Pain Physician 2012; 15:E777-E806 • ISSN 2150-1149

Systematic Review

An Update of the Appraisal of the Accuracy and Utility of Cervical Discography in Chronic Neck Pain

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Dr. Falco is a consultant for St. Jude Medical Inc. and Joimax Inc. Dr. Helm is a clinical investigator with Epimed and receives research support from Cephalon/ Teva, AstraZeneca, and Purdue Pharma, LP. He has attended an Advisory Group meeting for Activas. Dr. Hirsch has received fees from CareFusion in the past 12 months. He participated in an Aetrium focus group and received compensation..

Manuscript received:
Accepted for publication:

Free full manuscript:
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Background: Chronic neck pain represents a significant public health problem. Despite high prevalence rates, there is a lack of consensus regarding the causes or treatments for this condition. Based on controlled evaluations, the cervical intervertebral discs, facet joints, and atlantoaxial joints have all been implicated as pain generators. Cervical provocation discography, which includes disc stimulation and morphological evaluation, is occasionally used to distinguish a painful disc from other potential sources of pain. Yet in the absence of validation and controlled outcome studies, the procedure remains mired in controversy.

Study Design: A systematic review of the diagnostic accuracy of cervical discography.

Objective: To systematically evaluate and update the diagnostic accuracy of cervical discography.

Methods: The available literature on cervical discography was reviewed. Methodological quality assessment of included studies was performed using Quality Appraisal of Reliability Studies (QAREL). Only diagnostic accuracy studies meeting at least 50% of the designated inclusion criteria were utilized for analysis. However, studies scoring less than 50% are presented descriptively and analyzed critically.

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

Results: A total of 41 manuscripts were considered for accuracy and utility of cervical discography in chronic neck pain. There were 23 studies evaluating accuracy of discography. There were 3 studies meeting inclusion criteria for assessing the accuracy and prevalence of discography, with a prevalence of 16% to 53%.

Based on modified Agency for Healthcare Research and Quality (AHRQ) accuracy evaluation and United States Preventive Services Task Force (USPSTF) level of evidence criteria, this systematic review indicates the strength of evidence is limited for the diagnostic accuracy of cervical discography.

Limitations: Limitations include a paucity of literature, poor methodological quality, and very few studies performed utilizing International Association for the Study of Pain (IASP) criteria.

Conclusion: There is limited evidence for the diagnostic accuracy of cervical discography. Nevertheless, in the absence of any other means to establish a relationship between pathology and symptoms, cervical provocation discography may be an important evaluation tool in certain contexts to identify a subset of patients with chronic neck pain secondary to intervertebral disc disorders.

Based on the current systematic review, cervical provocation discography performed according to the IASP criteria with control disc(s), and a minimum provoked pain intensity of 7 of 10, or at least 70% reproduction of worst pain (i.e. worst spontaneous pain of 7 = 7 x 70% = 5), may be a useful tool for evaluating chronic pain and cervical disc abnormalities in a small proportion of patients.

Key words: Chronic cervical pain, cervical intervertebral disc, cervical discography, provocation discography, analgesic discography, pain generator, false-positives, diagnostic accuracy, sensitivity, specificity, outcomes

Pain Physician 2012; 15:E777-E806

Chronic pain in the United States has reached crisis levels, with an explosion of diagnostic and therapeutic measures (1). Chronic spinal pain is common in the general adult population, with low back and neck pain constituting the majority of the disorders (1-10). The most commonly used modalities of treatment, including cervical spine surgery and cervical epidural injections, have risen dramatically over the past 2 decades (3,11-47). Studies of the prevalence of chronic neck pan and its impact on general health have shown that 14% of patients report Grade II-IV neck pain, with a high pain intensity leading to disability. Grade 0 refers to no neck pain; Grade I represents pain of low intensity causing few activity limitations; Grade II indicates pain of high intensity, but with few activity limitations; Grade III is associated with pain of high intensity and high levels of disability associated with moderate limitations in activities; and Grade IV refers to pain with high levels of disability and several activity limitations (5,6). Chronic recurrent neck pain is a common problem in the adult population, with a typical 12-month prevalence of 30%-50% (2,4,20,24).

In addition to cervical disc herniation, cervical facet joint and discogenic pain are other common causes of chronic neck pain, with or without upper extremity radiation (2,3,24,32-35). Pain emanating from a degenerative disc may result in discogenic pain secondary to chemical irritation or predominantly axial pain secondary to internal disc disruption (48-50). Axial neck pain may be related to either a disc, facet joint, or soft tissue pathology. However, there is a lack of consensus regarding the causes and treatment of chronic neck pain without disc herniation and radiculitis.

Cervical provocation discography, an image-guided procedure in which a contrast agent is injected into the nucleus pulposus of the intervertebral disc, includes disc stimulation and morphological assessment. It is intended to both identify a painful cervical intervertebral disc and depict internal derangements (51-54).

Pathophysiology of cervical discogenic pain depends on the sensory nerves which innervate the discs (55-63). In the lumbar spine, sensory nerves usually innervate only the outermost portion of the annulus, but in degenerated discs, the innervation extends deeper and is more widespread; some fibers even penetrate the nucleus pulposus (64-72). It is well established that aging is associated with fissures and tears in the annulus in the lumbar discs. In addition, multiple types of chemical changes occur in the degenerated discs, with the subsequent release of inflammatory substances (70,73-87). In the cervical spine, neurons innervating cervical intervertebral discs can be divided into neurons and autonomic neurons. Dorsal root ganglia neurons can be divided in to the large and small neurons containing neuropeptides, and small neurons devoid of neuropeptides (57,88). Large dorsal root ganglion neurons are involved in proprioception (89). Sensory neurons involved in inflammatory-related pain perception are typically small, nerve growth factor (NGF)–dependant peptide containing neurons that are immunoreactive for substance *P* (SP), and calcitonin gene-related peptide (CGRP) (88-90). Further, it has been shown small, nonpeptide-containing neurons that bind isolectin B4 (IB4) from *Griffonia simplicifolia* may be involved in various pain states such as neuropathic pain from injured nerves (90,91). In an evaluation of the sensory and autonomic innervation of the cervical intervertebral discs in rats, Fujimoto et al (57) concluded that C5-C6 was innervated multisegmentally from neurons stemming from the C2-C8 dorsal root ganglia, stellate and other sympathetic ganglia, and parasympathetic ganglion including the nodose ganglion. Overall, 79.6% of the nerve fibers innervating the intervertebral disc were sensory and 20.4% were autonomic. In addition, 23.9% of the nerve fibers innervating the intervertebral discs were afferent sensory pain-related nerves, 8.9% were efferent sympathetic nerves, and 11.5% were efferent parasympathetic nerves. They postulated that these

findings may explain the broad array of referral patterns associated with chronic discogenic pain.

Cloward (49,50) described 2 types of pain during cervical disc stimulation: pain arising from internal disc disruption (i.e., discogenic pain) and neurogenic pain that stems from a herniated disc fragment causing nerve root or dural irritation. Cloward (61) stimulated cervical discs mechanically and electrically to verify that the evoked pain originated in the discs themselves, rather than from irritation of adjacent structures. Cloward (50) also proposed that disc-related pain is mediated through sinuvertebral nerves, which in the cervical region are very small and undetectable by conventional dissection methods. However, subsequent anatomical studies did visually identify cervical sinuvertebral nerves and confirmed Cloward's (50) experimental observations and inferences (48,62,63,69). Intervertebral disc innervation in the cervical spine is analogous to that in the lumbar spine, with cervical discs receiving innervation posteriorly from the sinuvertebral nerves, laterally from the vertebral nerve, and anteriorly from the sympathetic trunks (62,69).

In a report published in 1964, Holt (92) questioned the validity of cervical discography, citing a 100% false-positive rate in asymptomatic prisoners. Contrast extravasation occurred in all patients, and 93% of discs. He concluded that fissures and pain provocation were normal features in people without neck pain. In an observational study, Klafta and Collis (93,94) found that cervical discography was less accurate than myelography in predicting surgical findings. In 1988, Simmons et al (95) re-evaluated Holt's data (96) in the lumbar spine, finding the methodology so riddled with flaws as to render the findings irrelevant.

Multiple investigators (97-100) have re-examined Holt's conclusions. These studies have established fissures to be normal age-related findings that do not necessarily cause symptomatology, and found that demonstrating them with discography is immaterial (52,99). Thus, reproduction of a patient's typical pain is now considered to be the critical component of cervical discography (52). Supporting this assertion, Schellhas et al (97) found that pressurizing normal discs failed to provoke pain in both symptomatic and asymptomatic patients, whereas abnormal discs tended to produce concordant pain only in symptomatic individuals. Over 30 years ago, Roth (100) and Kofoed (101) proposed the concept of analgesic discography. During this time frame, cervical discography was increasingly used for surgical planning (102,103). As the centerpiece of ongoing controversy, cervical discography has been reviewed in multiple publications (7,25-35,49-56,92-94,97-105).

Building on a foundation first established by Cloward (49,50), Lotz and Ulrich (48) classified pain emanating from a degenerative disc into 2 distinct types: 1) radicular pain secondary to stenosis and/or nerve root irritation; and 2) predominantly axial pain due to internal disc disruption. They suggested that painful discs are characterized by a confluence of nerve in-growth, inflammation, and mechanical hypermobility. Not only cervical intervertebral discs, but other structures such as zygapophysial joints, muscles, and ligaments, can be potential sources of neck pain (7,30,31,49,50,55,56,61-63,98-101,104-116). Studies conducted using controlled diagnostic blocks have implicated the facet joints in between 36% to 60% of patients with chronic neck pain (112-116). Discography studies have also been characterized by wide variations in epidemiology, with reported prevalence rates ranging between 16% and 41% (31,32). Investigations have also found pain referral maps for cervical discogenic pain to be indistinguishable from those for facet joint pain (30,52,97,104,115). Since pain radiation patterns are more closely related to level than structure, and advanced imaging modalities are incapable of discerning nonspecific from nociceptive degeneration, a pivotal question arises about how best to correlate symptoms with pathology.

The major obstacle confronting proponents of cervical discography is the lack of consensus as to what constitutes a positive response. Widespread variations in criteria exist not only for pain provocation (i.e., designation of concordance and threshold for a positive response), but also for morphological classification. Whereas some investigators have interpreted certain patterns of contrast dispersion as being indicative of disc pathology, others have found a lack of correlation between morphology and pain reproduction (27,28,33,34,51-54,94,117).

Imaging studies such as radiographs, myelography, computed tomography (CT), CT-myelography, and magnetic resonance imaging (MRI) are incapable of identifying a degenerated disc as painful (28,33-35,54,87,97,100,103,111,118-149). Consequently, the referral patterns can only be used to suggest which segment(s) is most likely to be the source of pain and, therefore, the levels in which the investigation should focus (52).

Multiple questions have been raised regarding the utility of cervical discography, including the high

reported false-positive rate in select subpopulations; the lack of standardization; the discrepancies regarding the need for "control levels," pain concordance, and pain intensity threshold; and utilization (33-35,51-54,123). In a systematic review of lumbar provocation discography conducted by Wolfer et al (150), the authors re-analyzed the published data on false-positive rates using the International Association for the Study of Pain (IASP) criteria. They found the false-positive rate in subjects without co-existing psychopathology and prior surgery to be very low, and indicated that Level II-2 evidence supported lumbar discography as a diagnostic tool (151).

Shah et al (33) provided an extensive systematic and narrative review of discography in all regions as a diagnostic test for spinal pain. They provided systematic assessment evaluating quality assessment utilizing Agency for Health care Research and Quality (AHRQ) and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria (152,153). They reviewed 9 studies and concluded that there was moderate evidence supporting the role of discography in identifying a subset of patients with cervical discogenic pain. The authors provided an overview on the various assumptions, caveats, analogies, and convictions regarding discography and discogenic pain. They called for future research that investigates the precise mechanism of how discography induces pain and correlates with functional activities. Further, they also called for external validation — not based on subjective pain assessments — of the ability of discography to precisely identify the disc as the pain generator.

In a systematic review of cervical discography as a diagnostic test for chronic spinal pain in 2009, Manchikanti et al (35) reviewed multiple studies with methodological assessment. They concluded that based on the studies utilizing the IASP criteria, the data showed a prevalence rate ranging between 16% and 20%. They concluded that the indicated level of evidence was Level II-2 based on modified U.S. Preventive Services Task Force (USPSTF) criteria (151).

Among the various treatments available for managing axial discogenic pain, epidural injections are one of the most common nonsurgical interventions (3,36,37,154-157). Traditionally, epidural injections have not been recommended for axial neck or low back pain, but they are considered to be reasonable in disc herniation and spinal stenosis causing radicular pain (3,38-40,154,156,157). The evidence for cervical epidural injections in disc herniation and radicular pain, though controversial, is good to fair (3). The evidence for epidural injections as a treatment for axial discogenic pain is based on a single report of discogenic neck pain (after excluding facet joint pain) in patients without disc herniation or radiculopathy (36,37). The evidence for surgical interventions for cervical discogenic pain appears to be fair. The systematic review (35) also showed that cervical discography plays a significant role in selecting surgical candidates and improving outcomes, despite concerns regarding the false-positive rate, lack of standardization, and associated potential confounding factors.

Based on the literature that systematic reviews are time-sensitive, specifically in evolving specialties (158), this systematic review is undertaken to update and reassess the accuracy of cervical provocation discography in the diagnosis of discogenic pain, based on the latest systematic review published in 2009 (35).

1.0 METHODS

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and meta-analysis of diagnostic accuracy studies (125,153,159-175).

1.1 Definition and Criteria

The IASP criteria (165) for cervical discogenic pain includes reproduction of a patient's typical pain with disc stimulation, while injection of 2 adjacent intervertebral discs fails to provoke pain. In addition, the pain cannot be ascribed to some other source innervated by the same segments that innervate the putatively symptomatic disc.

In contrast to provocation discography, no standards have been established by the IASP for analgesic discography. Due to the questions and controversy surrounding provocation discography, pain relief following local anesthetic injected into one or more discs is theoretically a more self-evident and robust method to determine the degree to which one or more discs are contributing to the patient's symptoms (176). It is asserted that there are multiple false-positives with provocation discography when analgesic discography is used as the reference standard. Combining local anesthetic in equal concentration with contrast media during disc injection may enhance accuracy and estimate the degree of pain caused by one or more of the injected discs. This paradigm is similar to the one several investigators have employed for identifying a painful nerve root. In a study by Dooley et al (177), the authors

found that the combination of concordant pain provocation and analgesic response to nerve root infiltration was more accurate than either test alone in predicting surgical findings. Further, adding local anesthetic to the injected contrast mixture is considered to be less traumatic than functional anesthetic discography, which requires a large bore needle to accommodate the insertion of a catheter (176,178). However, the addition of local anesthetic to all injected discs will not necessarily distinguish all symptomatic from asymptomatic discs, which is contingent upon disc injection order, the ability of a patient to distinguish baseline from procedure-related pain, and often requires a patient to perform physical maneuvers designed to provoke pain. Although post-procedure relief of pain may help to confirm one or more positive provocative responses and help assuage concerns of false-positive responses (150), the evidence for analgesic discography for cervical pain is lacking even more than in the lumbar spine. Osler (143) reported that the symptoms of a painful disc are produced by tears in the annulus following acute trauma or stemming from chronic degeneration, resulting in stimulation of the small unmyelinated nerve fibers that innervate the disc capsule. He suggested that analgesic discography adds a new dimension to the treatment of this discogenic syndrome because the results of surgery ultimately depend on the accuracy of diagnostic tests employed.

1.2 Criteria for Considering Studies for the Review

1.2.1 Types of Studies

Diagnostic accuracy studies of cervical discs – provocation and analgesic discography.

1.2.2 Types of Participants

Participants of interest were adults aged at least 18 years with chronic neck pain of at least 3 months duration.

Participants must have failed previous pharmacotherapy, exercise therapy, etc., prior to discography.

1.2.3 Types of Interventions

The interventions were cervical provocation and analgesic discography.

1.2.4 Types of Outcome Measures

- The primary outcome parameter was pain provocation and pain relief when analgesic discography was performed.
- 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.

1.3 Literature Search

Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. EMBASE from 1980
   www.embase.com
3. Cochrane Library
   www.thecochranelibrary.com/view/0/index.html
4. U.S. National Guideline Clearinghouse (NGC)
   www.guideline.gov
5. Previous systematic reviews and cross references
6. Clinical Trials
   clinicaltrials.gov

The search period was from 1966 through June 2012.

1.4 Search Strategy

The search strategy emphasized chronic neck pain and diagnostic interventional techniques with special emphasis on provocation and analgesic discography.

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.

1.5 Data Collection and Analysis

This systematic review focused only on invasive diagnostic studies – provocation and analgesic discography. The population of interest was patients suffering with chronic neck pain with or without upper extremity pain for at least 3 months. Only the diagnostic accuracy of cervical discography with respect to chronic neck pain was evaluated. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

The quality of each individual article used in this assessment was based on Quality Appraisal of Reliability Studies (QAREL) checklist (Table 1) (166). This checklist has been validated and utilized in multiple systematic

Table 1. *Quality Appraisal of Diagnostic Reliability (QAREL) checklist.*

Item	Yes	No	Unclear	N/A
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?				
2. Was the test performed by examiners representative of those who would normally perform the test in practice?				
3. Were raters blinded to the reference standard for the target disorder being evaluated?				
4. Were raters blinded to the findings of other raters during the study?				
5. Were raters blinded to their own prior outcomes of the test under evaluation?				
6. Were raters blinded to clinical information that may have influenced the test outcome?				
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?				
8. Was the order in which raters examined subjects varied?				
9. Were appropriate statistical measures of agreement used?				
10. Was the application and interpretation of the test appropriate?				
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?				
12. If there were dropouts from the study, was this less than 20% of the sample.				
TOTAL				

Lucas N, et al. Reliability of physical examination for diagnosis of myofascial trigger points. *Clin J Pain* 2009; 25:80-89 (166).

reviews (167-169). Each study in the final sample of eligible manuscripts was assessed using a 12-item appraisal checklist designed to assess the quality and applicability of studies. The face validity of these checklists was established by consultation with methodology experts (166) and comparison with quality appraisal checklists used in other systematic reviews examining diagnostic reliability (179-182). This checklist was also developed in accordance to the Standards for the Reporting Studies of Diagnostic Accuracy Studies (STARD) (170) and the QUADAS (153,164) appraisal tool. Studies were not given an overall numeric quality score; instead each item was considered separately and graded as "yes," "no," "unclear," or "not applicable."

1.5.1 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.

1.5.2 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 non-eligible patients to return to work
   E. Ability to work

1.5.3 Clinical Relevance

The clinical relevance of the included studies were evaluated according to 5 questions recommended by the Cochrane Back Review Group (Table 2) (183,184). Each question was scored 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.

1.5.4 Methodological Quality or Validity Assessment

Each study was evaluated by at least 2 authors for stated criteria and any disagreements discussed with a third reviewer. Authors with a perceived conflict of interest for any manuscript were recused from reviewing the manuscript.

Only diagnostic accuracy studies meeting at least 50% of applicable inclusion criteria were included for analysis. Studies scoring less than 50% are reported descriptively with critical analysis.

1.5.5 Data Extraction & 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. Data were analyzed separately based on whether the intervention was provocation or analgesic.

1.6 Analysis of Evidence

The analysis of the evidence was performed based on USPSTF criteria as illustrated in Table 3, which has been utilized by multiple authors (33-35,168,169,172-175,185,186)

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

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

1.7 Outcome of the Studies

Outcome evaluations included prevalence of cervical discogenic pain, false-positive results, and its role in assessing patients for surgery.

Table 2. *Clinical relevance questions.*

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

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (184).

Table 3. *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 (151-173).

2.0 Results

Figure 1 shows a flow diagram of study selection. There were 41 studies considered for inclusion (27-32,92-94,97,98,102-105,117,118,122,123,133-135,138,143,144,187-202).

2.1 Diagnostic Accuracy Studies

Table 4 illustrates the characteristics of studies of cervical discography considered for inclusion. Table 5 shows characteristics of outcome studies.

Accuracy and reliability was evaluated in multiple studies as shown in Tables 4 and 5. Based on a cadaveric study, a good correlation was demonstrated between discography and microanatomic appearance. Overall, of the 23 studies evaluating the reliability of discography, 17 studies showed reproducibility. Similarly, with regard to whether or not discography improves surgical outcomes in patients undergoing cervical fusion, the results were superior in patients after discography in 14 studies, compared to 4 studies in which no significant improvement was noted.

2.1.1 Methodological Quality Assessment

A methodological quality assessment of diagnostic accuracy studies meeting inclusion criteria was carried out utilizing QAREL criteria as shown in Table 6. Studies achieving 50% or higher scores were included. Scores of 67% or higher were considered to constitute high quality, studies scoring over 50% were considered to be moderate quality, and studies scoring less than 50% were excluded.

There were 3 studies evaluating provocation discography based on IASP criteria (31,32,138).

2.1.2 Clinical Relevance

Among the 3 studies assessed for clinical relevance, all met all 5 criteria (31,32,138). Table 7 illustrates the assessment of clinical relevance.

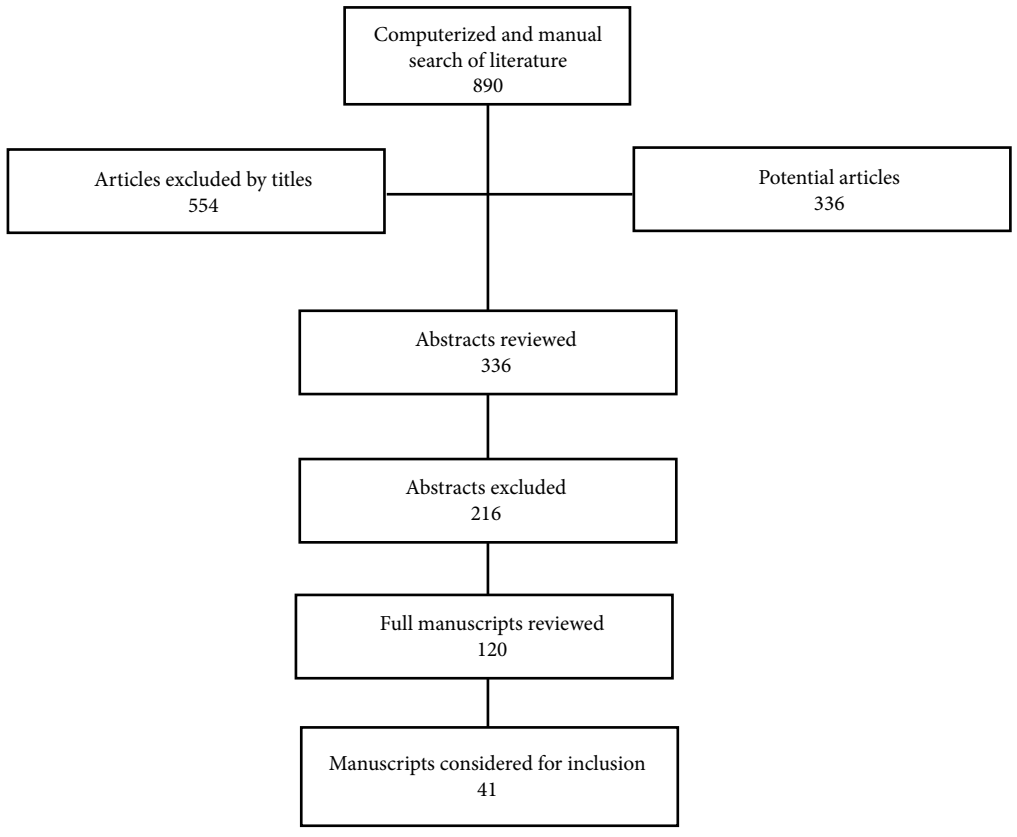

Fig. 1. *The flow diagram illustrating published literature evaluating provocation and analgesic cervical discography*

Table 4. Study *characteristics of cervical discography studies considered for inclusion*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Grubb & Kelly, 2000 (30)	O	A series of 173 cervical discograms performed over 12 years was examined. Objective was to report the prevalence of cervical pathology to determine whether a reproducible pattern of concordant pain could be associated with each symptomatic level identified, and to calculate the rate of complications. Pain responses provoked and recorded during discography were grouped by disc level and examined for recurring patterns. The prevalence of disc pathology was calculated.	In all, 807 discs were injected with 404 concordant pain responses, in 50%, 3 or more abnormal disc levels were identified. Complications developed in 4 patients (2.3%). Surgical treatment was indicated as viable in only 35 or 173 patients.	Discography was concluded as a safe and valuable diagnostic procedure showing characteristic pain patterns that may have clinical significance. Since in more than half of the patients, 3 or more levels were identified as pain generators, it was suggested that treatment decisions based on information from few discs injected during discography may be tenuous. In this series only 10% of the patients evaluated with cervical discography were surgical candidates. An additional 10% also underwent operative intervention because of instability or neural compressive syndromes. Overall disc pathology produces predictable pain distributions. Discography should be performed at all assessable levels. Multilevel degenerative disc disease is frequent in the cervical spine; there is a low rate of occurrence of complications related to cervical discography.	Authors summarized that they believe that surgery rarely is necessary in the treatment of mechanical neck pain if, however, surgery is being considered because of severe and disabling symptoms even after exhaustive assessment and nonoperative treatment, then discography is not only useful, but necessary to determine surgical levels.
Bogduk & Aprill, 1993 (31)	O	To determine the prevalence of disc pain and zygapophysial joint pain occurring simultaneously in the same segment of the neck, 56 patients with post traumatic neck pain underwent both provocation discography and cervical zygapophysial joint blocks.	Both a symptomatic disc and a symptomatic zygapophysial joint were identified in the same segment in 41% of the patients. Discs alone were symptomatic in only 20% of the sample.	Authors indicated that the investigation of neck pain by discography alone or by zygapophysial blocks alone constitute an inadequate approach to neck pain which fails to identify the majority of patients whose symptoms stem from multiple elements in the 3 joint complexes of the neck.	Since provocation discography was positive along with a zygapophysial joint block in 41% of the patients and discs were positive alone in 20% of the sample, a high prevalence of 61% may be the final result of discogenic pain in the cervical spine. In addition, 35% of the patients did not undergo any investigations. Authors also postulated that if cervical segments are fully investigated it emerges that cervical discs are not the most common, primary source of neck pain.
Yin & Bogduk, 2008 (32)	O	This evaluation was undertaken to determine the prevalence of different cause of neck pain in a private practice clinic. Overall 88 patients were evaluated from a sample of 167 patients with 46% of the patients completing the investigations.	A large proportion of patients did not pursue investigations. Among the 46% of patients who completed investigations, the prevalence of discogenic pain was 16% and the prevalence of zygapophysial joint pain was 55% with diagnosis remaining elusive in 32% of those patients who completed investigations.	In a private practice setting, authors were able to complete investigation in less than 50% of the patients; however, patients who completed controlled blocks or more than one invasive test, a pathoanatomic diagnosis remained elusive in only 17%.	Authors described that this study was not designed to establish the prevalence of various causes of neck pain in the general community, or even a particular sample of that community. The prevalence was estimated in a private pain clinic with highly select group of patients. This study provided prevalence of discogenic pain in 16% of the patients even though a large proportion of the patients did not undergo the assessment.
Holt, 1964 (92)	O	50 convicts of the Missouri State Prison who were between the ages of 21 and 50 underwent cervical discography as volunteers. Three disc spaces were injected in each individual; however, none had a history of prior neck injury or neck or arm pain.	The results showed extravasation of contrast media occurred at 2 levels in all cases and in 80% of the remaining spaces in only 10 disc spaces out of the total 148, the contrast remained within the central confines of the anulus.	Authors concluded that cervical discography is a painful and expensive procedure and is without diagnostic value. They also claimed that reproduction of discogenic pain by injection of the responsible disc space seems likely to be fallacious. Injection into any cervical disc causes great pain and brings on tonic neck muscle contracture.	Injection of contrast into asymptomatic discs caused pain and extravasation was noted in majority of the discs.
Klafta & Collis, 1969 (93)	O	42 patients who underwent laminectomy following discography and myelography were included	The accuracy of discography and myelography was 55% and 72%, respectively, using surgical findings as standard	Success rates were 100% for disk protrusion, 63% for spondylosis, and 33% in patients with no pathologic findings. Follow-up period not noted.	The overall diagnostic accuracy of the cervical discogram was only 55% compared to the diagnostic accuracy of myelogram of 72% in pre-MRI era.

Table 4 (cont.). Study *characteristics of cervical discography studies considered for inclusion*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Schellhas et al, 1996 (97)	O	Authors designed the study to assess the accuracy of MRI and discography in identifying the sources of cervical discogenic pain. They included 10 lifelong asymptomatic subjects and 10 non-litigious chronic neck and head pain patients in the study performing discography from C3-C4 through C6-C7 after MRI. Disc morphology and provoked responses were recorded at each level studied.	Of 20 normal discs by MRI from the asymptomatic volunteers, 17 proved to have painless annular tears discographically. In the pain patients, 11 discs appeared normal on MRI; whereas, 10 of those proved to have annular tears discographically. Two of these 10 proved concordantly painful with intensity ratings of at least 7/10. Discographically normal discs (N=8) were never painful in either group; whereas, intensely painful discs all exhibited tears of both the inner and outer aspects of the anulus.	Despite the high prevalence of anatomic disc derangement, there were no intensely painful discs in this entire series of asymptomatic volunteers. The highest pain intensity rating was 6 of 10, and was unfamiliar to the patient. In clinical pain sufferers, 8 of the 10 annular tears found with discography in MRI normal-appearing discs proved concordantly painful when injected. Concordantly painful discs that were normal on MRI had intensity ratings of 7/10 or greater. Fifteen discs from this group exhibited a combination of intense, concordant pain and annular tears at discography.	Overall 8 of the 10 patients with chronic pain had positive responses indicating that discography is an important test in patients with chronic neck pain. The results are clarified with lack of painful response in asymptomatic subjects even though they had multiple abnormalities.
Parfenchuck & Janssen, 1994 (98)	O	The study was designed to correlate the morphology of cervical discs with MRI compared to provocative discography and subsequently CT in 52 patients with discogenic pain. The MRI was characterized with regard to the disc nucleus signal and posterior annulus status. Provocative discography was evaluated with regard to positive or negative responses. CT was performed after discography on each patient.	There was no correlation between pain response or morphology as seen on either discography or CT discography. A significant correlation was found between abnormality as seen on MRI and pain response on discography, but the false-positive and false-negative rates were high.	The authors concluded that several MRI pattens correlate well with positive or negative cervical discography responses while several other patterns were equivocal. They concluded that MRI is a useful adjuvant to cervical discography, but there are some MRI patterns that cannot be considered pathologic, and discography is required to diagnose discogenic pain syndromes.	Discography resulted in familiar pain of a moderate or severe intensity. Of the 62 painful discs, 45 were abnormal on MRI, constituting a sensitivity of 73% and a false-negative rate of 27% for MRI to detect painful discs. Of the 42 asymptomatic discs, 28 were normal on MRI constituting a specificity of 67% and a false-positive rate of 33% per MRI as a test of painful cervical discs. Discography appears to be more helpful than MRI.
Riley et al, 1969 (102)	R	93 patients with neck and arm pain, without evidence of nerve root or spinal cord compression, underwent anterior fusion	72% of patients obtained good or excellent results. Success rate 75% for one or 2-level fusions and 58% for >3 levels.	87 patients underwent discography, most at time of surgery. Follow-up period not noted. Discography usually gave only confirmatory diagnostic help when disc space narrowing and spur formation were observed on plain x-rays, and when myelographic changes were present.	Discography was mildly helpful in pre-MRI era.
Whitecloud & Seago, 1987 (103)	R	40 patients with neck pain and no neurologic deficits underwent anterior fusion based on discography	70% of patients reported good or excellent results at least 12 months after surgery	All patients had negative myelograms. 37 patients had history of trauma. 6 patients were lost to follow-up	Positive study with 70% of patients undergoing surgical intervention reporting good or excellent results.
April & Bogduk, 1992 (138)	R	This study evaluated prevalence of cervical zygapophysial joint pain in 318 consecutive patients with intractable neck pain who underwent provocation discography and cervical zygapophysial joint blocks. Provocation discography was the sole investigation in 152 patients. In 76 patients, both provocation discography and zygapophysial joint blocks were performed.	Provocation discography provided unambiguous information and was the sole investigation performed in 152 patients, in 127 of whom a symptomatic disc was found at one or more levels, whereas in 25 patients provocation discography was negative at the levels investigated.	In the 76 patients who underwent both provocation discography and zygapophysial joint blocks, discography was indeterminate in 6 patients, and discography as well as zygapophysial joint blocks were both positive in 26 patients and both negative in 12.	Overall, in this study, 53% of the sample suffered a symptomatic disc.

Table 4 (cont.). Study *characteristics of cervical discography studies considered for inclusion*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Zheng et al, 2004 (118)	O	55 patients (161 levels) with cervical discogenic pain underwent MRI and discography. Discs with abnormal MRI and positive discography underwent anterior discectomy and fusion	Positive discography found in 49% of injected discs. 63% of dark discs, 45% of speckled and 29% of white discs. Discography positive in 59% of herniated or torn discs, 35% of bulging and 29% of flat discs. 76% of patients obtained good or excellent result at mean 3.6 year follow-up	Fusion done on 79 levels. MRI findings correlated with discography in 24% of patients and 64% of injected levels. In 79 positive discograms, 73% had abnormal MRI. In 82 levels with negative discograms, only 40 had normal MRI	A positive evaluation in post-MRI era. The combination of clinical symptoms, MRI, and discography provides the most information for decision-making and can improve the management of cervical discogenic pain.
Siebenrock & Aebi, 1994 (122)	R	27 patients with neck pain underwent anterior fusion and discography	At mean 16-month follow-up, 73% reported good to excellent results	39 levels fused. Included patients with neurologic deficits. Patients with trauma history did better than those w/o trauma	A positive study in post-MRI era.
Motimaya et al, 2000 (123)	R	16 patients underwent anterior discectomy and fusion	79% of patients had good to excellent results several months after surgery	95% of patients had involvement of C5-6 or C6-7. Follow-up period, inclusion criteria, or outcome measures not noted	A positive study in post-MRI era.
Ohnmeiss et al, 2000 (133)	R	The study was designed to investigate the relation between cervical discography pain responses and radiographic images in 161 patients studying 269 discs in patients suffering with chronic neck, should or arm pain.	There was significant relationship between the radiograph image of the disc and the result of clinical pain provocation. Among the 35 discs appearing as normal, clinical pain was provoked in only 14.3%, among 234 discs appearing as abnormal, clinical pain was provoked in 77.8%.	Authors concluded that there was good agreement between the radiographic appearance of the disc and pain provocation results. Discs that were painless but disrupted were found among older patients. Among such patients, discography may be particularly helpful in differentiating clinically significant abnormalities from those associated with aging.	Study illustrates significant correlation between radiographic findings and provocation discography.
Viikari-Juntura et al, 1989 (135)	Cadaveric study	This study was designed to test the value of MRI and discography in visualizing disc degeneration in the cervical spine experimentally on cadavers. Plain x-rays, MRI, discograms, and macroanatomic appearance of the cervical spines of 10 cadavers were compared.	At levels C4-C5 to C7-T1, general disc degeneration seen in discography correlated well with macroanatomy. The nuclear shape in MRI showed a weak correlation with macroanatomy and general disc degeneration in discography; whereas, nuclear intensity and MRI underestimated such changes. MRI showed posterior extension of the nucleus in most cases where moderate or severe leaking was seen in discography.	The MRI of this study correlated only moderately with macroanatomy and discography. The good sensitivity obtained for nuclear extension MRI nevertheless increased information of structural changes not available by other noninvasive and nonirradiative methods of examination. Overall discography showed good correlation with macroanatomy, whereas nuclear intensity in MRI underestimated such changes.	The cadaveric study shows excellent correlation with macroanatomy.
Osler, 1987 (143)	R	63 patients with neck pain without neurological deficits underwent analgesic discography followed by anterior discectomy and fusion.	81% of the patients had excellent or good results. All patients had analgesic response to intradiscal 2% lignocaine injection.	Authors concluded that analgesic discography is the most effective test for location of the lesion in the painful disc syndrome.	A positive study in pre-MRI era.
Simmons & Segil, 1975 (191)	R	56 patients with cervical disc disease who returned for follow-up. Symptomatic levels were determined by discography.	72% of patients had good or excellent results. Discography was at least twice as accurate as myelography, radiography, or clinical exam in assessing pathology	58 patients in series (n = 114) lost to follow-up. Inclusion criteria or follow-up period not noted. Diagnostic accuracy of discography was 91% compared to 43% for clinical examination, 46.5% for radiography, and 45.6% for myelography.	A positive study in pre-MRI era.

Table 4 (cont.). Study *characteristics of cervical discography studies considered for inclusion*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Chirls, 1970 (193)	R	300 patients with neck pain and no neurologic deficits underwent myelography and discography. 250 had fusion based on positive discogram(s)	Myelography was negative in 35% of cases. 86% of patients had good or excellent results	26 patients had multiple levels fused. Outcome measures and follow-up period not noted. Results not noted in 35% of patients.	A positive study in pre-MRI era.
Palit et al, 1999 (196)	R	38 patients with nonradicular neck pain underwent anterior discectomy and fusion based on positive MRI or CT scan and discography. All patients underwent cervical discography based on IASP guidelines with a concordant disc and controlled discs.	At mean 53-month follow-up, 79% of patients were satisfied with outcome	21 patients underwent single level, 16 patients 2-level, and one patient had a 3 level fusion. Only 5 patients returned to work	A positive evaluation in post-MRI era with evaluation of the role of cervical discography performed according to IASP standards.
Hubach, 1994 (197)	P	193 patients with cervical radiculopathy and/or myelopathy underwent anterior discectomy and fusion. During the operation a discography was performed on the symptomatic level(s) and the adjacent levels. All levels with positive discography were fused.	At mean 10.4 year follow-up, 82% of patients had good or excellent results. The first 23 patients underwent fusion without discography. and 35% developed adjacent segment pain. In the 156 patients who had fusion based on intraoperative discography, 12% developed adjacent segment pain	Mean 2.3 levels fused per patient. Patients were fused if intraoperative discography revealed abnormalities. 14 patients lost to follow-up.	A positive study in pre-MRI era.
Simmons et al, 1969 (198)	R	84 patients with neck pain underwent anterior discectomy and fusion. 31 patients had clinical, myelographic, and discographic assessment.	81% obtained good or excellent results at mean 34-mo follow-up	Included patients with neurological signs and symptoms	A positive study in pre-MRI era.
Connor & Darden, 1993 (199)	R	31 patients with neck pain without radicular pain underwent cervical discography followed by anterior cervical discectomy and fusion.	Of the 22 patients who underwent anterior cervical discectomy and fusion on the basis of cervical discography, one patient had an excellent result (5%), 9 patients had good results (41%), and 6 patients each had fair and poor results (54%).	Diagnostic cervical discography was found not to provide the degree of clinical predictive value necessary to substantiate its potential risks and complications.	Negative study of cervical discography in decision-making for anterior cervical discectomy and fusion in post-MRI era.
Williams et al, 1968 (200)	R	45 patients had preoperative discograms followed by anterior cervical discectomy and fusion. 30 patients underwent disc excision at level of pain reproduction.	Of the 30 patients undergoing disc excision at level of pain reproduction, 19 reported good to excellent results, whereas 4 reported fair results and 7 reported poor results.	When symptoms occur in the absence of clearly defined neurological signs, the chance of a long-term good or excellent result is materially reduced. The value of discography and myelography was not clearly defined by this evaluation.	One of the early negative outcome studies of cervical discography followed by cervical discectomy and interbody fusion.

R = Retrospective; O = Observational; MRI = Magnetic Resonance Imaging; Computed Tomography; IASP = International Association for the Study of Pain

Table 5. *Characteristics of studies of surgical outcomes.*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Zheng et al, 2004 (118)	O	55 patients (161 levels) with cervical discogenic pain underwent MRI and discography. Discs with abnormal MRI and positive discography underwent anterior discectomy and fusion	Positive discography found in 49% of injected discs. 63% of dark discs, 45% of speckled and 29% of white discs. Discography positive in 59% of herniated or torn discs, 35% of bulging and 29% of flat discs. 76% of patients obtained good or excellent result at mean 3.6 year follow-up	Fusion done on 79 levels. MRI findings correlated with discography in 24% of patients and 64% of injected levels. In 79 positive discograms, 73% had abnormal MRI. In 82 levels with negative discograms, only 40 had normal MRI	A positive evaluation in post-MRI era. The combination of clinical symptoms, MRI, and discography provides the most information for decision-making and can improve the management of cervical discogenic pain.
Motimaya et al, 2000 (123)	R	16 patients underwent anterior discectomy and fusion	79% of patients had good to excellent results several months after surgery	95% of patients had involvement of C5-6 or C6-7. Follow-up period, inclusion criteria, or outcome measures not noted	A positive study in post-MRI era.
Palit et al, 1999 (196)	R	38 patients with nonradicular neck pain underwent anterior discectomy and fusion based on positive MRI or CT scan and discography. All patients underwent cervical discography based on IASP guidelines with a concordant disc and controlled discs.	At mean 53-month follow-up, 79% of patients were satisfied with outcome	21 patients underwent single level, 16 patients 2-level, and one patient had a 3 level fusion. Only 5 patients returned to work	A positive evaluation in post-MRI era with evaluation of the role of cervical discography performed according to IASP standards.
Siebenrock and Aebi, 1994 (122)	R	27 patients with neck pain underwent anterior fusion and discography	At mean 16-month follow-up, 73% reported good to excellent results	39 levels fused. Included patients with neurologic deficits. Patients with trauma history did better than those w/o trauma	A positive study in post-MRI era.
Hubach, 1994 (197)	P	193 patients with cervical radiculopathy and/or myelopathy underwent anterior discectomy and fusion. During the operation a discography was performed on the symptomatic level(s) and the adjacent levels. All levels with positive discography were fused.	At mean 10.4 year follow-up, 82% of patients had good or excellent results. The first 23 patients underwent fusion without discography. and 35% developed adjacent segment pain. In the 156 patients who had fusion based on intraoperative discography, 12% developed adjacent segment pain	Mean 2.3 levels fused per patient. Patients were fused if intraoperative discography revealed abnormalities. 14 patients lost to follow-up	A positive study in pre-MRI era.
Connor & Darden, 1993 (199)	R	31 patients with neck pain without radicular pain underwent cervical discography followed by anterior cervical discectomy and fusion.	Of the 22 patients who underwent anterior cervical discectomy and fusion on the basis of cervical discography, one patient had an excellent result (5%), 9 patients had good results (41%), and 6 patients each had fair and poor results (54%).	Diagnostic cervical discography was found not to provide the degree of clinical predictive value necessary to substantiate its potential risks and complications.	Negative study of cervical discography in decision-making for anterior cervical discectomy and fusion in post-MRI era.
Siebenrock & Aebi, 1993 (134)	R	29 patients with discogenic syndrome confirmed by cervical discography underwent operative procedures. The patients were evaluated postoperative for change of symptoms, pain character and intensity, neurological deficits, working and sporting disability, and mobility of the cervical spine.	73% of patients showed a good to excellent result. A fair result was found in 23%, and an unsatisfactory result in 4%.	Authors concluded that in the literature a good to excellent outcome is seen in 30% to 46% in similar patient groups after cervical fusion without preoperative assessment by discography.	Compared to the literature with 30% to 46% success rate with good to excellent outcome, good to excellent result in 73% patients is a positive result.

Table 5 (cont.). *Characteristics of studies of surgical outcomes.*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Osler, 1987 (143)	R	63 patients with neck pain without neurological deficits underwent analgesic discography followed by anterior discectomy and fusion.	81% of the patients had excellent or good results. All patients had analgesic response to intradiscal 2% lignocaine injection.	Authors concluded that analgesic discography is the most effective test for location of the lesion in the painful disc syndrome.	A positive study in pre-MRI era.
Whitecloud and Seago, 1987 (103)	R	40 patients with neck pain and no neurologic deficits underwent anterior fusion based on discography	70% of patients reported good or excellent results at least 12 months after surgery	All patients had negative myelograms. 37 patients had history of trauma. 6 patients lost to follow-up	Positive study with 70% of patients undergoing surgical intervention reporting good or excellent results.
Kikuchi et al, 1981 (141)	R	138 patients with cervicobrachial pain underwent disc excision and anterior fusion	80% of patients improved 1-year after surgery	Results superior to 61% success rate in 54 patients who underwent fusion without discography	A positive study in pre-MRI era.
Simmons & Segil, 1975 (191)	R	56 patients with cervical disc disease who returned for follow-up. Symptomatic levels were determined by discography.	72% of patients had good or excellent results. Discography was at least twice as accurate as myelography, radiography, or clinical exam in assessing pathology	58 patients in series (n = 114) lost to follow-up. Inclusion criteria or follow-up period not noted. Diagnostic accuracy of discography was 91% compared to 43% for clinical examination, 46.5% for radiography, and 45.6% for myelography.	A positive study in pre-MRI era.
Chirls, 1970 (193)	R	300 patients with neck pain and no neurologic deficits underwent myelography and discography. 250 had fusion based on positive discogram(s)	Myelography was negative in 35% of cases. 86% of patients had good or excellent results	26 patients had multiple levels fused. Outcome measures and follow-up period not noted. Results not noted in 35% of patients.	A positive study in pre-MRI era.
Simmons et al, 1969 (198)	R	84 patients with neck pain who underwent anterior discectomy and fusion. 31 patients had clinical, myelographic, and discographic assessment.	81% obtained good or excellent results at mean 34-mo follow-up	Included patients with neurological signs and symptoms	A positive study in pre-MRI era.
Schaerer, 1968 (202)	R	247 patients with neck pain underwent anterior discectomy and fusion. 196 patients presented a picture of discogenic pain syndrome without nerve root involvement and all of them underwent cervical discography.	76% of patients had good or excellent results. Results not differentiated between patients with and without neurological symptoms	All 196 patients without neurological symptoms or trauma history underwent discography. Follow-up not noted	A positive study in pre-MRI era.
Roth, 1976 (100)	R	71 patients with neck pain without neurologic deficits underwent anterior discectomy and fusion	93% of patients had good or excellent outcomes	All patients had analgesic response to intradiscal lidocaine injection, but only 30% had concordant pain provocation. Follow-up period not noted	A positive report in pre-MRI era.
Riley et al 1969 (102)	R	93 patients with neck and arm pain, without evidence of nerve root or spinal cord compression, underwent anterior fusion	72% of patients obtained good or excellent results. Success rate 75% for one or 2-level fusions and 58% for >3 levels	87 patients underwent discography, most at time of surgery. Follow-up period not noted. Discography usually gave only confirmatory diagnostic help when disc space narrowing and spur formation were observed on plain x-rays, and when myelographic changes were present.	Discography was mildly helpful in pre-MRI era.

Table 5 (cont.). *Characteristics of studies of surgical outcomes.*

Study	Study Design	Patients and Interventions	Results	Comments	Summary of Results
Klafta & Collis, 1969 (93)	O	42 patients who underwent laminectomy following discography and myelography	The accuracy of discography and myelography was 55% and 72%, respectively, using surgical findings as standard	Success rates were 100% for disk protrusion, 63% for spondylosis, and 33% in patients with no pathologic findings. Follow-up period not noted	The overall diagnostic accuracy of the cervical discogram was only 55% compared to the diagnostic accuracy of myelogram of 72% in pre-MRI era.
Williams et al, 1968 (200)	R	45 patients had preoperative discograms followed by anterior cervical discectomy and fusion. 30 patients underwent disc excision at level of pain reproduction.	Of the 30 patients undergoing disc excision at level of pain reproduction, 19 reported good to excellent results, whereas 4 reported fair results and 7 reported poor results.	When symptoms occur in the absence of clearly defined neurological signs, the chance of a long-term good or excellent result is materially reduced. The value of discography and myelography was not clearly defined by this evaluation.	One of the early negative outcome studies of cervical discography followed by cervical discectomy and interbody fusion.

R = Retrospective; O = Observational; P = Prospective; MRI = Magnetic Resonance Imaging; IASP = International Association for the Study of Pain

Adapted, modified, and updated from Cohen and Hurley. The ability of diagnostic spinal injections to predict surgical outcomes. *Anesth Analg* 2007; 105:1756-1775 (142).

Table 6. *Quality Appraisal of Diagnostic Reliability of cervical discography studies.*

	Bogduk & Aprill (31)	Yin & Bogduk (32)	April & Bogduk (138)
1. Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	+	+	+
2. Was the test performed by examiners representative of those who would normally perform the test in practice?	+	+	+
3. Were raters blinded to the reference standard for the target disorder being evaluated?	–	–	–
4. Were raters blinded to the findings of other raters during the study?	NA	NA	NA
5. Were raters blinded to their own prior outcomes of the test under evaluation?	NA	NA	NA
6. Were raters blinded to clinical information that may have influenced the test outcome?	–	–	–
7. Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	+	+	+
8. Was the order in which raters examined subjects varied?	+	+	+
9. Were appropriate statistical measures of agreement used?	+	+	+
10. Was the application and interpretation of the test appropriate?	+	+	+
11. Was the time interval between measurements suitable in relation to the stability of the variable being measured?	NA	NA	NA
12. If there were dropouts from the study, was this less than 20% of the sample.	+	+	+
TOTAL	7/9	7/9	7/9

Y=yes; N=no; U=unclear; N/A=not applicable

2.1.3 Prevalence of Discogenic Pain

Table 4 illustrates the study characteristics of the included studies evaluating discography, all of which were conducted in accordance with IASP criteria (31,32,138).

Table 8 shows the potential prevalence of cervical discogenic pain based on cervical discography in patients with chronic neck pain. Yin and Bogduk showed 16% prevalence (32), Bogduk and April found a prevalence of 20% (31), and April and Bogduk reported a prevalence rate of 53% (138). It appears that the prevalence is highly dependent on the setting and selection of patients for discography.

Table 7. *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
Bogduk & Aprill (31)	+	+	+	+	+	5/5
Yin & Bogduk (32)	+	+	+	+	+	5/5
April & Bogduk (138)	+	+	+	+	+	5/5

+ = positive; - = negative

Scoring adapted from Staal JB, et al. Injection therapy for subacute and chronic low back pain. Cochrane Database Syst Rev 2008; 3:CD001824 (184).

Table 8. *Provocation discography utilizing IASP criteria.*

Study	Methodological Criteria	Number of Subjects	Prevalence Estimates
Bogduk &Aprill (31)	7/9	56	20%
Yin & Bogduk (32)	7/9	88	16%
April & Bogduk (138)	7/9	318	53%

2.1.4 Analysis of Evidence

Based on this systematic review, the evidence for cervical discography as a diagnostic tool is limited.

3.0 Complications

The most recognized complication of any discography procedure is bacterial discitis, with a reported incidence that is typically less than 1% (203-205). The most common microbe in discitis is Staphylococcus epidermidis, but streptococcus and Escherichia coli are also frequently implicated. Escherichia coli can be inoculated from the hypopharynx (206). A face mask for the patient might help prevent the patient's own oral flora from contaminating the sterile field as the result of an inadvertent cough or sneeze during the performance of a cervical discography.

Despite appropriate treatment of discitis with intravenous antibiotics, disc infection can accelerate or precipitate further disc degeneration and vertebral endplate destruction. Other complications from discitis include the development of epidural or retropharyngeal abscesses (199,207,208). In a combined animal and human study by Osti et al (204), the intradiscal injection of cefazolin mixed with contrast resulted in no cases of discitis in 4 sheep (20 discs) and 127 patients (336 discs) who underwent lumbar discography. As a result, it is believed that antibiotic injection in the disc during discography is sufficient prophylaxis to prevent the occurrence of discitis. In addition to intradiscal antibiotics, some physicians administer intravenous antibiotics prophylactically 30 minutes prior to the procedure. Changes in pain or quality of symptoms after discography should raise the suspicion for discitis. Screening is performed by erythrocyte sedimentation rate. If elevated, MRI is the current gold standard for detection of discitis (209,210).

Further complications include a vasovagal response, a hematoma that can include neural compromise within the spinal canal, an allergic drug reaction, headache, herniated cervical disc, quadriplegia, pneumothorax with lower cervical disc injections, thecal sac puncture, and arachnoiditis along with complications (203,205,211-234).

Toxicity of local anesthetic has been extensively discussed (218). Local anesthetics relieve pain by inhibiting sensitization of nerve endings (218) and by reducing proinflammatory cytokine production (219-221). Among the local anesthetics, bupivacaine has been one of the most commonly used local anesthetic for injection therapy, and is considered one of the safest drugs in terms of its potential for nerve or tissue toxicity (218). A number of invitro studies have demonstrated a dose- and time-dependent chondrotoxic effect of bupivacaine, especially at clinically applied concentrations from 0.1% to 1% (222-225). In evaluations of the effects of bupivacaine on cell viability, studies have shown that bupivacaine may be toxic to intervertebral disc cells (226-229). Some (230), but not all (231) studies have demonstrated synergistic toxic effects when steroids are combined with local anesthetic invitro.

4.0 Discussion

Based on the comprehensive evaluation of the available literature, this systematic review shows limited evidence in diagnosing discogenic pain and improving outcomes. The prevalence of cervical discogenic pain was found to be between 16% and 53% based on IASP criteria (31,32,138). Overall it appears that discography may serve an important adjuvant to improve surgical outcomes when IASP criteria are utilized test in diagnostically ambiguous cases. The results of this evaluation are similar to the previous evaluation (35) in which the indicated level of evidence was shown to be II-3, and consistent with that conclusion that cervical provocation discography had moderate validity and predictive value.

This systematic review faced significant challenges, which included the paucity of available literature and widespread discrepancies in methodology and outcome measurements. Although a significant number of studies were evaluated, only 3 studies (31,32,138) utilized IASP criteria requiring a concordantly painful disc and 2 negative control discs, one above and one below the affected level.

The validity of a diagnostic test can be determined by evaluating treatment outcomes. Multiple studies have been published assessing the predictive value of cervical discogenic pain prior to anterior cervical interbody fusion. These findings must be examined in the context of lack of standardization, evolution of both discography and surgical treatment, and lack of evidence supporting arthrodesis for degenerative spondylosis (195,235-241). Deyo et al (235) concluded that the evidence supporting cervical fusion to treat discogenic pain is weak and conflicting. In a Cochrane review, Jacobs et al (236) determined that discectomy alone provides comparable symptomatic relief to fusion, yet is associated with shorter recuperation times and hospital stays. Thus, the limitations of published outcome studies include methodological flaws: lack of prospective studies comparing outcomes between cohorts who were screened with preoperative discography and those who were not, publication bias, and wide variability in outcome measures and follow-up periods.

Despite these limitations, Cohen and Hurley (142) concluded that when all data are assembled, a pattern emerges whereby higher success rates tend to be reported when discography is used as a screening tool before cervical fusion than when surgery is based solely on imaging and clinical findings. Even then, only one study by Palit et al (196) utilized controlled provocation discography. Thus, the results of these evaluations must be considered with caution.

The characteristics of discography studies reporting surgical outcomes are presented in Table 5. Among the total 18 studies evaluating surgical outcomes based on cervical discography (93,100,102,103,118,122,123,134,141,143,191,193,196-200,202), 14 studies reported positive results (100,103, 118,122,123,134,141,143,191,193,196,197,198,202) and 4 studies reported negative results (93,102,199,200). Of note, 12 studies were conducted in the pre-MRI era (9 3,100,102,103,141,143,191,193,197,198,200,202) which undermines its validity in an era of advanced imaging, and 6 studies were done when MRI was widely available (118,122,123,134,196,199).

Among the post-MRI positive reports, Palit et al (196) evaluated outcomes in 38 patients who underwent anterior cervical discectomy and fusion for the management of non-radicular neck pain based on discography results. Significant improvements in mean numerical rating pain scores (8.3 vs 4.1; $P \leq 0.001$) and Oswestry disability scores (57.5 to 38.9; $P \leq 0.001$) were reported, with 79% of patients being satisfied with the results. Despite improvements in pain and function, these benefits did not translate into return-to-work. This may be partly attributable to the fact that Oswestry Disability Index scores are not validated instruments for neck pain, no differences were noted based on gender or worker's compensation status, and return-to-work tends to be more refractory to unidimensional therapy than other outcome measures (237).

Validity is exemplified by disc stimulation symptom mapping (97,104) in pain patients and asymptomatic volunteers. Ohnmeiss et al (133) found a significant relationship between imaging and symptom provocation, with 86% of normal-looking discs either producing no pain (60%) or atypical pain (26%). Conversely, 78% of disrupted discs were clinically painful on injection. Viikari-Juntura et al (135) demonstrated that discography provides additional information regarding structural changes not available by any other noninvasive and nonirradiative methods of examination. In general, nuclear signal changes observed on MRI in cadavers tended to underestimate the degree of pathology appreciated with discography or gross examination. Parfenchuck and Janssen (98) found that while certain MRI patterns correlated well with positive and negative cervical discography responses, many other patterns revealed equivocal responses. They concluded that MRI is a useful adjunct to cervical discography, but that some

MRI patterns should not be considered pathologic, and discography is necessary to identify a painful disc(s).

The proportion of cervical discs identified as symptomatic varies among studies. Grubb and Kelly (30) found that 50% of discs are capable of producing concordant pain upon injection. Schellhas et al (97) reported that among 11 discs that appeared normal on MRI in pain patients, 10 proved to have annular tears discographically. Two of these 10 elicited concordant pain with an intensity rating exceeding 6/10. Discographically normal discs (n = 8) were never painful in either pain patients or an asymptomatic cohort, whereas intensely painful discs all exhibited tears of both the inner and outer annulus.

Hamasaki et al (144) retrospectively reviewed 15 cases of foraminal cervical disc herniations. Using MRI and CT-myelography, less than half of the cases were identified. In contrast, all were clearly noted on CT-discography. These findings are similar to those found by Lejeune et al (242) in a study evaluating the diagnosis and outcomes for foraminal lumbar disc herniation. The authors concluded that a majority of foraminal-type cervical disc herniations may be missed with conventional MRI or CT-myelography, but correctly diagnosed with CT discography.

Zheng et al (118) evaluated cervical discography results in 59 patients and 161 disc levels. There were 79 positive levels, yielding a per disc prevalence rate of 49%. Fifty-nine percent of small herniated and torn discs were discographically positive. The false-positive rate of MRI was calculated to be 51% and the false-negative rate was 27%. The most important criterion for determining a symptomatic disc was moderate or severe reproduction of the patient's typical pain. The presence of a control disc was not considered a diagnostic criterion in this study.

Holt's 1964 study (92) in asymptomatic prisoners reflected negatively on cervical discography. But this study (92) has been repeatedly refuted and better overriding data have since been generated. Holt utilized an irritant contrast in a population with significant psychosocial issues (i.e. prisoners), and failed to employ fluoroscopic guidance. Even aside from these significant flaws, the technique itself was suspect. Extravasation of contrast material was noted with every injection, which continued even after reducing the volume. Furthermore, Holt considered "pain provocation" as being "without value."

The main criticism regarding studies attempting to quantify false-positive discography rates is that disc stimulation in asymptomatic volunteers may not reflect pain provocation in non-painful discs in subjects with spine pain (142). Moreover, the hallmark of a positive discogram has become concordant pain provocation, which is not possible in people devoid of spine symptoms. "False" pain provocation may be produced in markedly degenerative discs in the lumbar spine, especially in the elderly (142,243-246). Cohen et al (247,248) estimated that 15% to 25% of degenerative discs failed to elicit concordant pain during disc stimulation in the lumbar spine.

False-positive results with cervical provocation discography are a serious concern. But these rates vary as a function of the diagnostic criteria. False-positive responses to disc stimulation can arise if the threshold for reproduction of pain is set too low. A disc is not necessarily the source of a patient's pain if the pain that is reproduced is minor or trivial. Schellhas et al (97) compared the responses to discography in asymptomatic volunteers and patients with neck pain. They found that the numerical rating pain score produced by discography in asymptomatic subjects was significantly lower ($P \leq 0.0001$) than in patients with neck pain. Figure 2 illustrates the distribution of pain scores evoked by cervical discography in a histogram format. It was unusual for volunteers to report pain greater than 5/10 and no asymptomatic subject experienced pain exceeding 6/10. Consequently, Schellhas et al (97) recommended adding an operational criterion whereby the patient must rate the intensity of produced pain as ≥ 7 on a 10-point numerical pain rating scale or an equivalent magnitude on another suitable scale. The emphasis then shifts from the baseline pain score to how intensely the patient rates the evoked pain. Bogduk (52) pointed out that this criterion guards against diagnosing a moderately painful disc that could nevertheless be asymptomatic. The downside of this argument is the intrinsic potential for contradictions. Theoretically, a functional patient with 10/10 baseline pain could be deemed "positive" if 7/10 pain is elicited (i.e., 70% of baseline pain was provoked), whereas a disabled patient with 4/10 pain in whom disc stimulation provokes 6/10 pain (i.e., 150% of baseline) would be designated as "negative." This recommendation was used in most recent systematic review by Manchikanti et al (35).

Among the multitude of approaches described by various experts to overcome methodological biases (159,160,185,202,249), the AHRQ criteria appear to be the most widespread and comprehensive. Methodological challenges encountered in this systematic re-

view included the "gold standard" dilemma, spectrum and selection biases, subjective bias inherent in soft outcomes, observer variability, complex relations, clinical impact, small sample size, and the rapid evolution of knowledge and techniques (250). The second major criticism of discography is that disc stimulation may provoke pain in normal discs. However, the reported incidence of false-positive discography is contingent on multiple factors, including but not limited to investigator perspective (i.e., most studies that report high false-positive rates were done by spine surgeons), injection technique and needle placement, the population studied, and the criteria used to designate a discogram as "positive" (i.e., IASP or non-validated, individually developed criteria) (142). The "accepted" false-positive rates for cervical discography range from less than 5% to 27%, being higher in patients with chronic neck pain than in asymptomatic subjects (97,118,142). However, utilizing IASP criteria, the false-positive rate may be reduced significantly.

The literature is replete with controversies regarding a patient's ability to accurately report pain during discography, along with multiple other potential confounding factors (150,251-259). Factors besides diagnostic criteria that may influence the false-positive or false-negative rate include inappropriate patient selection, excessive or inadequate use of superficial anesthesia, needle insertion site, injection into the annulus or close to a vertebral endplate, chronological order of injection (i.e., injecting an intensely painful disc first), and insufficient or excessive sedation (142,243,249-251,257,260). Wolfer et al (150) have demonstrated that wen using strict validation criteria, the false-positive rate for lumbar discography is negligible (≤ 5%) in patients without somatization disorder or failed back surgery syndrome. Although no such review has been done for cervical discography, based on the present analysis, and extrapolated from the lumbar spine, the evidence for the validity of cervical discography indicated limited evidence.

The singular purpose of cervical discography is to identify a painful cervical intervertebral disc(s) (52). The premise upon which disc stimulation is based is that if a particular disc is painful, then stressing it under circumstances that simulate physiological conditions should reproduce the patient's pain. If the disc is not the source of a patient's pain, then stressing it either should not be painful or should produce pain that is not the patient's typical pain. Thus, disc stimulation is analogous to palpation for tenderness. Since cervical discography is a provocation test, similar to other examination tests, it is prone to false-positive results in certain circumstances.

In formal terms, disc stimulation tests the hypothesis that if a disc is the source of a patient's pain, then stressing the disc should reproduce their pain; however, simply reproducing pain cannot distinguish between a painful and non-painful disc. Thus, disc stimulation at a single segmental level does not provide a valid diagnosis. According to IASP (51), in order to maintain validity, provocation must be subjected to anatomical controls. The diagnostic criteria for discogenic pain (51) are that provocation of the target disc reproduces the patient's pain, whereas stimulation of adjacent discs does not reproduce pain.

The use of diagnostic injections to identify the source of low back pain dates back to the 1920s when von Gaza (261) used nerve blocks to illuminate obscure pain pathways. In the 1930s, Steindler and Luck (262) utilized procaine injections to identify specific pain generators in patients with chronic low back pain. In the intervening years, spinal injections have been periodically advocated as both diagnostic and prognostic screening tools before surgery, but their use in this capacity has been sporadic and inconsistent (142). In the midst of an explosive growth in surgery for spinal pain and exploding costs of a multitude of interventions (10-47), a reductionist approach emphasizing precision diagnosis, together with high tech interventions (263), has begun to emerge. Yet, spinal diagnostic interventions, including cervical provocation discography continue, to be controversial as screening tools for surgical intervention (24,33,34). Of all the diagnostic interventions, cervical discography probably remains the most controversial, next to thoracic discography. The main criticism of cervical discography, as with any other provocation test, is that disc stimulation may provide pain in normal discs.

In their systematic and narrative review of discography as a diagnostic test for spinal pain, Shah et al (33) discussed various issues starting with historical context, basic principles, lack of a gold standard, methodological quality criteria of provocation discography, multiple assumptions about discogenic pain including pressure pain thresholds, intradiscal distention, caveats about discogenic pain, analogies, and finally, convictions. They concluded that, overall, discography is a useful imaging tool. Historically, provocation discography is the only test which has the ability to evoke pain, which makes it unique among imaging studies. This provocative component has preserved the role of discography, but con-

tinues to generate controversy. Nonetheless, increased utilization of discography and increased physician-specialty representation among physicians performing discography suggests that discography has shed its pariah status (11,12,14,24). In addition, the renaissance era of discography was ushered in by the concept of discogenic pain, a term synonymous with internal disc disruption. Crock (264) defined internal disc disruption as "alteration in the internal architecture of the disc, specifically excluded the escape of a disc fragment from the confines of the space (annulus)", and suggested that discography "provides the single, most valuable, special investigation in cases of disc disruption."

Basic principles of a diagnostic test are to ascertain the disease or health status in a patient. Consequently, diagnostic accuracy studies assess a diagnostic test's ability to detect the target condition. The measurements of the index test's performance are reported as statistics: sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, diagnostic odds ratios, and receiver operator characteristic curves. In a clinical setting where the physician doesn't know the disease status of the patient, the predictive values are relevant; the physician obtains a diagnostic test result (positive or negative) and wants to predict the truthfulness of the patient's test result (249,265-269). However, the measurements are influenced by how one defines a positive or negative result and the prevalence of a disease in a population (33). As a tool to evaluate pain, the sensitivity of discography can approach 100% in absolute and relative — relative to other imaging modalities — terms, depending on the definition of a negative result. If a negative disc is defined as the one that is pain free and pathology free, then a false-negative could only occur when the patient is overly sedated; there is an unrecognized equipment malfunction during the intradiscal injection; intradiscal pathology is missed that could be detected by direct pathological inspection such as annular injection, partial nuclear filling due to the presence of a septum or intranuclear homogeneity, or lack of continuity between the nuclear cavity and the annulus (33). To develop any validity for discogenic pain, one should make certain assumptions that the disc is capable of pain generation. Consequently, discogenic pain has a structural and pathological basis that can be explained, discogenic pain can be reproduced by experimentally inducing physiological intradiscal loads, and discogenic pain may be managed. Even then, in judging the validity of provocation discography, one should not evaluate an unproven or poorly performed therapeutic technique.

Several authors challenged the concept that a "pain generator" can be confined to a discrete anatomic structure (33,268-271). Woolf (271) has proposed that a disease or anatomic-based classification of pain be replaced with a neurobiological mechanism-based classification. Advances in pain imaging, with respect to positron emission tomography (PET) scanning and functional MRI, illustrate the complexity of pain processing. In other specialties such as gastroenterology, in irritable bowel syndrome, rectal balloon distention of the sigmoid can evoke pain compared to controls, wherein pressure-evoked pain is thought to be due to altered sensory processing, either due to peripheral, spinal, or supraspinal sensitization (272). However, the increased selective attention and response is to a potentially threatening stimuli, which is a central component of sensitization (272). In this model of pain, the rectum is not the only "pain generator," per se, and one should not infer that removing or surgically treating the rectum would treat the pain. Hypothetically, a similar conceptual framework may apply to discography and discogenic pain. In fact, Giesecke et al (273) demonstrated that if equal amounts of pressure were applied to their patients, functional MRI could detect 5 common regions of neuronal activation in pain-related cortical areas in the chronic low back pain and fibromyalgia patients, but not the asymptomatic group. There are no readily available ways to measure the pain processes in an individual patient (274,275). Consequently, despite the limitations of the structural basis of spinal pain, discography is considered to be the criterion standard for diagnosing discogenic pain. Even then, a multitude of problems persist with cervical discography with regards to optimal criteria for therapeutic management based on the diagnostic information from provocation discography. Thus, we can have many controversies and differences, but questioning the validity of discography warrants questioning the role of the intervertebral disc as a discrete pain generator, or more specifically, challenges the concept of symptomatic internal disc disruption (33).

If conducted carefully and correctly, cervical discography should be a minimal risk procedure. Connor and Darden (199) reported that the weighted mean incidence of discitis following cervical discography was 6.4 per 1,000 cases, but this was a small study in which prophylactic antibiotics were not administered. When prophylactic antibiotics were administered, the discitis risk declines to less than 0.5% per patient (198,202,276).

Uncontrolled increases in disc pressure may accentuate bulging discs or precipitate prolapse in already deranged cervical disc(s) (199). Cervical discography is considered hazardous in patients with spinal stenosis or disc bulges that impinge or threaten to impinge on the spinal cord (52), and may worsen or precipitate a pre-existing protrusion. Injections done at C2-3 and C7-T1 are associated with additional hazards. At C2-3, the larynx may obstruct access to the disc, whereas at C7-T1 the apex of the lung may be encountered.

Cervical discography has clinical utility if, when considered in context with radiological imaging, patient selection, and historical and physical examination findings, it provides a suggestive diagnosis of discogenic pain. This can only be achieved by performing discography utilizing IASP standards. In addition, cervical discography may have therapeutic value by preventing unnecessary surgical intervention. To summarize, there is strong evidence for the utility of cervical discography as an intervertebral disc imaging tool and that intradiscal distention can produce pain. However, the indicated level of evidence supporting the role of discography in identifying patients with chronic cervical discogenic pain is Level II-2.

Ultimately, the number of studies available with statistically significant patient numbers and consistent use of IASP standards is lacking. Larger studies with preserved investigational criterion will need to be completed.

5.0 Conclusion

Based on a modified AHRQ accuracy evaluation and USPSTF level of evidence criteria, this systematic review indicates the strength of evidence as limited for the diagnostic accuracy of cervical discography.

Acknowledgments

The authors wish to thank Vidyasagar Pampati, MSc, for statistical assistance, Sekar Edem for assistance in the search of the literature; Bert Fellows, MA, and Laurie Swick, BS, for manuscript review; and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in preparation of this manuscript. The authors also thank Pain Physician for permission to reproduce Manchikanti et al's manuscript from 2009. We would like to thank the editorial board of Pain Physician for review and criticism in improving the manuscript.

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