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Systematic Review

# A Systematic Evaluation of Thoracic Interlaminar Epidural Injections

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**Background:** There is a paucity of literature on the use of epidural injections for the treatment of chronic mid and upper back pain due to disc herniation and radiculitis, axial or discogenic pain, spinal stenosis, post surgery syndrome, and post thoracotomy pain syndrome.

**Study Design:** A systematic review of therapeutic thoracic epidural injection therapy for chronic mid and upper back pain.

**Objective:** The objective of this systematic review is to determine the effects of thoracic interlaminar epidural injections with or without steroids, with or without fluoroscopy, and for various conditions including disc herniation and radiculitis, axial or discogenic pain, spinal stenosis, post thoracic surgery syndrome, and post thoracotomy pain syndrome.

**Methods:** The available literature on thoracic interlaminar epidural injections with or without steroids in managing various types of chronic mid and upper back 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, or 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 March 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:** For this review, 17 studies were identified, including studies examining adverse reactions. Only 2 studies were included: one randomized trial and one non-randomized or observational study.

The results of this systematic review evaluating the effectiveness of thoracic epidural injections with or without steroids in managing chronic thoracic pain shows fair evidence with one randomized trial in patients with various causes; whereas the evidence is limited based on one non-randomized study evaluating chronic pain in post thoracotomy syndrome.

**Limitations:** The limitations of this study include paucity of evidence.

**Conclusion:** The evidence based on this systematic review for thoracic epidural injection in treating chronic thoracic pain is considered fair and limited for post thoracotomy pain.

**Key words:** Spinal pain, chronic mid back pain, chronic upper back pain, post-thoracotomy pain, thoracic epidural injection, radiculopathy, herniation, steroids, local anesthetic, epidural steroid

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The prevalence of mid and upper back chronic pain is extremely low when compared to the prevalence of lower back and neck pain, likely due to the relative immobility and support of the thoracic region in contrast to the other regions of the spine (1-7). One report for back pain being of thoracic origin is 15%, compared to 44% neck and 56% low back (5); others have reported prevalences of 5% thoracic versus 24% cervical and 33% lumbar (6).

Kuslich et al (8) identified intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura as tissues capable of transmitting pain in the low back. Similarly, chronic thoracic or chest wall pain may be transmitted by either intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura, the tissues capable of transmitting pain in the mid back and upper back (9). Chronic, persistent thoracic and chest wall pain and rare radicular pain may be secondary to either disc herniation, discogenic pain, spinal stenosis, or post thoracic surgery syndrome. Post thoracotomy pain syndrome is separate from thoracic spinal pain.

In the United States, epidural injections are one of the most commonly utilized treatment modalities for managing chronic low back pain and lower extremity pain, in addition to numerous other modalities, including surgical interventions (10-33). Epidural injections are administered by accessing the thoracic epidural space by either a transforaminal or interlaminar approach. While significant differences have been described between these 2 approaches, interlaminar entry is considered to deliver the medication closer to the assumed site of pathology, while the transforaminal approach is considered the target-specific modality requiring the smallest volume to reach the primary site of pathology (31). However, the transforaminal approach has been associated with multiple complications (34-36).

Though thoracic epidural injections have been used in the acute setting for the relief of acute post thoracotomy pain, there is a paucity of literature concerning thoracic epidural injections with or without steroids for the treatment of chronic thoracic and chest wall pain of spinal origin and chronic post thoracotomy syndrome (34,37-42). Further, there have been very few studies addressing adverse outcomes and complications of thoracic epidural injections (31,35,36).

To date, there has been only one randomized double-blind trial (39) examining the effect of thoracic epidural injections in the management of chronic mid back, upper back, or chest wall pain secondary to disc herniation, radiculitis, or discogenic pain. However, thoracic epidural injections have been studied in the treatment of post thoracotomy pain (41,43,44). The use of thoracic epidural injection for pain relief is still for the most part being explored for post-thoracotomy treatment, often in conjunction with medical analgesia.

Limited studies have examined adverse outcomes of thoracic epidural injections (35,36,42,45-47). Overall, the thoracic epidural injection procedure itself does not appear to cause significant adverse outcomes.

The objective of this systematic review is to determine the effects of thoracic interlaminar epidural injections with or without steroids, with or without fluoroscopy, and for various conditions including disc herniation and radiculitis, axial or discogenic pain, spinal stenosis, post thoracic surgery syndrome, and post thoracotomy pain syndrome.

## 1.0 Methods

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and meta-analyses of randomized trials and observational studies (10,48-55), Consolidated Standards of Reporting Trials (CONSORT) guidelines for the conduct of randomized trials (56,57), Standards for Reporting Observational Studies (STROBE) (58-60), Cochrane guidelines (10,53,54), Chou and Huffman's guidelines (61), and quality of reporting of analysis (50).

### 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 Patients*

Patients of interest were adults aged at least 18 years with chronic thoracic and chest wall pain of at least 3 months duration.

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

#### *1.1.3 Types of Interventions*

The interventions were thoracic interlaminar epidural injections for chronic mid back and upper back pain. All randomized trials with proper inclusion criteria and appropriately performed non-randomized stud-

ies with proper technique preferably 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 conducted of 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 March 2012.

### 1.3 Search Strategy

The search strategy emphasized chronic thoracic pain, disc herniation, discogenic pain, post thoracic laminectomy syndrome, post-thoracotomy pain, thoracic spinal stenosis, and thoracic radiculitis treated with thoracic interlaminar epidural injections.

At least 2 of the review authors independently, in an unblinded, standardized manner, performed each search. Accuracy was confirmed by a statistician. 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 with chronic thoracic pain for at least 3 months. Only thoracic epidural injections with or without steroids 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*

The following are the inclusion and exclusion criteria:

1. Are the patients described in sufficient detail to allow one to decide whether they are comparable to those who are treated in interventional pain management clinical practices?
   A. Setting – office, hospital, outpatient, inpatient
   B. Physician – interventional pain physician, general physician, anesthesiologist, physiatrist, neurologist, rheumatologist, orthopedic surgeon, neurosurgeon, etc.
   C. Patient characteristics - duration of pain
   D. Non-interventional techniques or surgical intervention in the past
2. Is the intervention described in sufficient detail to enable one to apply its use to patients in interventional pain management settings?
   A. Nature of intervention
   B. Frequency of intervention
   C. Duration of intervention
3. Were clinically relevant outcomes measured?
   A. Proportion of pain relief
   B. Disorder/specific disability
   C. Functional improvement
   D. Allocation of eligible and ineligible patients to return to work
   E. Ability to work

#### *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) (52,62).

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 Methodologic Quality (Validity) Assessment*

Even though none of these instruments or criteria have been systematically assessed, the advantages and disadvantages of each system were debated.

The methodologic quality assessment was performed by 2 review authors who independently assessed, in an unblinded, standardized manner, the internal validity of all the studies.

The methodologic quality assessment was performed in a manner to avoid any discrepancies; if a discrepancy was found, it was evaluated by a third reviewer and settled by consensus.

The quality of each individual article used in this analysis was assessed by Cochrane review criteria (Table 2) (53) for randomized trials, and the Newcastle-Ottawa Scale for observational studies (Tables 3 and 4) (63).

Review authors with a perceived conflict of interest for any manuscript were recused from reviewing the manuscript(s).

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

Only the randomized trials meeting t at least 6 of 12 inclusion criteria were utilized for analysis. However, studies scoring lower were described and provided with an opinion and critical analysis.

Observational studies had to meet a minimum of 7 of the 13 criteria for cohort studies and 5 of 10 for 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 homogenous, 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 planned third author was called in to break the impasse.

#### *1.4.6 Measurement of Treatment Effect in Data Synthesis (Meta-Analysis)*

No meta-analysis was contemplated for thoracic epidurals due to the paucity of literature.

### 1.5 Summary Measures

Summary measures included 50% or more reduction of pain or at least a 3 point decrease in pain scores in at least 40% of the patients and a relative risk of adverse events including side effects.

### 1.6 Minimum Amount of Change

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 (64), chronic musculoskeletal pain (65), and chronic low back pain (48,50,52,65-67), which have been commonly utilized. Recent descriptions of clinically meaningful improvement showed either pain relief or functional status as 50% (68-84). 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, as clinically significant

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 in clinical 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 (62).

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:<br>–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"<br>–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<br>–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<br>–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"<br>–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 A. D. Furlan, V. Pennick, C. Bombardier, et al; Editorial Board, Cochrane Back Review Group, "2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group," *Spine (Phila Pa 1976)* vol. 34, no. 18, pp. 1929-1941, 2009 (53).

Table 3. *Newcastle-Ottawa quality assessment scale for 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 (63).

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 (e.g. 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 (63).

and functional status improvement of 40% or more.

### 1.7 Analysis of Evidence

The analysis of the evidence was performed based on USPSTF criteria as illustrated in Table 5, criteria which has been utilized by multiple authors (85).

The analysis was conducted using 3 levels of evidence ranging from good, fair, or limited (or poor).

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

### 1.8 Outcome of the Studies

In the randomized trials, a study was judged to be positive if the thoracic interlaminar epidural injection therapy 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 epidural injection therapy was effective, with outcomes reported at the reference point with positive or negative results at one month, 3 months, 6 months, and one year.

## 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) (51). There were 17 studies considered for inclusion (31,34,37-44,86-92).

Of the 17 thoracic epidural studies identified, only 2 studies were included (39,41). The 15 excluded studies were mainly assessments of post-thoracotomy pain and reviews (34,37,40,43,44,86-92). Table 6 illustrates other studies excluded (31,38,42).

Table 7 illustrates characteristics of studies considered for inclusion. There was only one randomized trial (39) and one observational study evaluating long-term follow-up (41).

### 2.1 Clinical Relevance

Of the 2 studies assessed for clinical relevance, both of them met criteria with scores of 5/5 and 4/5. Table 8 illustrates the assessment of clinical relevance.

### 2.2 Methodologic Quality Assessment

A methodologic quality assessment of the randomized controlled trials meeting inclusion criteria was carried out utilizing Cochrane review criteria as shown in Table 9. 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.

There was only one randomized trial evaluating long-term response of 12 months or longer (39).

A methodologic quality assessment of one observational study meeting inclusion criteria was carried out

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 (61,85).

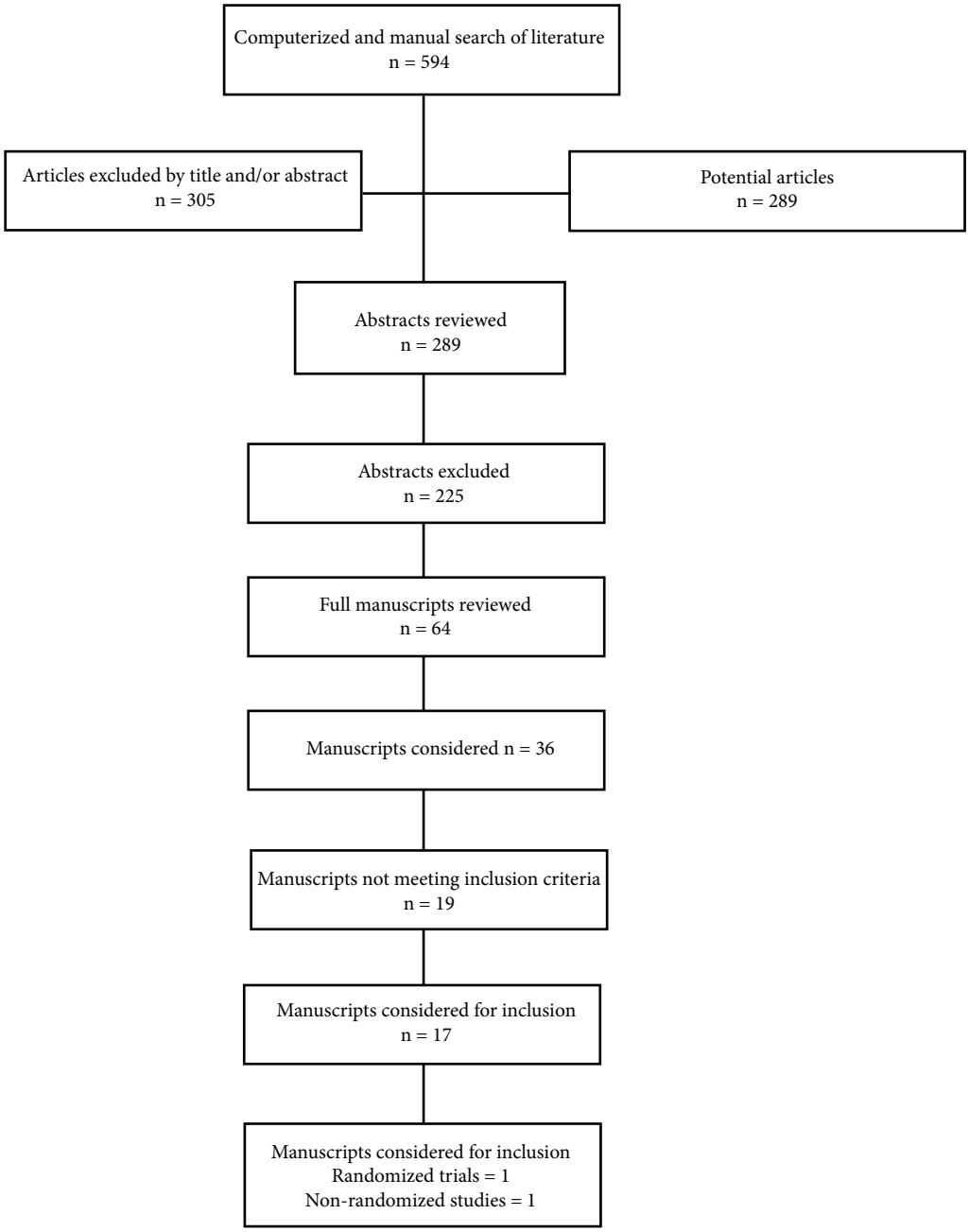


Fig. 1. *The flow diagram illustrating published literature evaluating thoracic epidural injections.*

utilizing Newcastle-Ottawa Scales as illustrated in Table 10. For case-control studies, 8 or higher was considered as high quality, 5 to 7 was considered as moderate quality, and less than 5 was considered low quality and those studies were excluded.

There was only one non-randomized or observational study evaluating long-term effectiveness of thoracic interlaminar epidural injections with follow-up of 6 months or longer (41).

### 2.3 Study Characteristics

Table 7 illustrates the study characteristics of the included studies.

### 2.4 Level of Evidence

Based on the USPSTF criteria, the evidence was considered at 3 levels – good, fair, and limited (or poor). The evidence for thoracic epidural injection in treating chronic thoracic pain is considered fair based on one randomized trial (39) and limited for post thoracotomy pain based on one observational study (41).

## 3.0 Complications and Side Effects

Very few studies have examined the adverse effects of thoracic epidural injections for the treatment of chronic mid and upper back pain (31,42). One study (31) examined the complication rate of thoracic fo-

Table 6. *List of excluded randomized trials and non-randomized studies.*

| Manuscript Author(s) | Condition Studied | Number of Patients | Reason for Exclusion | |
|---|---|---|---|---|
| | | | Follow-up Period | Other Reason(s) |
| Wang et al (31) | Thoracic transforaminal nerve block for various reasons for injection | 153 patients, 296 injections | NA | A retrospective evaluation using radiograph and reports of transforaminal epidurals |
| Fanciullo et al (38) | Frequency of epidural steroid injection | 36 | NA | Observational report with no follow-up results |
| Botwin et al (42) | Thoracic interlaminar | 21 | NA | Study of adverse effects |

Table 7. *Assessment of randomized trials and non-randomized studies for inclusion criteria.*

| Manuscript Author(s) | Type of Study | Number of Patients | Control vs. Intervention or Comparator vs. Treatment | Follow-up Period | Outcome Measures | Comment(s) |
|---|---|---|---|---|---|---|
| Manchikanti et al (39) | R, AC, F | 40<br>Local anesthetic only = 20<br>Local anesthetic with steroids = 20 | 6 mL of local anesthetic only or 6 mL of local anesthetic with 6 mg of nonparticulate betamethasone. | One year | NRS, ODI, employment status, opioid intake | Significant improvement with 50% or more pain relief and functional status improvement in 80% and 85% at one year in patients receiving local anesthetic or local anesthetic with steroids. This is the first randomized trial conducted in thoracic pain patients in contemporary practice under fluoroscopy. |
| Ayad et al (41) | P, B | 21 | 8 patients underwent conservative management whereas 13 patients underwent epidural injections with clonidine 150 mg, 80 mg of methylprednisolone acetate diluted in 8 mL of 0.5% lidocaine. | 6 months | VAS, sleep patterns, appetite changes, ADL | In this evaluation, allodynia in patients with post thoracotomy syndrome at least after 2 months were included for injection therapy with epidural injections. There was significant improvement which was different from the control group in patients receiving epidural injections. Sleep scores, appetite changes, activity scores also improved. Over 50% of the patients showed significant improvement of 50% or more.<br>This study had multiple issues with inclusion criteria including the number of patients as well as duration of pain. |

R = Randomized; AC = Active-control; F = Fluoroscopy; P = Prospective; B = Blind; NA = Not Applicable; NRS = Numeric Rating Scale; ODI – Oswestry Disability Index; VAS = Visual Analog Scale; ADL = Activities of Daily Living

Table 8. *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 |
|---|---|---|---|---|---|---|
| Manchikanti et al (39) | + | + | + | + | + | 5/5 |
| Ayad et al (41) | + | + | + | - | + | 4/5 |

+ = positive; - = negative ; U= unclear

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 (62).

Table 9. *Methodological quality assessment of the randomized trial.*

| | Manchikanti et al (39) |
|---|---|
| Randomization adequate | Yes |
| Concealed treatment allocation | Yes |
| Patient blinded | Yes |
| Care provider blinded | Yes |
| Outcome assessor blinded | No |
| Drop-out rate described | Yes |
| All randomized participants analyzed in the group | Yes |
| Reports of the study free of suggestion of selective outcome reporting | Yes |
| Groups similar at baseline regarding most important prognostic indicators | Yes |
| Co-interventions avoided or similar | Yes |
| Compliance acceptable in all groups | Yes |
| Time of outcome assessment in all groups similar | Yes |
| **Score** | 11/12 |

raminal injections at the same institution and found a complication rate of 4.1% (12 out of 296 injections). All of these were considered minor complications (lightheadedness, local numbness, muscle spasm, vasovagal response, headache) with one major complication of an avoidable pneumothorax.

Botwin et al (42) reviewed adverse effects of fluoroscopically guided interlaminar thoracic epidural injections for the treatment of spondylosis and herniated nucleus pulposus. A retrospective review of charts of 21 patients revealed a 20.5% minor complication rate, all without morbidity. Complications included pain at the injection site (7.7%), facial flushing (5.1%), headache (2.6%), insomnia the night of the injection (2.6%), and fever the night of the procedure (2.6%).

Manchikanti et al evaluated complications and side effects of epidural injections (45-47,93). Among 10,000 epidurals performed, 301 were performed in the thoracic region. The results illustrated intravascular entry in 4%; return of blood in 2.7%; profuse bleeding in 1.3%; local hematoma in 0.7%; bruising in 0.3%; vasovagal reaction, transient nerve root irritation, postlumbar puncture headache, and facial flushing in 0.33%; transient spinal cord irritation in 1%; dural puncture in 1.3%; and profuse bleeding in 1.3%.

## 4.0 Discussion

The results of this systematic review evaluating the effectiveness of thoracic epidural injections with or without steroids in managing chronic thoracic pain showed fair evidence with one randomized trial in pa-

Table 10. *Quality assessment of case control studies*.

| | Ayad et al (41) |
|---|---|
| **Selection** | |
| 1) Is the case definition adequate? | |
| a) yes, with independent validation * | |
| b) yes, e.g., record linkage or based on self-reports | X |
| 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 | X |
| a) study controls for _____ (Select the most important factor.) * | |
| b) study controls for any additional factor * (This criterion could be modified to indicate specific control for a second important factor.) | |
| **Exposure** | |
| 1) Ascertainment of exposure | |
| a) secure record (e.g., surgical records) * | X |
| b) structured interviews were blind to case/control status * | |
| c) interviews 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) Nonresponse rate | |
| a) same rate for both groups * | |
| b) nonrespondents described | X |
| c) rate different and no designation | |
| **SCORE** | **7/10** |

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of 2 stars can be given for Comparability.

G.A. Wells, B. Shea, D. O'Connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, "The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis," www.ohri.ca/programs/clinical_epidemiology/oxford.asp (63).

tients with various causes; whereas the evidence was poor or limited based on one non-randomized study evaluating chronic pain in post thoracotomy syndrome. The results of this systematic review are provided utilizing contemporary systematic review methodology of randomized trials and observational studies, even though most of the evidence was derived from randomized trials. This systematic review provides information that thoracic epidural injections may be effective and there may not be any significant difference with the addition of steroids when appropriately performed with fluoroscopy.

The scarcity of published reports to describe the effectiveness of thoracic epidural injections for the treatment of chronic pain is the obvious shortcoming of this review. Although the frequency of mid and upper back pain is lower than low back and neck pain, it is estimated that the prevalence is around 13% in the general population (1). Interestingly, despite its low frequency, pain in the thoracic spine causes as much disability as pain originating in other areas of the spine (7). The one randomized trial to date showed effectiveness for patients with chronic pain secondary to thoracic disc herniation or radiculitis and discogenic pain. This preliminary report established that if thoracic facet joint arthropathy is ruled out as a source of chronic pain, local anesthetics epidurally injected with or without steroids provide a promising alternative for the treatment of thoracic spine pain. Overall 80-85% of the patients showed an over 50% reduction in pain. Interestingly, the use of steroids did not show any benefit over the local anesthetic group. One limitation of this study is that the number of patients enrolled did not reach significance as determined by the sample size analysis, but the dramatic number of patients that reported over 50% relief at the 12 month follow-up represents a viable treatment option for this group of patients.

The adverse effects of thoracic epidural injections do not appear to be significant, especially when compared to lumbar and cervical injection complication rates. Also, as stated in several of the studies, no control or placebo groups are used in most reports. Though this is the norm for these types of studies, it is a shortcoming. There does not seem to be a consensus in the use of thoracic epidural analgesia for post-thoracotomy pain relief, with some studies finding no improvement with thoracic epidural injections, though various methodologies of treatment are still being investigated, i.e., perioperative and postoperative treatment with or without adjuvant medical management. Overall, use of thoracic epidural injection holds promise as treatment either alone or in conjunction with pain medication. Adverse effects appear to be about equal to adverse outcomes of more frequently used lumbar and cervical injections.

Multiple systematic reviews have been performed evaluating the role of epidural injections, most commonly in the lumbar spine, but also in the cervical spine (10,17,18,61,94-96). Multiple guidelines have been published over the years; however, due to the paucity of literature on thoracic epidural injections, this is the first systematic review ever performed for thoracic interlaminar epidural injections. This systematic review failed to show significant improvement over the general impressions that there is a substantial paucity of literature about thoracic epidural injections.

Various disadvantages of the single study included are the lack of placebo control with an active-control design and also that it is a preliminary report of 40 patients. Placebo control neural blockade has been described quite extensively as has its misinterpretations. Generally, it is not recognized that placebo solutions injected into active structures produce significant clinical or therapeutic effects (96-110). The underlying mechanism of action of epidurally administered steroids and local anesthetic injection is not well understood, but it is believed that both local anesthetics and steroids provide long-lasting relief by various mechanisms, despite the significant evidence for inflammatory theory in disc herniation and probably in discogenic pain (111-127).

In fact, Sato et al (117) and Tachihara et al (118) showed the prolonged analgesic effect of epidural bupivacaine in a rat model of neuropathic pain with repetitive administration, possibly by inducing plastic change in nociceptive input (117); the nerve root infiltration prevented mechanical allodynia, however, no additional benefit from using corticosteroid was identified by Tachihara et al (118).

## 5.0 Conclusion

Epidural injections for managing chronic thoracic pain showed fair evidence with one randomized trial in patients with various causes; whereas, for chronic pain from post-thoracotomy syndrome, the evidence was poor or limited based on one non-randomized study.

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