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Systematic Review

The Effectiveness of Medial Branch Blocks and Radiofrequency Neurotomy in Managing Chronic Thoracic Pain: A Systematic Review and Meta-Analysis

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Background: Extensive research into potential sources of thoracic pain with or without referred pain into the chest wall has demonstrated that thoracic facet joints can be a potential source of pain confirmed by precise, diagnostic blocks.

The objective of this systematic review and meta-analysis is to evaluate the effectiveness of medial branch blocks and radiofrequency neurotomy as a therapeutic thoracic facet joint intervention.

Methods: Systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies of medial branch blocks and the radiofrequency neurotomy in managing thoracic pain utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was performed. A comprehensive literature search of multiple databases of RCTs and observational studies of medial branch blocks and radiofrequency neurotomy in managing chronic thoracic pain were identified from 1996 to December 2022 with inclusion of manual searches of the bibliography of known review articles and multiple databases. Methodologic quality and risk of bias assessment was also conducted. Evidence was synthesized utilizing principles of quality assessment and best evidence synthesis, with conventional and single meta-analysis.

The primary outcome measure of success was 3 months of pain reduction for medial branch blocks and 6 months for radiofrequency thermoneurolysis for a single treatment. Short-term success was defined as up to 6 months and long-term was more than 6 months.

Results: This literature search yielded 11 studies meeting the inclusion criteria, of which 3 were RCTs and 8 were observational studies. Of the 3 RCTs, 2 of them assessed medial branch blocks and one trial assessed radiofrequency for thoracic pain.

The evidence for managing thoracic pain with qualitative analysis and single-arm meta-analysis and GRADE system of appraisal, with the inclusion of 2 RCTs and 3 observational studies for medial branch blocks was Level II.

For radiofrequency neurotomy, with the inclusion of one RCT of 20 patients in the treatment group and 5 observational studies, the evidence was Level III in managing thoracic pain.

Limitations: There was a paucity of literature with RCTs and real-world pragmatic controlled trials. Even observational studies had small sample sizes providing inadequate clinically applicable results. In addition, there was heterogeneity of the available studies in terms of their inclusion and exclusion criteria, defining their endpoints and the effectiveness of the procedures.

Conclusion: This systematic review and meta-analysis show Level II evidence of medial branch blocks and Level III evidence for radiofrequency neurotomy on a long-term basis in managing chronic thoracic pain.

Key words: Chronic spinal pain, thoracic facet or zygapophysial joint pain, facet joint nerve blocks, medial branch blocks, controlled comparative local anesthetic blocks, diagnostic accuracy, radiofrequency neurotomy

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Escalating morbidity and chronic disability account for almost 50% of the US healthcare burden, with low back and neck pain ranking as number one and three among the 30 leading causes and injuries (1-4). The healthcare burden is exacerbated by ever increasing costs as shown by Dieleman et al (5,6) with an estimated 53.5% increase in spending from $87.6 billion in 2013 to $134.5 billion in 2016 to manage low back and neck pain, which accounted for the highest amount of various disease categories. Among chronic pain disorders, the lifetime prevalence of chronic persistent spinal pain is reported in 25% to 60% of patients for at least one year, and even longer following an initial episode (3). Chronic axial spinal pain with or without extremity pain, chest wall pain or headache is one of the major causes of disability and healthcare costs. Historically, the focus has been on pain generators related to low back and neck. In fact, Linton et al (7) estimated the prevalence of thoracic pain in 15% of the general population in contrast to 56% in the low back and 44% in the neck. These findings were reinforced by other studies, including the study by Leboeuf-Yde et al (8) showing the prevalence of low back pain in the past year was most frequent in low back at 43%, followed by neck pain in 32%, and mid back pain in 13%. Historically, the causes of thoracic pain have not been studied as well as for the lumbar and cervical spine. Consequently, the role of thoracic facet joints as a causal chronic upper or mid back pain has received very little attention with only a few early publications discussing these joints as the source of pain (9-13). The initial descriptions of involvement of thoracic facet joints as a cause of chronic mid and upper back pain was provided in 1987 by Wilson questioning whether the thoracic facet in joint syndrome is a clinical entity (9). Subsequently, thoracic facet joint pain patterns were described by Dreyfuss et al (10) in 1994 and by Fukui et al (11) in 1997. Percutaneous facet denervation in chronic thoracic spinal pain was described by Stolker et al (13). Overall, the proportion of patients suffering from chronic upper or mid back pain secondary to thoracic disorders is relatively small, specifically in interventional pain management settings, ranging from 3% to 22% (12,13). An additional problem is related to the fact that thoracic procedures as the procedure codes are the same whether the procedures are performed in the cervical or thoracic spine as the cervical and thoracic spine is considered as one region (14). Conventional clinical and radiologic techniques are unreliable in diagnosing facet or zygapophysial joint pain (3). Consequently, controlled local anesthetic blocks of thoracic facet joints with medial branch blocks have shown a prevalence of thoracic facet joint pain in chronic pain as 34% to 48% of patients, with false positive rates of 42% to 48% in chronic mid back and upper back pain (3,15-17).

In recent years, multiple publications have shown emerging concepts in diagnosis (18,19) and management of lumbar and cervical facet joint pain (20,21). Systematic reviews have emphasized multiple of these aspects (22,23). The overall emerging evidence shows an approach of chronic pain model in the diagnosis of facet joint pain (18,19) with a double block paradigm and noninferiority of facet joint nerve blocks to radiofrequency neurotomy with lesser complications and higher success rate, even though the number of procedures performed are twice the number of radiofrequency neurotomy procedures (3,20,21). In one RCT (24) evaluating the comparative value of local anesthetic blocks with radiofrequency neurotomy in patients with clinically diagnosed cervical facet joint pain, pain treatment success of 61.1% was reported in both groups, either with local anesthetic alone or with local anesthetic and radiofrequency neurotomy at 3 months, whereas similar pain relief was reported in 55.6% in the denervation group and 51.3% in the bupivacaine alone group at 6 month follow-up with no significant difference among the groups, reinforcing long-term relief of local anesthetic medial branch blocks.

In addition, related to escalating utilization patterns of facet joint and other interventions (25-33), multiple local coverage determinations (LCDs) have been enacted (34). The study of utilization patterns of interventional techniques (26) has shown an increase of cervical and thoracic facet joint interventions to be 0.7% annually from 2010 to 2019, compared to a 0.3% decrease of lumbar facet joint interventions (26). A significant decrease was also noted related to the COVID-19 pandemic from 2019 to 2020 with 18.2% for cervicothoracic interventions and 18.5% for lumbar facet joint interventions. These changes in utilization patterns indicate lesser declines for cervicothoracic interventions compared to lumbosacral facet joint interventions and epidural injections (25-32).

Apart from various conservative modalities of treatments, medial branch blocks and radiofrequency neurotomy have been described as effective modalities of treatments after failure of conservative management in managing chronic mid back and upper back pain originating from thoracic facet joints (3). Even though available evidence has been assessed systematically (3,35-49),

the paucity of literature is obvious. Guidelines published in 2020, which performed systematic review without meta-analysis, showed Level II evidence with moderate strength of recommendation for thoracic facet joint nerve blocks with inclusion of 2 randomized controlled trials (RCTs) (38-40) and 3 observational studies (37,41,48) with long-term improvement. In contrast, the level of evidence was Level III with weak to moderate strength of recommendation with emerging evidence for thoracic radiofrequency ablation (RFA) with inclusion of one relevant RCT (42) and 3 observational studies (43,44,48). However, the level of evidence for thoracic intraarticular facet joint injections was even weaker with Level III with weak to moderate strength of recommendation with inclusion of one RCT with 6-month follow-up (40).

Consequently, the present systematic review and meta-analysis of RCTs and observational studies was undertaken to assess the updated review of thoracic medial branch nerve blocks and radiofrequency neurotomy in managing chronic thoracic spinal pain. Intraarticular injections were not included as there was only one RCT available for review with no observational studies.

Methods

A systematic review and meta-analysis were performed based on methodological and reporting quality of systematic reviews as described by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (50). Methodology from other reviews was also utilized (22,23,51-55).

Eligibility Criteria

RCTs and observational studies of therapeutic medial branch blocks and radiofrequency neurotomy with at least 3 months of follow-up for medial branch blocks and 6 months of follow-up for radiofrequency thermoneurolysis were included in this study. The studies with appropriate diagnosis established by diagnostic blocks or clinical diagnosis were included.

Studies without an appropriate diagnosis and case reports were excluded.

Information Sources

A comprehensive literature search was conducted to include randomized control trials published from all countries and in all languages. Searches were performed from the following sources without language restrictions.

1. PubMed from 1966 https://pubmed.ncbi.nlm.nih.gov/
2. Cochrane Library https://www.cochranelibrary.com/
3. Google Scholar https://scholar.google.com/
4. US National Guideline Clearinghouse (NGC) https://www.ahrq.gov/gam/index.html
5. Clinical Trials https://www.clinicaltrials.gov/
6. Previous systematic reviews and cross-references
7. All other sources including non-indexed journals and abstracts

The search period was from 1966 through December 2022

Search Strategy

The search strategy emphasized chronic thoracic pain treated with thoracic facet joint interventions. The search terms included: ((((((spinal pain, chronic mid back and upper back pain) OR chronic thoracic pain OR chronic back pain) OR facet joint pain) OR post thoracic surgery syndrome) OR zygapophysial)) AND ((((facet joint) OR zygapophyseal) OR zygapophysial) OR medial branch block OR intraarticular injection OR radiofrequency neurotomy) OR radiofrequency ablation.

Data Selection

In the identification of the relevant literature, the article selection and extraction of the data from the included studies was conducted independently, by 3 review authors (NNK MRS, RNJ). Any disagreements among the reviewer authors were resolved by the fourth author (ADK). All conflicts of interest of the reviewers with authorship of the article were resolved by assigning them to other reviewers.

Methodological Quality and Risk of Bias Assessment

RCTs were assessed for their quality or risk of bias methodologically with Cochrane review criteria (Appendix Table 1) (56), Interventional Pain Management Techniques–Quality Appraisal of reliability and Risk of Bias Assessment (IPM-QRB) (Appendix Table 2) (57), and Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies (IPM-QRBNR) was utilized for observational studies, as shown in Appendix Table 3 (58).

Risk of Bias and Methodologic Quality of Individual Studies

Trials that met the inclusion criteria and scored at least 9 of 13 using Cochrane review criteria (56) were considered high quality, while trials scoring 5-8 were

considered of moderate quality. Trials that scored less than 5 were considered of low quality and were excluded from the analysis.

Trials meeting the inclusion criteria were also assessed with IPM-QRB criteria (57). Studies scoring 32-48 were considered of high quality, those scored 16-31 were of moderate quality and those that scored below 16 were considered of low quality and were excluded from the analysis.

Based on IPM-QRBNR criteria (58), studies meeting the inclusion criteria but scoring less than 16 were considered low-quality and were excluded, studies scoring from 16 to 31 were considered moderate quality; and studies scoring from 32 to 48 were considered high-quality and were included.

The methodological quality of the trials was assessed by two authors, independently in an unblinded manner. If a discrepancy occurred, a third author was involved to resolve the conflict. When an issue of conflict of interest was raised in reviewing the manuscript (regarding authorship), the involved authors were not allowed to review those manuscripts for quality assessment.

Analysis of Evidence

At least two of the review authors (NNK, EK) independently, in a standardized manner, analyzed the evidence. Any disagreements between reviewers were resolved by two authors (MRS and ADK) and consensus was attained.

If there were any conflicts of interest (e.g., authorship), the reviewer of interest (LM) was recused from assessment and analysis.

Outcome Measures

An outcome is considered clinically significant if there is a reduction of 2 points on the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS), or at least 50% reduction in pain and improvement in the functional status. A positive study is said to be clinically significant and effective indicating that the primary outcome should be statistically significant at a *P*-value ≤ 0.05.

Qualitative Analysis of Evidence

The qualitative analysis of the evidence was performed based on best-evidence synthesis, modified, and collated using multiple criteria, including the Cochrane Review criteria and United States Preventive Services Task Force (USPSTF) criteria as illustrated in Table 1 (59). The analysis was conducted using five levels of evidence ranging from strong to opinion- or consensus-based.

Quantitative Analysis of Evidence

Quantitative evidence synthesis was performed utilizing conventional meta-analysis and a single-arm meta-analysis.

Software Review Manager (Rev Man 5.4) was used (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2008) for conventional or dual-arm meta-analysis.

Software Comprehensive Meta-Analysis Version 3.0 was used (Biostat Inc., Englewood, NJ) for single-arm meta-analysis.

The standardized mean differences (SMD) with 95% confidence intervals (CI) were reported for pain and improvement of function data.

Data were plotted by using forest plots to evaluate treatment effects. Heterogeneity was interpreted through I^2 statistics.

Results

Literature Search

The flow diagram based on 2020 PRISMA guidance (50) illustrates the search results and the final number of studies that were considered for inclusion (Fig. 1).

Table 1. *Qualitative modified approach to grading of evidence of therapeutic effectiveness studies*.

Level I	Strong	Evidence obtained from multiple relevant high-quality randomized controlled trials
Level II	Moderate	Evidence obtained from at least one relevant high-quality randomized controlled trial or multiple relevant moderate or low-quality randomized controlled trials
Level III	Fair	Evidence obtained from at least one relevant moderate or low-quality randomized trial or Evidence obtained from at least one relevant high-quality non-randomized trial or observational study with multiple moderate or low-quality observational studies
Level IV	Limited	Evidence obtained from multiple moderate or low-quality relevant observational studies
Level V	Consensus based	Opinion or consensus of large group of clinicians and/or scientists

Modified from: Manchikanti L, et al. A modified approach to grading of evidence. Pain Physician 2014; 17:E319-E325 (59).

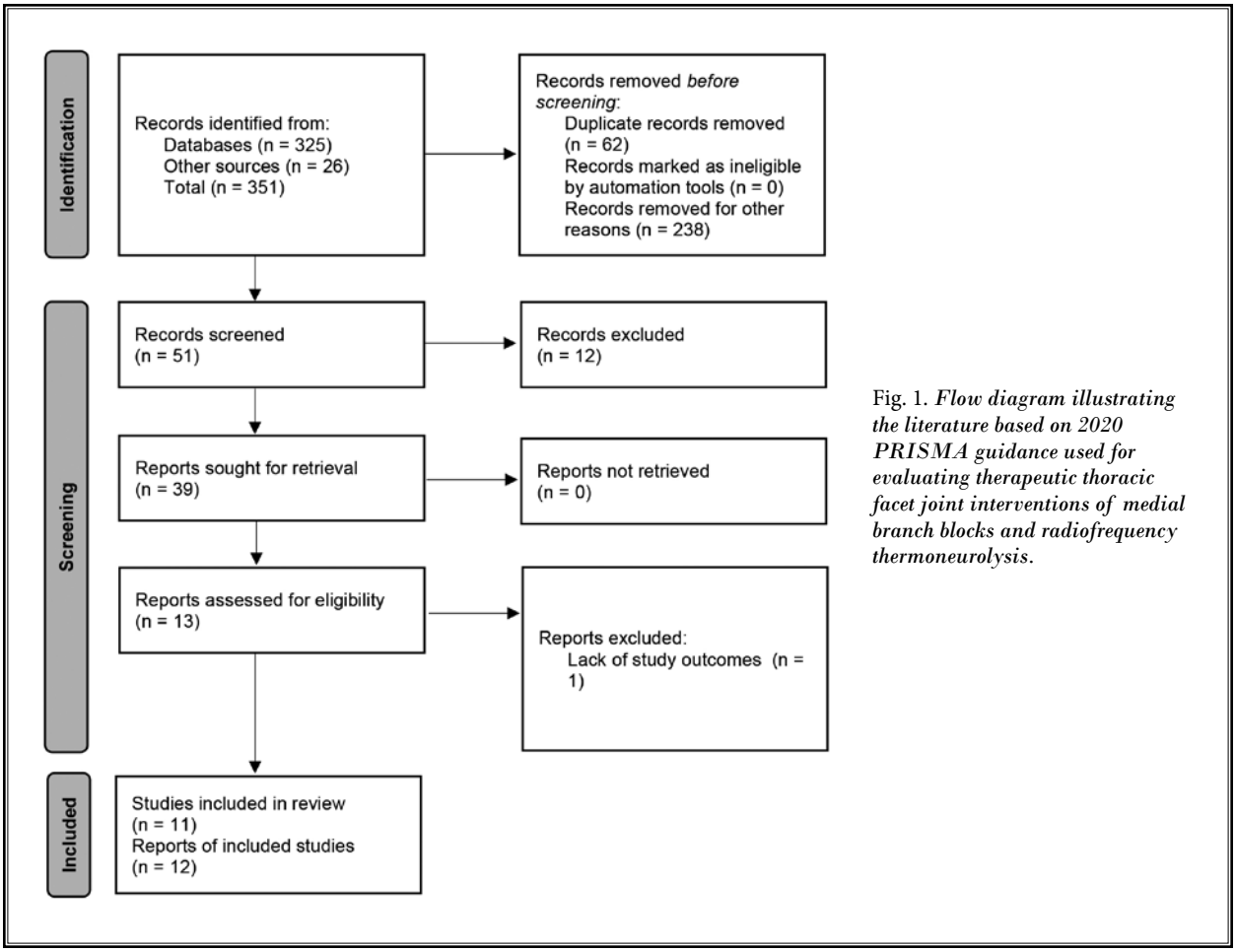

Fig. 1. *Flow diagram illustrating the literature based on 2020 PRISMA guidance used for evaluating therapeutic thoracic facet joint interventions of medial branch blocks and radiofrequency thermoneurolysis.*

The search criteria started with a total of 351 publications with 13 studies (37-49) considered for inclusion. Among the 13 studies considered for inclusion, one study was excluded due to lack of study outcomes (49). Overall, 11 studies (37-48) met inclusion criteria with one study with 2 reports (38,39). Of these included studies, there were 3 RCTs (39,40,42). The remaining 8 studies were of observational nature, either prospective or retrospective (37,41,43-48), as shown in Fig. 1.

Of the 3 RCTs, none were assessed with a placebo control, and two were active-controlled trials for medial branch blocks (39,40). The third study was for radiofrequency neurotomy (42). There was only one trial evaluating intraarticular injection (40). Consequently, assessment of intraarticular injections of thoracic facet joints was not included.

Among the 8 observational studies (37,41,43-47), 3 studies were of medial branch blocks (37,41,48) and 5 studies of radiofrequency neurotomy (43-47).

Study Characteristics

Study characteristics of RCTs and observational studies of medial branch blocks were shown in Table 2. The table shows study characteristics with intervention, results of pain relief and function, and overall results of positivity. There was one randomized active-controlled trial (42) evaluating radiofrequency neurotomy with a total of 40 patients with 20 patients undergoing radiofrequency neurotomy and 20 patients with alcohol injection with results showing significant improvement in both groups. The remaining studies were of observational nature (43-47). A total of 215 patients in 4 studies (43-45,47) underwent dual diagnostic blocks, whereas in one study, 184 patients were evaluated, and they underwent radiofrequency neurotomy after a single diagnostic medial branch block (46). In one study (43), cooled radiofrequency was utilized in 23 patients with 40 treatments with a 6-month follow-up, results showing 57% success rate. In this study, 974 patients

Table 2. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
THORACIC RADIOFREQUENCY									
Joo et al, 2013 (42) RA, AC Quality Scores: Cochrane = 12/13 IPM-QRB = 38/48	In this trial, 40 patients were included either with radiofrequency neurotomy in 20 patients, or alcohol injection in another 20 patients. However, all these patients have undergone radiofrequency neurotomy prior to the enrollment in the study and they required a repeat procedure with recurrent pain after successful treatment. These patients, even though were successfully treated with radiofrequency neurotomy, underwent dual diagnostic block, comparative local anesthetic blocks using lidocaine and bupivacaine. > 50% relief of the targeted pain lasting for more than 6 months was considered as a positive outcome.	Radiofrequency neurotomy was performed at 90°C for 90 seconds after the injection of 0.5 mL of 1% lidocaine to generate a single thermal RFA at each level. In the alcohol group, 1 mL of dehydrated alcohol was injected slowly over a period of 15 seconds.	100% vs. 100%s Recurrence of pain = 0% in both groups	95% vs. 100% Recurrence of pain = 5% in radiofrequency group; 0% in alcohol group	25% vs. 100% Recurrence of pain = 15% in radiofrequency group; 0% in alcohol group	P	P	NA	Positive trial In this study, the patients were selected who were successful prior to the initiation of the treatment with radiofrequency neurotomy. They also underwent repeat diagnostic blocks. The authors have outlined outcome criteria of 50% relief of more than 6 months as a successful outcome. However, the data is not reported in these aspects. It appears that 95% of the patients were positive for 6 months in radiofrequency group and 100% patients were positive for over 15 months in alcohol ablation group. Consequently, it appears that the alcohol ablation group was superior to radiofrequency ablation.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
Gungor & Candan, 2020 (43) Observational study Quality Score: IPM-QRBNR = 28/48	23 patients were selected from a total of 974 patients with a clinical diagnosis of thoracic facet joint related pain undergoing 40 treatments after dual diagnostic medial branch blocks, which were positive in 63 patients. Withdrawal rate was high with 38 of 15 patients withdrawing from the outcomes period without follow-up.	Cooled radiofrequency neurotomy was performed with a 17-gauge 75 mm 5.5 mm active-tipped CRFA electrode. Radiofrequency denervation was carried out at 60° for 150 seconds at each level.	53%	53%	38%	N	N	N	Negative study In this study, a large proportion of patients (974) were screened with 63 patients testing positive with dual diagnostic blocks and 38 patients enrolled for cooled radiofrequency neurotomy; however, with 15 patients lost to follow-up, only 23 patients remained even though they underwent 40 treatments. The relief patterns were very low with 20.72% reduction from 4 to 8 weeks and 53% during 2 to 6 month period. After 6 months, pain relief was 37.58%. Proportion of patients with >50% relief was not reported. The study is judged negative due to very high rate of lost to follow-up, lack of individuals with 50% improvement, and lackluster relief, which was focused only from 2 to 6 months.
Rohof & Chen, 2018 (44) Retrospective study Quality Score: IPM-QRBNR = 28/48	71 patients after controlled diagnostic blocks. Patients underwent bipolar radiofrequency neurotomy. Patients were assessed with > 50% relief at 12 months and also Numeric Rating Scale and pain levels and Pain Disability Index .	Bipolar radiofrequency neurotomy	82%	82%	82%	P	P	P	Positive study Positive study with 71% of the patients and appropriate outcome measures.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
Speldewinde, 2021 (45) Retrospective study Quality Score: IPM-QRBNR = 27/48	39 patients underwent dual diagnostic intraarticular blocks with at least 50% relief undergoing thermal radiofrequency neurotomy	Thermal conventional radiofrequency neurotomy. Radiofrequency neurotomy was performed after injection of 1 to 2 mL of local anesthetic at 80°C for 60 seconds with multiple lesions.	63%	46%	NA	P	P	NA	Positive study Weak positive study with 46% patients reporting > 50% relief for 6 months. In this study, the authors have studied specific joint groups with dual diagnostic blocks of 50% relief. Overall, they showed average duration of relief was 7.8 months with 46% showing > 6 months of > 50% relief. Secondary outcomes of physical and psychological function using Functional Rating Index and the Depression Anxiety Stress Scale showed significant improvements with small to moderate effect sizes with all achieving > 36% improvement in success. The primary outcome was duration of > 50% relief.
Akgul & Akgun, 2022 (46) Clinical, comparative retrospective study Quality Score: IPM-QRBNR = 28/48	184 patients were included in thoracic region from a total of 774 patients. Patients underwent radiofrequency neurotomy after single diagnostic medial branch block. In this study, there was a control group with 122 patients.	Conventional radiofrequency neurotomy performed at 80° for 90 seconds with a single lesion.	Significant pain relief and functional improvement at all levels	Significant pain relief and functional improvement at all levels	Increase in VAS	P	P	N	Positive study Positive study showing significant improvement at 3, and 6 months with non-significant improvement at 12 and 24 months. The study evaluated cervical, thoracic and low back pain with conventional radiofrequency neurotomy showing short-term relief. The study showed significant improvement in multiple parameters with physical functioning, physical health, body pain, general health, and emotional well being.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
Hambraeus et al, 2018 (47) Observational study Quality Score: IPM-QRBNR = 31/48	82 patients were treated in the thoracic region according to the Spine Intervention Society guidelines.	Dual diagnostic blocks of medial branches with 80% relief as the criterion standard were performed. Radiofrequency neurotomy procedure was performed at 80° for 60 seconds with multiple lesions varying from 3 to 15 variable on temperature of the tip.	76%	60%	49%	P	P	P	Positive study Positive study with over 60% success rate at 3 months and approximately 60% at 6 months with 45% at 12 months. In this study, they evaluated lumbar, cervical and thoracic regions. The relief was similar in all regions. The major disadvantages of this study is that even though they followed Spine Intervention Society guidelines, they utilized 1 mL of bupivacaine to each nerve and what appears to be the same drug injected twice, even though relief assessment was appropriate with 80% or more relief. The standard practice is 0.5 mL per nerve with a short- and long-acting local anesthetic. Additional issue is also related to the number of lesions. While they produced 3-15 lesions in cervical and lumbar regions, they produced only 3-5 lesions at each location in the thoracic spine, which is generally considered as excessive. It is impressive that they included only the data from the first denervation and follow-up visits within 1 year after the first denervation.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Characteristic / Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 1 year	
THORACIC FACET JOINT NERVE BLOCKS									
Manchikanti et al, 2010 & 2012 (38,39) RA, DB, AC Quality Scores: Cochrane = 11/13 IPM-QRB = 45/48	100 patients with 50 patients in local anesthetic alone and 50 patients with local anesthetic and steroid groups were available. All patients underwent dual diagnostic blocks with lidocaine and bupivacaine with 80% relief criterion standard. Outcome measures included Numeric Pain Scores and Oswestry Disability Index with significant relief defined as > 50% pain relief and/or positive change in Oswestry Disability Index scores.	Local anesthetic = 50 Local anesthetic with steroid = 50 The injections were carried out under fluoroscopic guidance with total volume of 1 to 1.5 mL per nerve.	79% vs 83%	79% vs 81%	80% vs 83%	P	P	P	Positive trial Positive study with long-term follow-up showing results up to 2 years with > 50% improvement in 80% of patients in local anesthetic group and 84% in patients with local anesthetic and steroids at 2-year follow-up. This is a high quality, double blind, active-controlled trial with long-term follow-up showing positive results.

were diagnosed with thoracic facet joint related pain based on clinical evaluation. Sixty-three patients were positive with dual diagnostic blocks. Of these, 38 patients completed cooled radiofrequency neurotomy. However, 15 patients were lost to follow-up. Consequently, only 23 patients undergoing 40 treatments were reported. They reported pain reduction of 21% during the early period of 4 to 8 weeks. In the second follow-up from 2 to 6 months, they reported 53% improvement of pain scores, whereas in the third follow-up from 6-12 months duration, improvement of the pain scores was 38%. Their primary outcome measure determined as the adequate reduction of pain scores (≥ 50%) was achieved only during the intermediate term relief period (2-6 months) with 53% reduction in NRS pain scores. Patients required repeat radiofrequency procedure at 24-36 months with the shortest pain relief of 30 weeks and the longest pain relief of 112 weeks.

In two RCTs (39,40) evaluating the role of facet joint nerve blocks with a total of 140 patients, of which 120 patients underwent medial branch blocks, the RCT by Manchikanti et al (39) with 100 patients showed ≥ 50% improvement in over 83% of the patients at 12 months with multiple injections. However, Lee et al (40) included only 20 patients with a single diagnostic block for inclusion showing improvement of 40% at 6-month follow-up with medial branch blocks compared to 65% of the patients with intraarticular steroid injections in 20 patients. However, in this study, the 3-month results were not available, which is the average relief with medial branch blocks. Consequently, this is considered as a positive study too since it did provide relief in 40% of the patients at 6-month follow-up. Further, there was no significant difference in reduction of NRS at any time. The data

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
Lee et al, 2018 (40) RA, AC Quality Scores: Cochrane = 12/13 IPM-QRB = 39/48	Total of 40 patients meeting inclusion criteria were included. Inclusion criteria was pain of greater than 6 months in upper or mid back with local or paramedian tenderness over the area of the facet joints and reproduction of pain with deep pressure. Age between 20 and 79. Greater than 80% temporary pain relief following a diagnostic thoracic medial branch block with 0.5 mL of 1% lidocaine. Failure to respond to physical therapy and medication. Sample size calculation showed required 20 subjects in each group. Thoracic medial branch block with injection of 0.5 mL of 0.25% bupivacaine with 10 mg, 0.25 mL of dexamethasone. Two medial branches were blocked to block one joint. Successful outcome was defined as 50% reduction in the NRS scores at 6 months, when compared to the pre-treatment NRS score.	Intraarticular steroid injections was performed with injection of 0.3 mL of contrast material, followed by injection of 10 mg, 0.25 mL of dexamethasone, mixed with 0.5 mL of 0.25% bupivacaine.	Medial branch blocks Baseline 5.4 ± 1.4, reduced to 3.2 ± 1.9 Intraarticular steroid injections Baseline 5.3 ± 1.3, reduced to 2.8 ± 1.5 No significant difference between the groups Patients with more than 50% reduction in NRS scores 3 months – not available	Medial branch blocks 5.4 ± 1.4, to 3.4 ± 1.9 Intraarticular steroid injection 5.3 ± 1.3 to 2.9 ± 1.5 at 6 months with no significant difference in pain scores Patients with more than 50% reduction in NRS scores 3 months – not available 6 months – 40% in medial branch block group, 65% in intraarticular injection group	NA	P	P	NA	Positive trial Positive study at 3 months and 6 months for both medial branch blocks and intraarticular injections based on decrease in NRS scores with no significant difference between the groups. However, judging based on greater than 50% improvement, even though there is no significant difference MBB group was successful in 40% of the patients and intraarticular steroid group was successful in 65% of the patients. Overall, it showed better results in intraarticular steroid group; however, there was no significant difference in any of the other factors, even after 6 months. Because therapeutic medial branch blocks average duration is about 3 months, this is considered as an overall positive study at 3 months and 6 months, for short-term as well as long-term considering that only single block was provided.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Study Characteristic Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term		
							> 6 mos.	≥ 1 year	
Manchikanti et al, 2006 (37) Prospective outcome study Quality Score: IPM-QRBNR = 33/48	55 consecutive patients, all meeting diagnostic criteria for thoracic facet joint pain with comparative local anesthetic blocks with 80% pain relief criteria. Outcomes were assessed with pain relief and functional improvement with significant improvement determined as > 50% improvement.	Therapeutic thoracic facet joint nerve blocks were performed under fluoroscopic guidance with bupivacaine with or without Sarapin and steroid with a total volume of 1 to 1.5 mL per nerve.	71%	71%	76%	P	P	P	Positive study Positive study with short- and long-term relief This is an observational outcome study with appropriate outcome parameters and 1-year follow-up.
Park et al, 2013 (41) Observational study Quality Scores: Quality Score: IPM-QRBNR = 28/48	53 patients with axial back pain with chronic facet joint pain for osteoporotic compression fractures in thoracolumbar region. Majority of the patients included osteoporotic fractures at T12 and L1. Selection criteria was based on clinical assessment and positive response with 80% pain relief with a single diagnostic medial branch block.	Therapeutic medial branch blocks of T11 and T12 and L1 and L2 were performed. Lidocaine 1% 0.5 mL was injected over each target nerve.	80%	80%	80%	P	P	P	Positive study Positive short- and long-term improvement. The authors in this study studied 53 patients with facet joint pain diagnosed clinically and with diagnostic medial branch block. The majority of the patients involved had thoracic or thoracolumbar pain. Therapeutic medial branch blocks provided average total pain relief per procedure (3.26, 41.83, and 13.26 weeks). 49 of the 53 patients received 4 procedures and reported greater than 11 weeks of relief varying from 11 to 52 weeks on average per procedure. Average total relief was variable between 41 to 43 weeks in 47 of 53 patients.

Table 2 cont. *Studies of the effectiveness of thoracic radiofrequency neurotomy, facet joint nerve blocks and intraarticular injections.*

Study Characteristic / Methodological Quality Scoring	Patients	Interventions	Pain Relief and Function			Results			Conclusion/Comments
			3 mos.	6 mos.	12 mos.	Short-Term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 1 year	
Chang, 2018 (48) Retrospective, observational data collected from 72 patients Quality Score: IPM-QRBNR = 31/48	72 patients underwent thoracic medial branch blocks. 20 patients refractory to medial branch blocks underwent PRF thoracic medial branch blocks	Pulsed radiofrequency treatment in patients with recurrence of pain after medial branch blocks.	Significant improvement in 52 of 72 patients	Significant improvement in 52 of 72 patients	Significant improvement in 52 of 72 patients	P	P	P	Positive study Positive study for medial branch blocks and pulsed radiofrequency neurotomy. All patients underwent thoracic medial branch blocks on multiple occasions with lidocaine mixed with bupivacaine with 1 to 2 blocks. Only 20 patients out of 72 patients required additional treatment, indicating significant improvement with medial branch blocks alone.

RA = randomized; AC = active control; DB: double blind; P = positive; N = negative; NA = not applicable

showed in medial branch block, the pain scores decreased from 5.4 ± 1.4 before treatment to 3.2 ± 1.9 at 3 months, and 3.4 ± 1.9 at 3 months. In the intraarticular group, the changes were from baseline of 5.3 ± 1.3 to 2.8 ± 1.5 at 3 months, and 2.9 ± 1.5 at 6 months. There was no significant difference between the groups. Inclusion criteria was also based on clinical findings and confirmation with 80% pain relief with a single diagnostic block with 0.5 mL of lidocaine. Overall, the selection criteria were stringent by Manchikanti et al (39) with 80% relief as criterion standard with comparative local anesthetic blocks. However, Lee et al's (40) inclusion criteria were based on clinical criteria.

Among the observational studies, there was a total of 3 studies (37,41,48), which included 160 patients with all of them showing positive results. Manchikanti et al (37) evaluated 55 consecutive patients with selection criteria of dual diagnostic blocks of 80% concordant pain relief and with appropriate outcome parameters with at least 50% pain relief and improvement in Oswestry Disability Index (ODI) as the criterion standard. They showed a success rate of 71% at 3 and 6 months and 76% at 12 months with positive results. Park et al (41) evaluated 53 patients with a single block with facet joint pain after osteoporotic compression fractures showing with therapeutic facet joint nerve blocks of 80% pain relief at 3, 6, and 12 months with positive short- and long-term relief. Finally, Chang (48) evaluated patients with pulsed radiofrequency after they have not responded to therapeutic medial branch blocks. Overall, it appears to be very successful even though data is not available. Of the 72 patients, only 20 patients required pulsed radiofrequency. Thus, all observational studies were positive.

Methodological Quality and Risk of Bias Assessment

The results of methodological quality assessment of the RCTs meeting the inclusion criteria were carried out using Cochrane review criteria and IPM-QRB and observational studies utilizing IMP-QRBNR criteria are illustrated in Tables 3-5.

Utilizing the Cochrane quality assessment and the previously established score ranges in the methods section of this study, all 3 trials

Table 3. *Methodological quality assessment of randomized trials of thoracic facet joint nerve blocks and radiofrequency thermoneurolysis utilizing Cochrane review criteria.*

	Manchikanti et al (38,39)	Lee et al (40)	Joo et al (42)
Randomization adequate	Y	Y	Y
Concealed treatment allocation	Y	Y	Y
Patient blinded	Y	Y	Y
Care provider blinded	Y	N	N
Outcome assessor blinded	N	Y	Y
Drop-out rate described	Y	Y	Y
All randomized participants analyzed in the group	Y	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	N	Y	Y
Co-intervention avoided or similar in all groups	Y	Y	Y
Compliance acceptable in all groups	Y	Y	Y
Time of outcome assessment in all groups similar	Y	Y	Y
Are other sources of potential bias not likely	Y	Y	Y
SCORE	11/13	12/13	12/13

Y = yes; N = no; U = nuclear
Source: Furlan AD, et al; Editorial Board of the Cochrane Back, Neck Group. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. Spine (Phila Pa 1976) 2015; 40:1660-1673 (56).

(39,40,42) scored between 9 and 13, thus meeting our criteria of high-quality studies.

Based on the IPM-QRB criteria for randomized trials, all 3 trials (39,40,42) scored between 32 and 48, hence they are of high quality. Thus, all 3 trials were judged as high quality based on Cochrane review criteria and IPM-QRB criteria for randomized trials.

Based on the IPM-QRBNR criteria for observational studies, one study (37) scored between 32 and 48, hence was of high quality, while 7 studies (41,43-48) scored between 16 and 31, thus are considered as moderate quality.

Analysis of Evidence

The evidence was analyzed based on qualitative and quantitative analysis.

Qualitative Analysis

Overall, 3 RCTs (39,40,42) and 8 observational studies (37,41,43-48) were included in this analysis. Of these, 2 RCTs (39,40) and 3 observational studies (37,41,48) evaluated facet joint nerve blocks. Both RCTs were active-controlled trials.

Based on the qualitative analysis, both RCTs (39,40) and 3 observational studies (37,41,48) evaluating thoracic facet joint nerve blocks showed positive results.

Radiofrequency neurotomy was evaluated in one RCT (42) and 5 observational studies (43-47). The RCT showed significant relief.

Overall, the number of patients included in the radiofrequency neurotomy studies were 376 patients with only one study of 23 patients showing negative results (43) and all others showing positive results (42,44-47). Thus, qualitative analysis of radiofrequency neurotomy shows positive results with one RCT (42) of a small sample size and 5 observational studies (43-47) with one negative study (43).

Overall, the evidence is Level II for facet joint blocks with one large RCT (38,39) with appropriate outcome parameters and one smaller RCT (40) showing positive results with addition of 3 observational studies (37,41,48).

For radiofrequency neurotomy, the evidence is Level III based on one small RCT (42) and 5 observational studies (43-47) with all of them showing positive results except one small observational study (43).

Quantitative Analysis

Pain and Functionality at 3 Months

Figure 2A shows the results of a single meta-analysis utilizing local anesthetic with steroids. There were 2 RCTs (38,40) and 2 observational studies (37,41) used to assess pain scores at 3 months using NRS or VAS in

Table 4. *Methodologic quality assessment of randomized trials of thoracic facet joint nerve blocks and radiofrequency thermoneurolysis utilizing IPM – QRB criteria.*

		Manchikanti et al (38,39)	Lee et al (40)	Joo et al (42)
I.	TRIAL DESIGN AND GUIDANCE REPORTING			
1.	CONSORT or SPIRIT	3	2	2
II.	DESIGN FACTORS			
2.	Type and Design of Trial	2	2	2
3.	Setting/Physician	2	2	2
4.	Imaging	3	3	3
5.	Sample Size	3	1	1
6.	Statistical Methodology	1	1	1
III.	PATIENT FACTORS			
7.	Inclusiveness of Population			
	• For facet or sacroiliac joint interventions:	2	2	2
8.	Duration of Pain	2	2	2
9.	Previous Treatments	2	2	2
10.	Duration of Follow-up with Appropriate Interventions	3	2	2
IV.	OUTCOMES			
11.	Outcomes Assessment Criteria for Significant Improvement	4	2	2
12.	Analysis of all Randomized Participants in the Groups	2	2	2
13.	Description of Drop Out Rate	2	2	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	2	2	2
15.	Role of Co-Interventions	1	1	1
V.	RANDOMIZATION			
16.	Method of Randomization	2	2	2
VI.	ALLOCATION CONCEALMENT			
17.	Concealed Treatment Allocation	2	2	2
VII.	BLINDING			
18.	Patient Blinding	1	1	1
19.	Care Provider Blinding	1	1	0
20.	Outcome Assessor Blinding	0	1	0
VIII.	CONFLICTS OF INTEREST			
21.	Funding and Sponsorship	2	2	2
22.	Conflicts of Interest	3	2	3
TOTAL		45	39	38

Source: Manchikanti L, et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. Pain Physician 2014; 17:E263-E290 (57).

patients who underwent MBB. As shown in Fig. 2A, the pooled mean difference of pain scores from the baseline to 3-month follow-up was 3.997 points decreased (95% CI: -4.089 to -3.904, $P < 0.0001$).

Figure 2B shows the results of a single meta-analysis utilizing steroids with local anesthetic and MBB technique. There was one RCT (38) and 2 observational studies (37,41) used to assess functionality scores at 3 months using ODI. As shown in Fig. 2, the pooled mean difference of functionality scores from the baseline to 3-month follow-up was 18.413 points decreased (95% CI: -19.287 to -17.539, $P < 0.0001$).

Figure 3 shows the results of a single meta-analysis of RFA. There was one RCT (42) and 2 observational studies (44,46) used to assess pain scores at 3 months using NRS or VAS in patients who underwent RFA. As shown

Table 5. *IPM checklist for assessment of nonrandomized or observational studies of thoracic facet joint nerve blocks and radiofrequency thermoneurolysis utilizing IPM – QRBNR criteria.*

		Manchikanti et al (37)	Park et al (41)	Gungor & Candan (43)	Rohof & Chen (44)	Speldewinde (45)	Akgul & Akgun (46)	Hambraeus et al (47)	Chang (48)
I.	STUDY DESIGN AND GUIDANCE REPORTING								
1.	STROBE or TREND GUIDANCE	3	2	2	2	1	3	1	2
II.	DESIGN FACTORS								
2.	Study Design and Type	2	2	2	1	1	1	1	2
3.	Setting/Physician	2	2	2	2	2	2	2	2
4.	Imaging	3	3	3	3	3	3	3	3
5.	Sample Size	0	0	0	0	0	1	1	1
6.	Statistical Methodology	1	1	1	1	1	1	1	1
III.	PATIENT FACTORS								
7.	Inclusiveness of Population								
	• For facet or sacroiliac joint interventions:	4	4	4	2	4	3	4	4
8.	Duration of Pain	2	2	2	2	1	2	2	2
9.	Previous Treatments	2	2	2	2	1	2	2	2
10.	Duration of Follow-up with Appropriate Interventions	3	2	2	3	2	2	2	2
IV.	OUTCOMES								
11.	Outcomes Assessment Criteria for Significant Improvement	4	1	1	3	4	1	3	3
12.	Description of Drop Out Rate	1	1	1	1	1	1	1	1
13.	Similarity of Groups at Baseline for Important Prognostic Indicators	0	0	0	0	0	0	2	0
14.	Role of Co-Interventions	2	2	2	2	2	2	2	2
V.	ASSIGNMENT								
15.	Method of Assignment of Participants	2	2	2	2	2	2	2	2
VI.	CONFLICTS OF INTEREST								
16.	Funding and Sponsorship	2	2	2	2	2	2	2	2
TOTAL		33	28	28	28	27	28	31	31

Source: Manchikanti L, et al. Development of an interventional pain management specific instrument for methodologic quality assessment of nonrandomized studies of interventional techniques. Pain Physician 2014; 17:E291-E317 (58).

in Fig. 3, the pooled mean difference of pain scores from the baseline to 3-month follow-up was 4.894 points decreased (95% CI: -5.058 to -4.731, $P < 0.0001$).

Pain and Functionality at 6 Months

Figure 4 shows the results of a single meta-analysis of medial branch blocks utilizing local anesthetic and steroids. There were 2 RCTs (39,40) and one observational study (37) used to assess pain scores at 6 months using NRS or VAS in patients who underwent MBB with local anesthetic and steroids. As shown in Fig. 4, the pooled mean difference of pain scores from the baseline to 6-month follow-up was 4.367 points decreased (95% CI: -4.522 to -4.212, $P < 0.0001$).

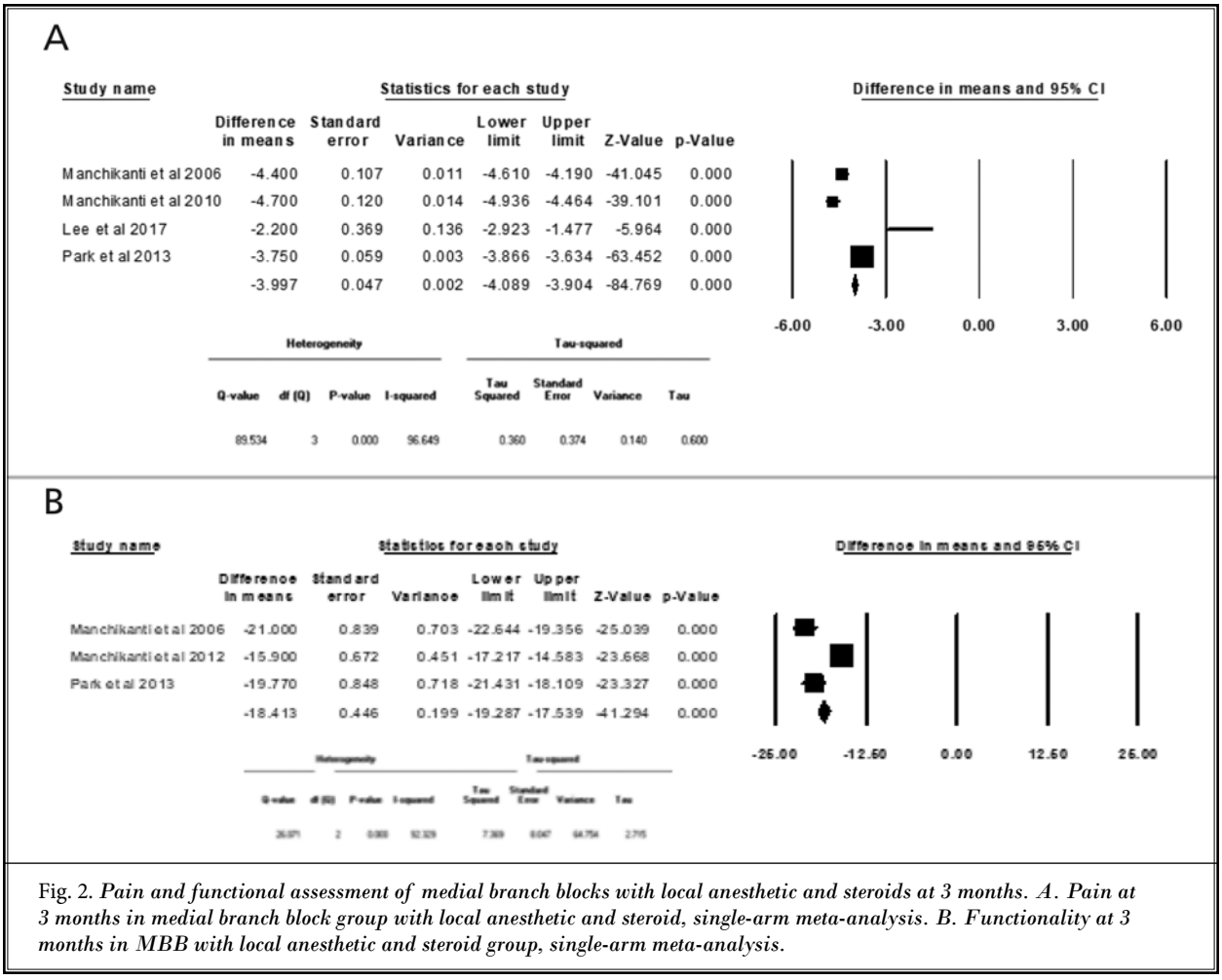

Fig. 2. *Pain and functional assessment of medial branch blocks with local anesthetic and steroids at 3 months. A. Pain at 3 months in medial branch block group with local anesthetic and steroid, single-arm meta-analysis. B. Functionality at 3 months in MBB with local anesthetic and steroid group, single-arm meta-analysis.*

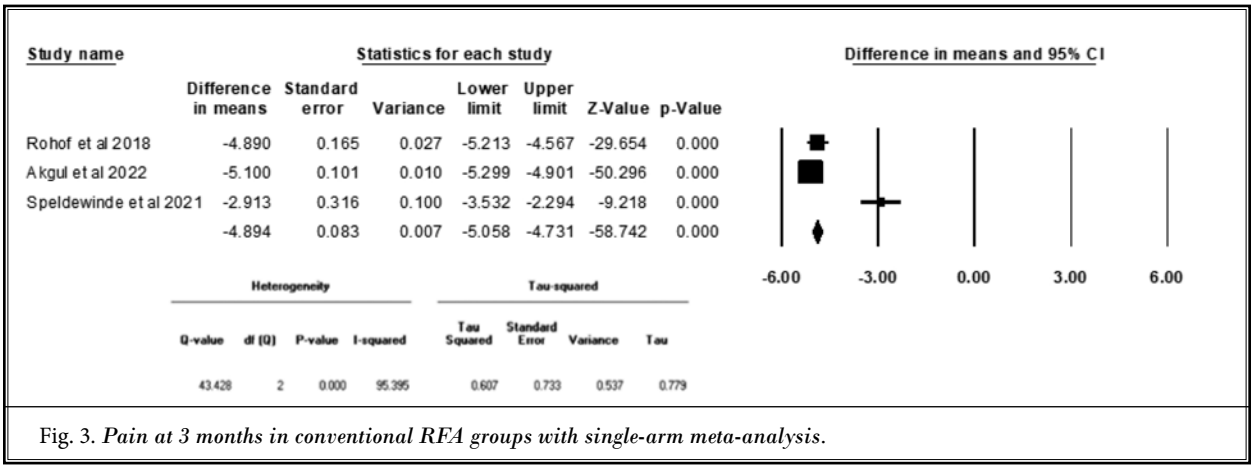

Fig. 3. *Pain at 3 months in conventional RFA groups with single-arm meta-analysis.*

Pain and Functionality at 12 Months

Figure 5A shows the results of a single meta-analysis for medial branch blocks with local anesthetic and steroids. There was one RCT (39) and 2 observational studies (37,41) used to assess pain scores at 12 months using NRS or VAS in patients who underwent MBB with local anesthetic and steroids. As shown in Fig. 5A, the pooled mean difference of

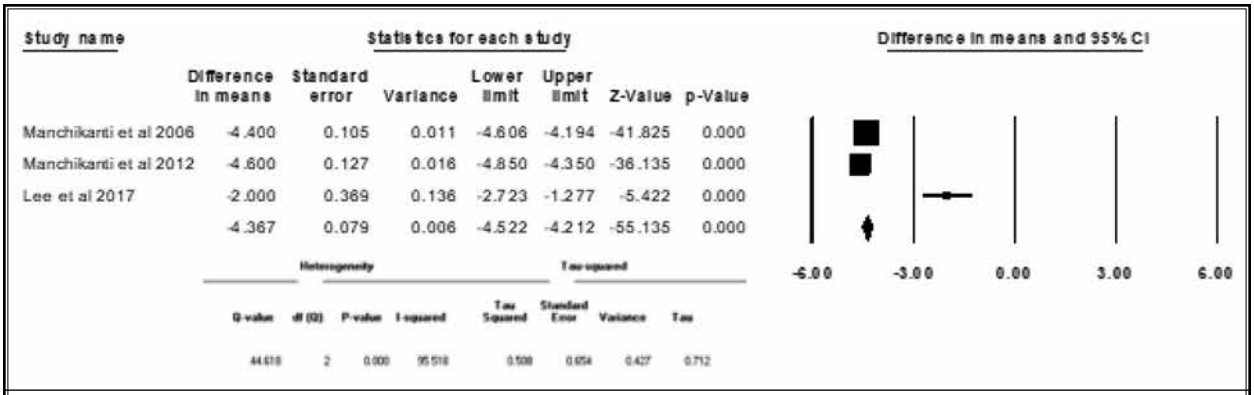

Fig. 4. *Single meta-analysis of medial branch blocks utilizing local anesthetics with steroids at 6 months.*

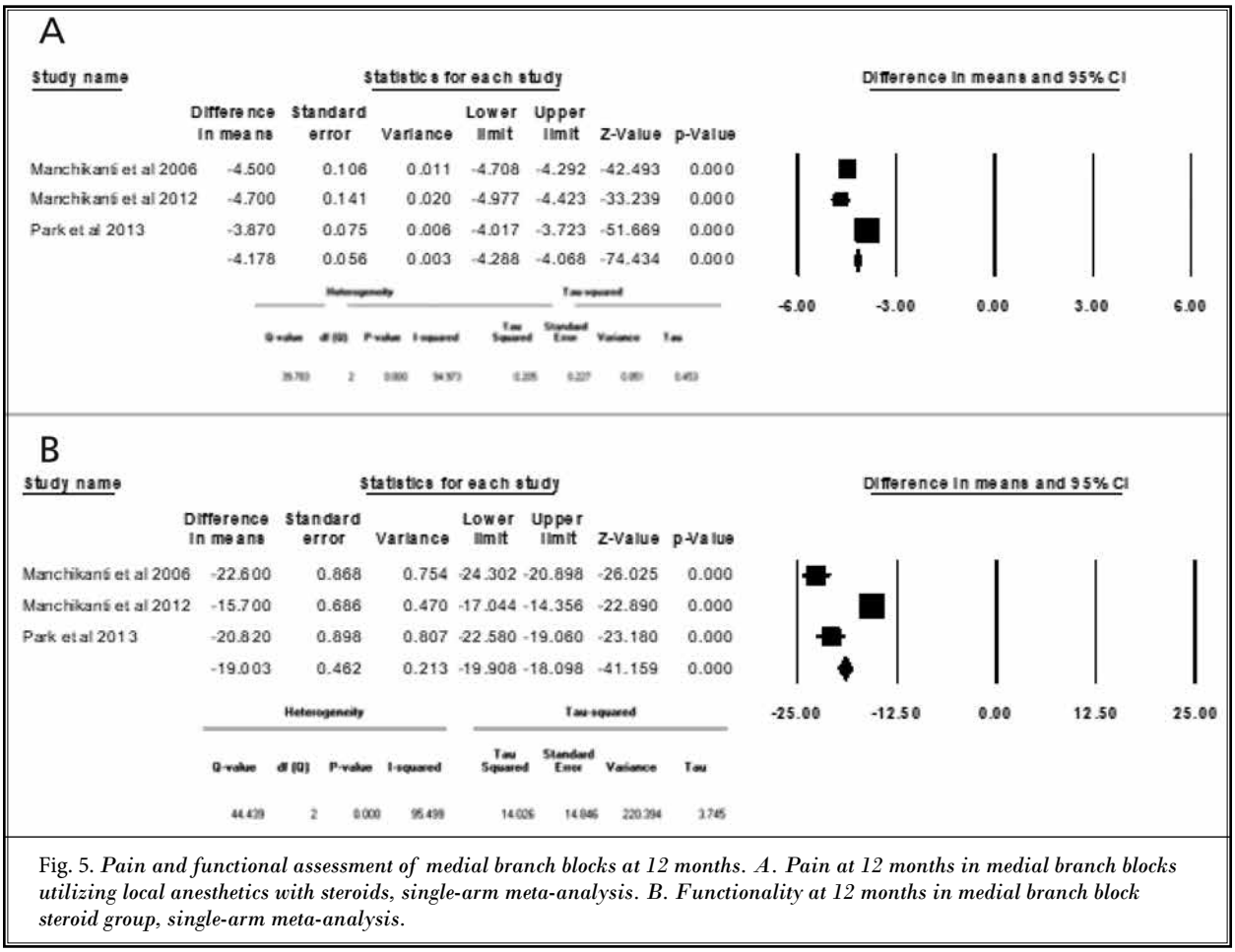

Fig. 5. *Pain and functional assessment of medial branch blocks at 12 months. A. Pain at 12 months in medial branch blocks utilizing local anesthetics with steroids, single-arm meta-analysis. B. Functionality at 12 months in medial branch block steroid group, single-arm meta-analysis.*

pain scores from the baseline to 12-month follow-up was 4.178 points decreased (95% CI: -4.288 to -4.068, $P < 0.0001$).

Figure 5B shows the results of a single-arm meta-analysis utilizing the steroid group. There were 3 trials (37,39,41) used to assess functionality scores at 6 months using ODI. As shown in Fig. 5B, the pooled mean difference of functionality scores from the baseline to 12-month follow-up was 19.003 points decreased (95% CI: -19.908 to -18.098, $P < 0.0001$).

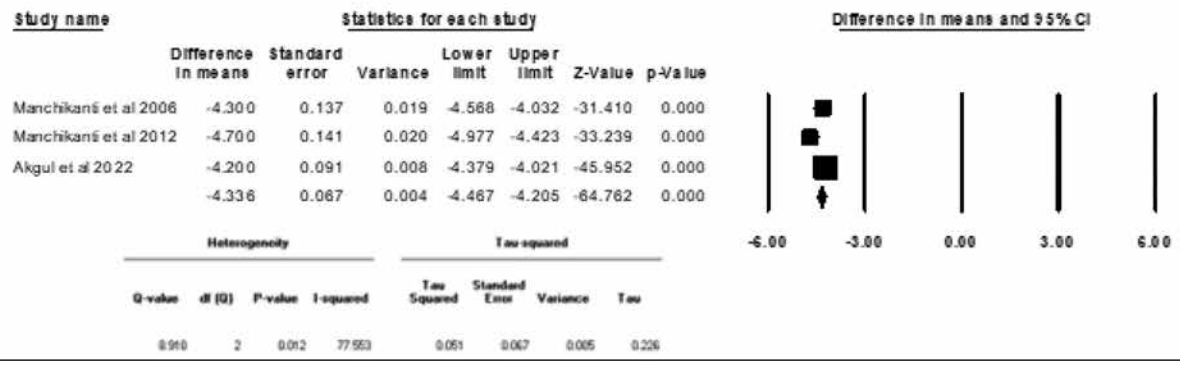

Fig. 6. *Pain at 24 months in medial branch block utilizing local anesthetic and steroids, single-arm meta-analysis.*

Pain and Functionality at 24 Months

Figure 6 shows the results of a single meta-analysis of MBB utilizing local anesthetic and steroids. There were 3 trials (37,39,46) used to assess pain scores at 24 months using NRS or VAS in patients who underwent the steroid group in MBB. As shown in Fig. 5A, the pooled mean difference of pain scores from the baseline to 24-month follow-up was 4.336 points decreased (95% CI: -4.467 to -4.205, $P < 0.0001$).

Discussion

This systematic review and meta-analysis of RCTs and observational studies of the effectiveness of thoracic facet joint nerve blocks and radiofrequency neurotomy in managing chronic thoracic pain showed Level II evidence for long-term effectiveness of 6 months or longer for thoracic facet joint nerve or medial branch blocks and Level III evidence for conventional radiofrequency neurotomy. The evidence synthesis included both a qualitative and quantitative analysis of both procedures. Related to lack of studies, analysis was not performed for thoracic intraarticular facet joint injections.

The qualitative analysis in managing thoracic facet joint pain with facet joint nerve blocks presented with 2 RCTs with one RCT with 2-year follow-up (38,39) with inclusion of 100 patients with local anesthetic or local anesthetic and steroids shown as high quality with significantly positive response at 6 and 12 months, with a second RCT (40) with inclusion of only 40 patients and providing data for 6 months with no significant difference in NRS scores at one, 3, and 6 months. However, the significant improvement judged by > 50% improvement showed 40% improvement with medial branch blocks and 65% improvement with diagnostic blocks. The study was well performed. A sample size determination was carried out. They used a single block diagnostic algorithm with 80% pain relief in chronic thoracic pain. Medial branch blocks were performed with injection of local anesthetic mixed with dexamethasone. Three observational studies (37,41,48) with a total of 160 patients yielded positive results with one high quality (37) and 2 moderate quality studies (41,48) showing positive results. The studies were clinically applicable.

For radiofrequency neurotomy procedures, the evidence included one small RCT (42) comparing radiofrequency neurotomy with alcohol injection in 20 patients each with appropriate diagnostic criteria showed significant improvement at 3 and 6 months, followed by 5 observational studies (43-47) with inclusion of 376 patients involving either conventional radiofrequency neurotomy or bipolar radiofrequency neurotomy with selection criteria involving diagnostic blocks showed positive results at 3 and 6 months in all studies. However, in one study involving 23 patients with 40 treatments utilizing cooled radiofrequency neurotomy, the results were negative. All the studies were clinically applicable. Due to a single high quality RCT with a small sample size with low clinical applicability and the study was downgraded by application of GRADE criteria, the evidence was shown to be of Level III.

With changes in policies in the USA and emerging guidelines, it is conceivable that radiofrequency neurotomy will increase much faster while intraarticular injections and medial branch blocks will continue to decline (34,60). As no systematic reviews with meta-analysis are available for thoracic facet joint interventions, the value and validity of this publication is only as reliable as the validity of the primary studies included. As described earlier, most of the studies of radiofrequency neurotomy in this systematic review and meta-

analysis are observational studies with a single RCT (42) with a small number of patients (20 in each group), the remaining were observational studies, similar to cervical spine (23). Consequently, numerous issues have been highlighted in reference to systematic reviews in interventional pain management. These have been discussed in guidelines and multiple other systematic reviews extensively (3,4,22,23,51-55,61-69). Significant discussions continue with descriptions of placebo and inappropriately converted placebo analysis of active control trials. Manchikanti et al (64) have shown sodium chloride solution injected into the epidural space is not a placebo. Similarly, it has been widely publicized that epidural injection of local anesthetic is an active agent with only short-term differences in improvement with local anesthetic alone compared to local anesthetic with steroids (61,62). Ironically, in contrast to numerous descriptions, the articles included in this analysis showed similar improvement with therapeutic medial branch blocks with local anesthetic injection with or without steroids compared to radiofrequency neurotomy, however, requiring early repeat injections similar to a short-acting compared to a long-acting drug or any other technique. It is also crucial that real-world evidence be applied in analysis of the evidence with higher clinical relevancy. The majority of the trials and studies included in this analysis showed only moderate clinical relevance due to extensive lesioning and time-consuming techniques. Dal-Re´ et al (66) discussed the issues related to real-world evidence focusing on pragmatic RCTs in contrast to explanatory RCTs, which are used to test hypotheses on whether the intervention causes an outcome of interest in ideal circumstances; pragmatic RCTs aim to provide information on the relative merits of real-world clinical alternatives in routine care. A critical aim of an explanatory RCT is to ensure internal validity (prevention of bias), in contrast to a pragmatic RCT which focuses on maximizing external validity (generalizability of the results to many real-world settings), preserving internal validity as much as possible. Dal-Re´ et al (66) also noted that a genuinely pragmatic RCT should fulfill at least two fundamental features, including conduct of the study resembling usual clinical practice and the results being applicable clinically to multiple other settings. It is crucial in interventional pain management to identify real-world trials with high clinical applicability. This is the first systematic review comparing thoracic medial branch blocks and radiofrequency neurotomy utilizing a single-arm meta-analysis. Single-arm meta-analysis essentially showed significant improvement with conventional radiofrequency neurotomy and therapeutic medial branch blocks. Even though not well appreciated, single-arm analysis should be made a crucial part of meta-analysis in elucidating the effectiveness of both groups and real-world RCTs.

The results of the present analysis echoed the systematic reviews performed in cervical and thoracic regions; however, the results are similar to previous systematic reviews (2,33,23,67,68).

Facet joint guidelines from American Society of Interventional Pain Physicians (ASIPP), while showing Level II evidence with moderate strength of recommendation for diagnostic accuracy, showed Level III evidence with weak to moderate strength of recommendation with emerging evidence for thoracic RFA with inclusion of one relevant RCT and 3 observational studies. The present systematic review and meta-analysis included the same studies with the addition of 3 observational studies (45-47). Even then, the evidence yielded the same level of Level III with weak to moderate strength of recommendation with qualitative and quantitative analysis, including a single arm meta-analysis. In contrast, the guidelines showed the level of evidence as II with moderate strength of recommendation for thoracic facet joint nerve blocks with inclusion of 2 RCTs and 2 observational studies with long-term improvement. The present systematic review and meta-analysis, which included a single arm meta-analysis, included 2 RCTs (39,40) and 3 observational studies (37,41,48) yielding the same level of evidence with Level II and moderate strength of recommendation.

As shown earlier in multiples studies, systematic reviews and guidelines, selection criteria are crucial. The majority of the studies for radiofrequency neurotomy, as well as facet joint nerve blocks incorporated diagnostic blocks with controlled comparative local anesthetic blocks. It provides appropriateness and clinical applicability, whereas some studies were based on only either clinical assessment or a single block.

Facet joint interventions showed an overall 2.9% annual increase from 2010 to 2019 compared to an annual increases of 14.2% from 2000 to 2010, with 19.3% COVID-19 pandemic-related decline from 2019 to 2020. In addition, the analysis of expenditures for facet joint interventions in the Medicare population (28) also showed an increase in expenditures of 79% from 2009 to 2018 in the form of total cost for facet joint interventions. Inflation-adjusted costs with 2018 US dollars, however, showed an overall increase of 53%

instead of 79% with an annual increase of 4.9%. Further, cervical facet joint injection procedures increased by 2% annually from 2010 to 2019, whereas cervical radiofrequency neurotomy procedures increased by 8.9%. In comparison, lumbosacral facet joint blocks increased at an annual rate of 0.8% from 2010 to 2019, whereas radiofrequency neurotomy procedures during the same period increased 7.4%. During the COVID-19 pandemic overall facet joint interventions decreased 19.3%, with cervical/thoracic facet joint blocks decreasing 20.2%, lumbar/sacral facet joint blocks decreasing 20.7%, with cervical/thoracic facet neurolysis decreasing 14.1%, and lumbosacral facet neurolysis procedures decreasing 7.3% (25). In contrast, epidural procedures showed an overall decrease of inflation-adjusted costs of 2%, whereas prior to inflation adjustment, total expenditures increased by 14.6%, an annual increase of 1.5% (27). Spinal cord stimulation procedures also increased in utilization and costs; however, utilization of percutaneous adhesiolysis procedures and vertebral augmentation procedures have declined significantly (29,30). In addition, recent evaluations assessing the impact of the COVID-19 pandemic showed an 18.7% reduction in overall interventional techniques from 2019 to 2020 (25).

However, separate data for thoracic facet joint interventions is not available as these are included as part of cervicothoracic CPT coding system.

In summary, from a clinical perspective, one challenge in many patients with thoracic pain is the overlap in characteristics and descriptions of presenting symptoms, whether the true source of their pain is thoracic discogenic, facetogenic and/or muscular in origin. At present, there is no literature that precisely correlates facet joint imaging with clinical signs and symptoms. Furthermore, unlike cervical and lumbar discogenic pain which have very well-defined dermatomal distributions, thoracic discogenic pain, in many cases, presents less clear on physical examination. In this regard, many patients initially present with thoracic imaging reflecting minor or moderate thoracic disc herniation and are treated with a thoracic epidural without easing pain symptoms. In these patients, the true source of pain is thoracic facet joint arthritis, and the patient would benefit from thoracic medial branch blocks and radiofrequency ablation.

Conclusion

The present systematic review and meta-analysis of RCTs and observational studies of thoracic therapeutic facet joint nerve blocks and radiofrequency neurotomy provided Level II evidence with moderate recommendation for the short and long-term effectiveness of facet joint nerve blocks and Level III evidence for radiofrequency neurotomy in managing thoracic facet joint pain after the diagnosis of facet joint pain with dual controlled diagnostic blocks with at least 80% criterion standard for the diagnosis.

Author Contributions

The study was designed by LM, MRS and JAH.

Statistical analysis was performed by EK and NNK.

All authors contributed to preparation of the manuscript, reviewed, and approved the content with final version.

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Appendix Table 1. *Sources of risk of bias and Cochrane Review rating system.*

Bias Domain	**Source of Bias**		**Possible Answers**
Selection	(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 dice (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, preordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and preordered list of treatment assignments.	Yes/No/Unsure
		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.	
Selection	(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
Performance	(3) Was the patient blinded to the intervention?	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
Performance	(4) Was the care provider blinded to the intervention?	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
Detection	(5) Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for each primary outcome separately. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or:	Yes/No/Unsure
		• 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., cointerventions, 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	
Attrition	(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
Attrition	(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 noncompliance and cointerventions.	Yes/No/Unsure
Reporting	(8) Are reports of the study free of suggestion of selective outcome reporting?	All the results from all prespecified 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

Appendix Table 1 cont. *Sources of risk of bias and Cochrane Review rating system.*

Bias Domain	**Source of Bias**		**Possible Answers**
Selection	(9) Were the groups similar at baseline regarding the most important prognostic indicators?	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
Performance	(10) Were cointerventions avoided or similar?	If there were no cointerventions or they were similar between the index and control groups.	Yes/No/Unsure
Performance	(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 for 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
Detection	(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 primary outcome measures.	Yes/No/Unsure
Other	(13) Are other sources of potential bias unlikely?	Other types of biases. For example: • When the outcome measures were not valid. There should be evidence from a previous or present scientific study that the primary outcome can be considered valid in the context of the present. • Industry-sponsored trials. The conflict of interest (COI) statement should explicitly state that the researchers have had full possession of the trial process from planning to reporting without funders with potential COI having any possibility to interfere in the process. If, for example, the statistical analyses have been done by a funder with a potential COI, usually "unsure" is scored.	Yes/No/Unsure

Adapted and modified from: Furlan AD, et al; Editorial Board of the Cochrane Back, Neck Group. 2015 Updated method guideline for systematic reviews in the Cochrane Back and Neck Group. Spine (Phila Pa 1976) 2015; 40:1660-1673 (56).

Appendix Table 2. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
I.	TRIAL DESIGN AND GUIDANCE REPORTING	
1.	CONSORT or SPIRIT	
	Trial designed and reported without any guidance	0
	Trial designed and reported utilizing minimum criteria other than CONSORT or SPIRIT criteria or trial was conducted prior to 2005	1
	Trial implies it was based on CONSORT or SPIRIT without clear description with moderately significant criteria for randomized trials or the trial was conducted before 2005	2
	Explicit use of CONSORT or SPIRIT with identification of criteria or trial conducted with high level reporting and criteria or conducted before 2005	3
II.	DESIGN FACTORS	
2.	Type and Design of Trial	
	Poorly designed control group (quasi selection, convenient sampling)	0
	Proper active-control or sham procedure with injection of active agent	2
	Proper placebo control (no active solutions into active structures)	3
3.	Setting/Physician	
	General setting with no specialty affiliation and general physician	0
	Specialty of anesthesia/PMR/neurology/radiology/ortho, etc.	1
	Interventional pain management with interventional pain management physician	2
4.	Imaging	
	Blind procedures	0
	Ultrasound	1

Appendix Table 2 cont. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
	CT	2
	Fluoro	3
5.	Sample Size	
	Less than 50 participants in the study without appropriate sample size determination	0
	Sample size calculation with less than 25 patients in each group	1
	Appropriate sample size calculation with at least 25 patients in each group	2
	Appropriate sample size calculation with 50 patients in each group	3
6.	Statistical Methodology	
	None or inappropriate	0
	Appropriate	1
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	
7a.	For epidural procedures:	
	Poorly identified mixed population	0
	Clearly identified mixed population	1
	Disorders specific trials (i.e. well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post surgery syndrome)	2
7b.	For facet or sacroiliac joint interventions:	
	No diagnostic blocks	0
	Selection with single diagnostic blocks	1
	Selection with placebo or dual diagnostic blocks	2
8.	Duration of Pain	
	Less than 3 months	0
	3 to 6 months	1
	> 6 months	2
9.	Previous Treatments	
	Conservative management including drug therapy, exercise therapy, physical therapy, etc.	
	Were not utilized	0
	Were utilized sporadically in some patients	1
	Were utilized in all patients	2
10.	Duration of Follow-up with Appropriate Interventions	
	Less than 3 months or 12 weeks for epidural or facet joint procedures, etc. and 6 months for intradiscal procedures and implantables	0
	3 to 6 months for epidural or facet joint procedures, etc., or 1 year for intradiscal procedures or implantables	1
	6 months to 17 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables	2
	18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables	3
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	
	No descriptions of outcomes OR < 20% change in pain rating or functional status	0
	Pain rating with a decrease of 2 or more points or more than 20% reduction OR functional status improvement of more than 20%	1

Appendix Table 2 cont. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
	Pain rating with decrease of ≥ 2 points AND ≥ 20% change or functional status improvement of ≥ 20%	2
	Pain rating with a decrease of 3 or more points or more than 50% reduction OR functional status improvement with a 50% or 40% reduction in disability score	2
	Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores	4
12.	Analysis of all Randomized Participants in the Groups	
	Not performed	0
	Performed without intent-to-treat analysis without inclusion of all randomized participants	1
	All participants included with or without intent-to-treat analysis	2
13.	Description of Drop Out Rate	
	No description of dropouts, despite reporting of incomplete data or ≥ 20% withdrawal	0
	Less than 20% withdrawal in one year in any group	1
	Less than 30% withdrawal at 2 years in any group	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	
	Groups dissimilar with significant influence on outcomes with or without appropriate randomization and allocation	0
	Groups dissimilar without influence on outcomes despite appropriate randomization and allocation	1
	Groups similar with appropriate randomization and allocation	2
15.	Role of Co-Interventions	
	Co-interventions were provided but were not similar in the majority of participants	0
	No co-interventions or similar co-interventions were provided in the majority of the participants	1
V.	RANDOMIZATION	
16.	Method of Randomization	
	Quasi randomized or poorly randomized or not described	0
	Adequate randomization (coin toss, drawing of balls of different colors, drawing of ballots)	1
	High quality randomization (Computer generated random sequence, pre-ordered sealed envelopes, sequentially ordered vials, telephone call, pre-ordered list of treatment assignments, etc.)	2
VI.	ALLOCATION CONCEALMENT	
17.	Concealed Treatment Allocation	
	Poor concealment of allocation (open enrollment) or inadequate description of concealment	0
	Concealment of allocation with borderline or good description of the process with probability of failure of concealment	1
	High quality concealment with strict controls (independent assignment without influence on the assignment sequence)	2
VII.	BLINDING	
18.	Patient Blinding	
	Patients not blinded	0
	Patients blinded adequately	1
19.	Care Provider Blinding	
	Care provider not blinded	0
	Care provider blinded adequately	1
20.	Outcome Assessor Blinding	
	Outcome assessor not blinded or was able to identify the groups	0
	Performed by a blinded independent assessor with inability to identify the assignment-based provider intervention (i.e., subcutaneous injection, intramuscular distant injection, difference in preparation or equipment use, numbness and weakness, etc.)	1

Appendix Table 2 cont. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
VIII.	CONFLICTS OF INTEREST	
21.	Funding and Sponsorship	
	Trial included industry employees	-3
	Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts	-3
	Industry or organizational funding with reimbursement of expenses with some involvement	0
	Industry or organization funding of expenses without involvement	1
	Funding by internal resources only with supporting entity unrelated to industry	2
	Governmental funding without conflict such as NIH, NHS, AHRQ	3
22.	Conflicts of Interest	
	None disclosed with potential implied conflict	0
	Marginally disclosed with potential conflict	1
	Well disclosed with minor conflicts	2
	Well disclosed with no conflicts	3
	Hidden conflicts with poor disclosure	–1
	Misleading disclosure with conflicts	–2
	Major impact related to conflicts	–3
TOTAL		48

Source: Manchikanti L, et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. Pain Physician 2014; 17:E263-E290 (57).

Appendix Table 3. *IPM checklist for assessment of nonrandomized or observational studies of IPM techniques utilizing IPM-QRBNR.*

		Scoring
I.	STUDY DESIGN AND GUIDANCE REPORTING	
1.	STROBE or TREND Guidance	
	Case Report/Case Series	0
	Study designed without any guidance	1
	Study designed with minimal criteria and reporting with or without guidance	2
	Study designed with moderately significant criteria or implies it was based on STROBE or TREND without clear description or the study was conducted before 2011 or similar criteria utilized with study conducted before 2011	3
	Designed with high level criteria or explicitly uses STROBE or TREND with identification of criteria or conducted prior to 2011	4
II.	DESIGN FACTORS	
2.	Study Design and Type	
	Case report or series (uncontrolled – longitudinal)	0
	Retrospective cohort or cross-sectional study	1
	Prospective cohort case-control study	2
	Prospective case control study	3
	Prospective, controlled, nonrandomized	4
3.	Setting/Physician	
	General setting with no specialty affiliation and general physician	0
	Specialty of anesthesia/PMR/neurology, etc.	1
	Interventional pain management with interventional pain management physician	2

Appendix Table 3 cont. *IPM checklist for assessment of nonrandomized or observational studies of IPM techniques utilizing IPM-QRBNR*.

		Scoring
4.	Imaging	
	Blind procedures	0
	Ultrasound	1
	CT	2
	Fluoro	3
5.	Sample Size	
	Less than 100 participants without appropriate sample size determination	0
	At least 100 participants in the study without appropriate sample size determination	1
	Sample size calculation with less than 50 patients in each group	2
	Appropriate sample size calculation with at least 50 patients in each group	3
	Appropriate sample size calculation with 100 patients in each group	4
6.	Statistical Methodology	
	None	0
	Some statistics	1
	Appropriate	2
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	
7a.	For epidural procedures:	
	Poorly identified mixed population	1
	Poorly identified mixed population with large sample (≥ 200)	2
	Clearly identified mixed population	3
	Disorders specific trials (i.e. well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post-surgery syndrome)	4
7b.	For facet or sacroiliac joint interventions:	
	No specific selection criteria	1
	No diagnostic blocks based on clinical symptomatology	2
	Selection with single diagnostic blocks	3
	Selection with placebo or dual diagnostic blocks	4
8.	Duration of Pain	
	Less than 3 months	0
	3 to 6 months	1
	> 6 months	2
9.	Previous Treatments	
	Conservative management including drug therapy, exercise therapy, physical therapy, etc.	
	Were not utilized	0
	Were utilized sporadically in some patients	1
	Were utilized in all patients	2
10.	Duration of Follow-up with Appropriate Interventions	
	Less than 3 months or less for epidural or facet joint procedures, etc., and 6 months for intradiscal procedures and implantables	1
	3-6 months for epidural or facet joint procedures, etc., or one year for intradiscal procedures or implantables	2
	6-12 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables	3
	18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables	4

Appendix Table 3 cont. ***IPM checklist for assessment of nonrandomized or observational studies of IPM techniques utilizing IPM-QRBNR.***

		Scoring
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	
	No descriptions of outcomes OR < 20% change in pain rating or functional status	0
	Pain rating with a decrease of 2 or more points or more than 20% reduction OR functional status improvement of more than 20%	1
	Pain rating with decrease of ≥ 2 points AND ≥ 20% change or functional status improvement of 20%	2
	Pain rating with a decrease of 3 or more points or more than 50% reduction OR functional status improvement with a 50% or 40% reduction in disability score	2
	Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores	4
12.	Description of Drop Out Rate	
	No description despite reporting of incomplete data or more than 30% withdrawal	0
	Less than 30% withdrawal in one year in any group	1
	Less than 40% withdrawal at 2 years in any group	2
13.	Similarity of Groups at Baseline for Important Prognostic Indicators	
	No groups or groups dissimilar with significant influence on outcomes	0
	Groups dissimilar without significant influence on outcomes	1
	Groups similar	2
14.	Role of Co-Interventions	
	Dissimilar co-interventions or similar co-interventions in some of the participants	1
	No co-interventions or similar co-interventions in majority of the participants	2
V.	ASSIGNMENT	
15.	Method of Assignment of Participants	
	Case report/case series or selective assignment based on outcomes or retrospective evaluation based on clinical criteria	1
	Prospective study with inclusion without specific criteria	2
	Retrospective method with inclusion of all participants or random selection of retrospective data	3
	Prospective, well-defined assignment of methodology and inclusion criteria (quasi randomization, matching, stratification, etc.)	4
VI.	CONFLICTS OF INTEREST	
16.	Funding and Sponsorship	
	Trial included industry employees with or without proper disclosure	-3
	Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts	-3
	Industry or organizational funding with reimbursement of expenses with some involvement or no information available	0
	Industry or organization funding of expenses without involvement	1
	Funding by internal resources only	2
	Governmental funding without conflict such as NIH, NHS, AHRQ	3
TOTAL MAXIMUM		48

Source: Manchikanti L, et al. Development of an interventional pain management specific instrument for methodologic quality assessment of non-randomized studies of interventional techniques. Pain Physician 2014; 17:E291-E317 (58).