evaluation ever published in cervical spine evaluating the role of therapeutic cervical medial branch blocks.

Table 9. *Study characteristics of randomized trial of cervical intraarticular injections.*

Study/ Characteristics	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 months Long-term relief > 6 months
RANDOMIZED					
Barnsley et al ,1994 (49) Randomized, double-blind, active-control	41 patients with involvement of one or more cervical zygapophysial joints after automobile accidents with median duration of pain of 39 months were randomly assigned into 2 groups.	Intraarticular injection of 5.7 mg betamethasone or 1 mL intraarticular bupivacaine	Pain relief	No significant difference in duration of pain relief. Median duration of time to return of pain to 50% was 3 days in the steroid group and 3.5 days in the local anesthetic group.	Negative Authors injected local anesthetic or steroid into the joint, thus this is not placebo controlled, it is rather an active-control trial.
Park & Kim, 2012 (145) Randomized, active control	This randomized trial was conducted in Korea with recruitment of the patients from March 2002 to February 2008. They selected 200 patients in each group either with therapeutic medial branch blocks or conservative management. Patients were selected for therapeutic medial branch blocks if they were positive for facet joint pain utilizing dual diagnostic blocks.	Intraarticular injections were performed with 0.5 mL of 1% lidocaine and 5 mg of triamcinolone and 187.5 international units of hyaluronidase. Patients also received either Botox or trigger point injections if they required; however, these were of a small number.	Cervical range of motion, numeric rating scale for pain, comorbid tension type headache	Patients receiving intraarticular injections on one occasion showed increased cervical range of motion, increased mean numeric rating scale pain reduction, and decreased incidence of combined tension-type headache compared with control group receiving conservative management during the follow-up.	Undetermined This study shows positive results of intraarticular injections. The study is compounded with multiple deficiencies including trigger point injections and Botox injections in some patients. There was also higher than 20% withdrawal rate.

Table 10. *Methodological quality assessment of randomized trials.*

	Barnsley et al (49)	Manchikanti et al (51,52,126)	Lord et al (53)	Park & Kim (145)
Randomization adequate	Y	Y	Y	N
Concealed treatment allocation	Y	Y	Y	N
Patient blinded	Y	Y	Y	N
Care provider blinded	Y	Y	Y	N
Outcome assessor blinded	Y	N	Y	N
Drop-out rate described	Y	Y	Y	Y
All randomized participants analyzed in the group	Y	Y	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	Y	Y
Co-interventions avoided or similar	Y	Y	Y	Y
Compliance acceptable in all groups	Y	Y	Y	N
Time of outcome assessment in all groups similar	Y	Y	N	Y
Score	**12/12**	**11/12**	**11/12**	**6/12**

Y=yes; N=no; U=unclear

There were 3 randomized trials scoring high quality (49,51-53,126) and one trial scoring moderate quality (145).

A methodological quality assessment of the observational studies meeting inclusion criteria was carried out utilizing Newcastle-Ottawa Scales as illustrated in Tables 11 and 12. For cohort studies, studies achieving scores of 67% or higher were considered high quality; 50% or higher were considered as moderate quality; studies scoring less than 50% were considered low quality and were excluded.

For case-control studies, 67% or higher was considered as high quality, 50% or higher was considered as moderate quality, and less than 50% was considered low quality and those studies were excluded.

There were 6 observational studies (50,54,128,129,142,144) which were considered of moderate quality.

2.2 Clinical Relevance

of the 10 studies assessed for clinical relevance (49,50-54,126,128,129,142,144,145) with 3 duplicates (51,52,126), all studies met criteria with score of 3 of 5 or greater. Table 13 illustrates assessment of clinical relevance.

2.3 Meta-Analysis

No meta-analysis was feasible due to only one or 2 randomized trials in each category of radiofrequency neurotomy, medial branch nerve blocks, and intraarticular injections.

2.4 Analysis of Evidence

The evidence was synthesized based on the specific condition provided. Tables 14-16 illustrate the results of cervical facet joint interventions.

2.5 Summary of Evidence

In summary, the evidence is fair for radiofreqency neurotomy and therapeutic cervical medial branch blocks, whereas, it is limited for intraarticular injections.

3.0 Complications

Complications from intraarticular injections, or medial branch blocks or radiofrequency thermoneurolysis in the cervical spine are exceedingly rare (1,36,41-43,49-55,126,127,132-149,154-186). However, serious complications with cervical facet joint injections may occur. Complications include those related to placement of the needle, the temperature, and those related to the administration of various drugs.

Proximity of the needle to the vertebral artery, spinal cord, and nerve root creates risk for injury and makes precise and accurate needle placement exceedingly important. Complications may include dural puncture, spinal cord trauma, subdural injection, neural trauma, injection into the intervertebral foramen and intravertebral arteries; intravascular injection into veins or vertebral arteries; infectious complications including epidural abscess and bacterial meningitis; and side effects related to the administration of steroids, local anesthetics, and other drugs.

Okada (166) showed that in a series of cervical

Table 11. *Methodologic quality assessment of case control studies utilizing Newcastle-Ottawa quality assessment scale.*

	Sapir & Gorup (54)
Selection	
1) Is the case definition adequate?	X
a) yes, with independent validation *	
b) yes, e.g. record linkage or based on self reports	
c) no description	
2) Representativeness of the cases	
a) consecutive or obviously representative series of cases *	X
b) potential for selection biases or not stated	
3) Selection of Controls	
a) community controls *	X
b) hospital controls	
c) no description	
4) Definition of Controls	
a) no history of disease (endpoint) *	
b) no description of source	
Comparability	
1) Comparability of cases and controls on the basis of the design or analysis	
a) study controls for _____ (Select the most important factor.) *	X
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)	
Exposure	
1) Ascertainment of exposure	
a) secure record (eg surgical records) *	X
b) structured interview where blind to case/control status *	
c) interview not blinded to case/control status	
d) written self report or medical record only	
e) no description	
2) Same method of ascertainment for cases and controls	
a) yes *	X
b) no	
3) Non-Response rate	
a) same rate for both groups *	X
b) non respondents described	
c) rate different and no designation	
SCORE	7/12

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (88).

facet joint injections, a communicating pathway existed in 80% of subjects between the facet joint and interlaminar space, the opposite facet joint, extradural space, and interspinous space when volumes in excess of 1 mL were used. Others (156) also have shown that extraarticular leaks have been observed in up to 7% of the cases, even with low volumes.

Manchikanti et al (183) in a prospective, non-ran-

Table 12. *Methodological quality assessment of cohort studies utilizing Newcastle-Ottawa quality assessment scale.*

	Manchikanti et al (50)	Cohen et al (128)	Macvicar et al (129)	Speldewinde (142)	Govind et al (144)
Selection					
1) Representativeness of the exposed cohort					
a) truly representative of the average _____ (describe) in the community	X	X	X	X	X
b) somewhat representative of the average pain patients in the community					
c) selected group of users e.g. nurses, volunteers					
d) no description of the derivation of the cohort					
2) Selection of the non exposed cohort					
a) drawn from the same community as the exposed cohort *	X	X	X	X	X
b) drawn from a different source					
c) no description of the derivation of the non exposed cohort					
3) Ascertainment of exposure					
a) secure record (eg surgical records) *	X	X	X	X	X
b) structured interview *					
c) written self report					
d) no description					
4) Demonstration that outcome of interest was not present at start of study					
a) yes *	X	X	X	X	X
b) no					
Comparability					
1) Comparability of cohorts on the basis of the design or analysis					
a) study controls for _____ (select the most important factor)*					
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)					
Outcome (Exposure)					
1) Assessment of outcome					
a) independent blind assessment *					X
b) record linkage *	X	X	X	X	
c) self report					
d) no description					
2) Was follow-up long enough for outcomes to occur					
a) yes (select an adequate follow up period for outcome of interest)*	X	X	X	X	X
b) no					
3) Adequacy of follow up of cohorts					
a) complete follow up - all subjects accounted for *					
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost)*	X	X	X	X	X
c) follow up rate < ____% (select an adequate %) and no description of those lost					
d) no statement					
SCORE	**7/12**	**7/12**	**7/12**	**7/12**	**7/12**

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (88).

Table 13. *Clinical relevance of included studies.*

Manuscript Author(s)	A) Patient description	B) Description of interventions and treatment settings	C) Clinically relevant outcomes	D) Clinical importance	E) Benefits versus potential harms	Total Criteria Met
Barnsley et al (49)	+	+	+	+	+	5/5
Manchikanti et al (50)	+	+	+	+	+	5/5
Manchikanti et al (51,52,126)	+	+	+	+	+	5/5
Lord et al (53)	+	+	+	+	+	5/5
Sapir & Gorup (54)	+	+	+	+	+	5/5
Cohen et al (128)	+	+	+	–	+	4/5
Macvicar et al (129)	+	+	+	+	+	5/5
Speldewinde (142)	+	+	+	+	+	5/5
Govind et al (144)	+	+	+	+	+	5/5
Park & Kim (145)	+	+	+	+	+	5/5

+ = positive; - = negative; U = unclear

Scoring adapted from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (87).

Table 14. *Results of randomized trials and observational studies of cervical conventional radiofreqency neurotomy.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief			Results	
				3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 months	Long-term relief > 6 months
Lord et al, 1996 (53)	RA, Sham control, DB	11/12	24	NA	1 of sham 7 of active	58% in active treatment group	P	P
Sapir and Gorup, 2001 (54)	P	7/12	46	NA	NA	Mean VAS change 4.6 ± 1.8	P	P
Macvicar et al, 2012 (129)	P	7/12	104	NA	74% & 61%	74% & 61%	P	P
Speldewinde, 2011 (142)	P	7/12	130	NA	76%	76%	P	P
Govind et al, 2003 (144)	P	7/12	49	NA	88%	88%	P	P
Cohen et al, 2007 (128)	R	7/12	92	NA	55%	55%	P	P

RA = randomized; DB = double-blind; P = prospective; R = retrospective; vs = versus; P = positive

Table 15. *Results of randomized trials and observational studies of cervical facet joint interventions.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief			Results	
				3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 months	Long-term relief > 6 months
Manchikanti et al, 2008, 2010, 2006 (51,52,126)	RA, DB, AC	11/12	Group I-no steroid = 60 Group II-steroid = 60	83% versus 85%	87% versus 95%	85% versus 92%	P	P
Manchikanti et al, 2004 (50)	P	7/12	100	92%	82%	56%	P	P

RA = randomized; DB = double-blind; AC = active-control; P = prospective; P = positive

Table 16. *Results of randomized trials of cervical intraarticular injections.*

Study	**Study Characteristics**	**Methodological Quality Scoring**	**Participants**	**Pain Relief**			**Results**	
				3 mos.	**6 mos.**	**12 mos.**	**Short-term relief ≤ 6 months**	**Long-term relief > 6 months**
Park & Kim, 2012 (145)	RA, AC	6/12	200	SPP	SPP	SPP	U	U
Barnsley et al, 1994 (49)	RA, DB, AC	12/12	41	20%	20%	20%	N	N

RA = randomized; DB = double-blind; AC = active-control; SPP = significant proportion of patients; N = negative; U = Unclear

domized study of patients undergoing interventional techniques from May 2008 to December 2009 investigated the incidence in characteristics of adverse effects and complications of facet joint nerve blocks. The study was carried out over a period of 20 months including almost 7,500 episodes of 43,000 facet joint nerve blocks with 3,370 episodes in the cervical region. The results showed there were no major complications. Multiple side effects and complications observed included overall intravascular penetration in the cervical region of 20%, local bleeding in 66.9%, oozing with 28.9% of encounters, local hematoma seen only in 2.3% of the patients with profuse bleeding, bruising, soreness, nerve root irritation, and all other effects such as vasovagal reactions observed in 1% or less of the episodes. They concluded that the study illustrated that major complications are extremely rare and minor side effects are common.

Vertebral artery and ventral ramus damage, along with a risk of embolus resulting in serious neurological sequelae with spinal cord damage and cerebral infarction, are exceedingly rare, but are potential complications with cervical facet joint injections.

Other minor complications include lightheadedness, flushing, sweating, nausea, hypotension, syncope, pain at the injection site, and headaches. Side effects related to the administration of steroids are generally attributed to the chemistry or to the pharmacology of the steroids (1,163). These include suppression of pituitary-adrenal axis, hyperadrenocorticism, Cushing's syndrome, osteoporosis, avascular necrosis of the bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia.

Reported complications of radiofrequency thermoneurolysis include a worsening of the usual pain, burning or dysesthesias, decreased sensation and allodynia in the skin in the region of the facets denervated, transient leg pain, persistent leg weakness, and inadvertent lesioning of the spinal nerve or ventral ramus resulting in motor deficits, sensory loss, and deafferentation pain.

A spinal cord lesion can lead to quadriplegia, motor weakness, loss of proprioception and sensory function, bowel and bladder dysfunction, Brown-Sequard syndrome, and spinal cord infarction.

4.0 Discussion

The evidence for radiofrequency neurotomy is fair based on one high quality randomized trial (53) and multiple moderate quality observational studies (54,128,129,142,144). The evidence for therapeutic medial branch blocks is fair based on one high quality randomized trial (51,52,126) and one moderate quality observational study (50). However, the evidence for intraarticular injections is poor. The results showed no change from the previous review (36), based on 2 randomized trials (49,145) with one high quality randomized trial (49) showing negative evidence and one moderate quality randomized trial (145) showing undetermined results.

Even though there are multiple studies evaluating various aspects of cervical facet joint interventions, most studies failed to meet the inclusion criteria. In addition, the evidence appears to be the best when the patients are selected with controlled local anesthetic blocks specifically utilizing 80% or high pain relief as the criterion standard. However, this aspect has not been systematically evaluated in the cervical spine. Similar to previous evaluations, radiofreqency neurotomy showed significant evidence even though it has not reached the good evidence level due to the lack of high quality randomized trials for both short-term and long-term improvement. Similarly, therapeutic medial branch blocks also continue to show fair evidence with limited high quality randomized trials. Further, intraarticular injections continue to show limited evidence even though there was an additional moderate quality randomized trial (145), which is opposed by a high quality randomized trial (49) revealing negative results. Thus, the evidence from this systematic review, applying contemporary and strict criteria with robust outcomes, provides appropriate and sound guidance in managing chronic cervical facet joint pain in practical settings.

The results of this systematic review are similar to some previous systematic reviews (36,40), while it is discordant with others (47,150). Further, this is updated evidence using the latest trials with strict adherence to systematic assessment of the evaluation. Disappointingly, there were not enough homogenous studies to provide meta-analysis in an appropriate manner. In this systematic assessment, one randomized trial and 5 observational studies were included in assessing the effectiveness of radiofrequency neurotomy. The randomized trials pertain to Lord et al's (53) percutaneous radiofrequency neurotomy study published in 1996. This randomized, double-blind clinical trial includes 24 patients comparing percutaneous radiofrequency neurotomy to a sham treatment wherein the procedural technique was the same but radiofrequency was not applied in the control group. Patients with cervical spine pain from automobile accidents were included in the study after comparative diagnostic blocks identified those with cervical facet joint derived neck pain. At 3 months all patients were formally interviewed by completing the visual analogue scale and the McGill Pain Questionnaire. At 27 weeks, one patient in the control group and 7 in the active treatment group remained free of pain. The median time for return of pain to at least 50% of the preoperative level was 263 days in the active group and 8 days in the placebo group. This study found that radiofrequency neurotomy can provide pain relief for a moderate proportion of patients lasting from months to over a year.

This is a meticulously performed study on a small number of patients; however, the technique is not commonly utilized in the United States. Carragee et al (150) criticized the differences in baseline characteristics of patients among both groups and the nature of the blinding. Carragee et al (150) reported that blinding was in doubt, as 42% of the active group developed long-term anesthetic or dysesthetic areas of skin and none of the patients in the control group developed changes. They stated that these changes revealed the treatment assigned in nearly half of the active treatment group. With regards to the baseline characteristics the results showed no significant differences based on these differences and also based on litigation. The results showed that 58% of patients in the control group and 25% in the active-treatment group had a return of their accustomed pain in the period immediately after the radiofrequency procedure at the 3-month follow-up. Lord et al (53) were unable to avoid such an issue and in fact, this is a problem with any of the sham procedures in interventional pain management. In fact, Dreyfuss and Baker (151) supported Lord et al (53) for maintaining blinding of subjects admirably well and the evidence of the difficulty of performing such a study is demonstrated by an extremely limited number of published sham studies involving an invasive treatment. However, Carragee et al (152) maintained their criticism. The small number of patients included in this study also has been an issue; however, the study met inclusion criteria.

All other radiofrequency neurotomy studies were of observational nature. Sapir and Gorup (54) in 2001 examined the efficacy of radiofrequency medial branch

neurotomy to treat cervical zygapophysial joint pain from whiplash in an observational study comparing the results of litigants and non-litigants. All patients were involved in an automobile accident at least 20 weeks prior to inclusion in the study and had failed conservative treatment. Those subjects with a positive response to confirmatory diagnostic blocks were enrolled into the study and divided into groups of litigants and non-litigants. Pain was evaluated prior to treatment based on the Visual Analogue Scale as well as other outcome measures such as self-report of improvement and change in medication usage. The administration of all questionnaires to the subjects was blind to their legal status, but the treatment operator was not blind to the legal status of the patient. Fifty patients were included in the study meeting the criterion of at least 80% pain relief from comparative diagnostic blocks and underwent radiofrequency neurotomy. Forty-six patients completed the study consisting of 29 (63%) litigants and 17 (37%) non-litigants. Twenty-one patients (14 litigants and 7 non-litigants) reported a recurrence of pain within one year and 25 patients (15 litigants and 10 non-litigants) remained asymptomatic at one year. Time to pain recurrence defined as 50% return of pain was approximately 8.3 ± 2.3 months in the 21 patients whose pain returned within one year. There was an overall VAS pain reduction of 4.6 ± 1.8 from radiofrequency neurotomy at one year with a small but statistically significant difference with litigants having a slightly greater reduction in pain. There were no clinically discernible treatment outcome differences between the litigant and non-litigant groups. In this study radiofrequency neurotomy of cervical facet joint neck pain was found to be an effective treatment for chronic cervical whiplash independent of litigation.

The results of the observational study by Cohen et al (128) showed the only clinical variable associated with success was paraspinal tenderness. Factors associated with treatment failure included radiation to the head, opioid use, and pain exacerbated by neck extension and/or rotation. They concluded that selecting patients based on key clinical variables may increase the chance of treatment success for cervical facet radiofrequency denervation.

The results of the study by MacVicar et al (129) showed that in the 2 practices, 74% and 61% of patients achieved a successful outcome. Relief lasted 17-20 months from the first radiofrequency, and 15 months for repeat treatments. Allowing for repeat treatment, patients maintained relief for a median duration of 20-26 months, with some 60% still having relief at follow-up. They concluded that cervical radiofrequency can be very effective when performed in a rigorous manner in appropriately selected patients. Chronic neck pain, mediated by the cervical medial branches, can be temporarily, but completely, relieved and patients fully restored to desired activities of daily living, if treated with radiofrequency neurotomy.

The results of the study by Speldewinde (142) showed that of 379 procedures, 272 (72%) were regarded as successful by the patients, irrespective of region treated. The results were highly significant by t-test, and the effect size was large as determined by the Cohen's d. Adverse events were infrequent and relatively minor. Repetitions of the procedure were highly successful. They concluded that neurotomy of the cervical, thoracic, lumbar, and sacroiliac joints were uniformly successful with 72% recipients obtaining an average of 86% reduction in pain for a period of 12 months.

Govind et al (144) evaluated radiofrequency neurotomy for the treatment of third occipital headache with a revised technique using a large gauge electrode ensuring minimum separation between the 3 electrode placements, and holding the electrode in place by hand. The revised technique was used to treat 51 nerves in 49 patients diagnosed as suffering from third occipital headache on the basis of controlled diagnostic blocks of the third occipital nerve. The criteria for successful outcome was complete relief of pain for at least 90 days associated with restoration of normal activities of daily living, and no use of drug treatment for headache. of the 49 patients, 43 (88%) achieved a successful outcome. The median duration of relief in these patients was 297 days, with 8 patients continuing to have ongoing relief. Fourteen patients underwent a repeat neurotomy to reinstate relief with 12 (86%) achieving a successful outcome with a median duration of relief in these patients of 217 days, with 6 patients having ongoing relief. This revised technique apparently improved the success rate greatly compared to the previous technique by Lord et al (143).

Among the excluded studies, the studies by McDonald et al (55) and Barnsley (127) are noteworthy as they showed significant progress on a long-term basis, even though they failed to meet the inclusion criteria. Thus, radiofrequency neurotomy showed fair evidence overall even though described as fair on the strict criteria.

In reference to medial branch blocks, 2 manuscripts were published by the same group of authors, a high quality randomized trial (51,52,126) and a moderate

quality observational study (50).

The outcome results of the randomized, double-blind controlled trial of therapeutic cervical medial branch nerve blocks in patients with function-limiting chronic neck pain showed significant improvement with decreased pain and improvement in functional status at completion of the 2-year follow-up in 85% of patients treated with local anesthetic only and 93% of the patients with local anesthetics and steroids (51,52,126). Over a period of 2 years, the average pain relief per procedure ranged from 17 to 19 weeks, with an average number of procedures of 5.7 with total relief of 83 ± 27.5 weeks in Group I and 89 ± 21.1 weeks in Group II. Opioid intake and employment status showed clinically important improvement, though it was not statistically significant. The results of this study were similar to lumbar and thoracic facet joint nerve blocks (105,117,118). There were no other studies available, either observational or randomized, evaluating the therapeutic outcomes of cervical medial branch blocks with a long-term follow-up of at least 2 years.

This randomized trial (51,52,126) was designed to reflect everyday clinical practice. The authors found that the 2 drugs used in combination with a local anesthetic, namely Sarapin, and a steroid did not differ significantly in their response. The small differences between the 2 treatments were unlikely to be of clinical importance even in larger studies. This is one of the largest studies with the longest follow-up of an interventional technique, specifically for facet joint nerve blocks, in managing chronic neck pain. This study resolves the issue of the addition of Sarapin and a steroid to local anesthetic to therapeutic cervical medial branch blocks.

The observational study by Manchikanti et al (50) also showed significant improvement differences in numeric pain scores and significant pain relief (50% or greater) at 3 months, 6 months, and 12 months, compared to baseline measurements. Functional improvement was demonstrated at 12 months from baseline. There was significant improvement with an increase in employment among the patients eligible for employment (employed and unemployed) from baseline to 12 months, and improved psychological functioning.

In reference to therapeutic intraarticular injections, the 2 studies showed contradictory results. The one high quality study by Barnsley et al (49) showed rather negative results, whereas one moderate quality randomized trial (145) showed undetermined results. It is rather surprising that one single intraarticular steroid injection provided significant relief for as long as one year. However, this study has numerous flaws and was not of high quality.

Multiple problems related to interventional techniques include the role of steroids versus local anesthetic, placebo response, and technical aspects in performing a procedure. Overall there is no significant evidence that steroids provide long-term relief compared to local anesthetic only. For medial branch blocks, there has been lack of additional effectiveness with the addition of a steroid (50-52,105,126,142,143).

The lack of additional effectiveness with the addition of a steroid beyond the effect provided by local anesthetic blocks with bupivacaine provides information that there is no significant role for steroids in cervical medial branch blocks. The basis for intraarticular injections has been that there is inflammation and steroids are used to treat the inflammation. The literature is replete with descriptions of epidural corticosteroids providing a certain level of efficacy by their anti-inflammatory, immuno-suppressive, anti-edema effects and inhibition of neurotransmission within the C-fibers (105-121,187-195). Similarly, local anesthetics also have been described to provide long-term symptomatic relief, even though the mechanism of this relief remains an enigma. It has been postulated that local anesthetics provide relief by suppression of nociceptive discharge (196), the block of the axonal transport (197,198), the block of the sympathetic reflex arc, the block of sensitization (199,200), and anti-inflammatory effects (201). The long-term effectiveness of local anesthetics has been shown in a host of previous studies following local anesthetic nerve blocks or epidural injections (187-195).

Lack of placebo in active control trials is a major misunderstanding and a limitation. However, the placebo control has been misunderstood in many cases. The reviewers have considered a local anesthetic injection as a placebo control, thus it is a well known fact that placebo control in any neural blockade is a difficult task. Further, it also adds ethical issues and difficulty with recruitment in the United States. However, multiple investigations performed in interventional pain management with descriptions of placebo control have been met with design flaws (202-210). The effect of any solution injected into a closed space such as an intraarticular space or epidural space or over a nerve has not been appropriately evaluated. Carrette et al (187,188), in widely acclaimed studies, showed that patients responded similarly to an intraarticular injection or epidural injection whether it contained a

sodium chloride solution or local anesthetic with a steroid; however, the response was low in both groups. Thus, their study (187) shows that sodium chloride solution injected into an intraauricular space has similar effects as local anesthetic with a steroid; the conclusion is that intraarticular steroids are not an effective therapy. The issue is also exemplified by Birkenmaier et al (211), utilizing either pericapsular injections or medial branch blocks, who went on to perform cryoneurolysis. Not surprisingly, the results were superior in patients who were diagnosed using medial branch blocks rather than pericapsular injections of local anesthetic. This study was the basis for Chou and Huffman (86) to discard the value of diagnostic lumbar facet joint nerve blocks. In addition, the literature shows differing effects with injections of various solutions such as local anesthetic, normal saline, or dextrose and also shows differing effects by injection into the disc, facet joint, or multifidus muscle (212-219). It has been shown that a small volume of local anesthetic or normal saline abolishes muscle twitch induced by a low current (0.5 mA) during electrode location (212-215). Further, there is direct evidence for spinal cord involvement in placebo analgesia (216). It also has been shown that epidurally administered sodium chloride solution provides significant improvement in the pain and function (220-222). The evidence cited above leads to the conclusion that the effect of local anesthetic on cervical facet joint nerve blocks cannot be attributed to placebo effect, even though some have mistakenly misinterpreted this to be the case for facet joint nerve blocks (204,205,223,224). Placebo effects are not expected to be seen in a high proportion of patients, nor are they expected to be long lasting with repeat interventions over a period of 2 years. However, the limitations of the lack of placebo must not be underestimated. If feasible, a placebo-controlled study with appropriate design that includes not injecting the placebo solution over the facet joint nerves, and subsequent results, would be highly valid and provide conclusive knowledge on the issue of placebo-controlled blocks. The issues related to placebo have been discussed extensively in recent years ultimately leading to the opinion that placebo effect is an inconsistent measure in clinical studies, unless it is designed appropriately (225-234).

Another issue is related to the reliability of the controlled, comparative local anesthetic blocks, which have been criticized, and their validity as precision diagnostic techniques has been questioned and debated (202,203,235-239). The issues related to the accuracy of diagnostic facet joint nerve blocks include the reference standard, prior exposure to opioids, sedation, systemic local anesthetic effect, and non-specific effect resulting in positive results (27,28,30,31,36,130,131,240-242). The validity of controlled facet joint nerve blocks as a gold standard or reference standard in the diagnosis of lumbar facet joint pain has been established (243,244). Reference standard is established in surgical situations via biopsy or autopsy. However, these are difficult to apply in the diagnosis of chronic spinal pain of facet joint origin. Thus, the long-term or dedicated clinical follow-up of the subjects appears to be the only solution in establishing a reference standard with controlled facet joint nerve blocks (245). Based on the criterion standard of long-term follow-up, controlled diagnostic lumbar facet joint nerve blocks have been shown to be valid utilizing the criteria of 80% pain relief and the ability to perform previously painful movements, with a sustained diagnosis of lumbar facet joint pain in at least 89.5% of the patients at the end of 2-year follow-up (243). However, the diagnosis was sustained in only 51% of the patients with 50% relief at the end of 2 years (243). Thus, the controlled diagnostic blocks utilized in this study appear to be reliable.

Overall the results of this systematic review are applicable to real world settings describing patients in real world settings; however, the results are not applicable unless controlled diagnostic blocks are performed prior to therapeutic modalities.

5.0 Conclusion

Based on the review of the included therapeutic studies described herein, the indicated evidence for cervical radiofrequency neurotomy is fair. The indicated evidence for cervical medial branch blocks is fair. The indicated evidence for cervical intraarticular injections with local anesthetic and steroids is limited.

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