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Non-Operative Management for Discogenic Back Pain: A Systematic Review

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Abstract

Study Design—Systematic review of the literature.

Objective—A systematic evaluation of the literature was performed to investigate current non-operative management for the treatment of discogenic low back pain.

Summary of Background data—Back pain is a major healthcare concern with up to 39% being discogenic in origin according to one study. Non-operative therapy is likely to be the initial treatment strategy for discogenic low back pain.

Methods—Pubmed, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for clinical studies evaluating non-operative methods of treating discogenic back pain that were published between 2000–2012. Only prospective randomized controlled studies that compared a non-surgical intervention with sham or placebo therapy were included. After removal of duplicate citations, a total of 226 articles were initially identified from the search terms. From these, we identified 11 randomized controlled trials (RCTs) from which data analysis was performed.

Results—The 11 RCTs investigated traction therapy, injections and ablative techniques. Results from five RCTs investigating methylene blue injection, steroid injection, ramus communicans ablation, intradiscal electrothermal therapy (IDET) and biacuplasty favored intervention over sham therapy. However, results from the study on methylene blue injections have not been replicated in other RCTs. Evaluation of the selection criteria utilized in the studies on ramus communicans ablation and intradiscal biacuplasty and a stratified analysis of results from the RCTs on IDET casts doubt on whether the conclusions from these RCTs can be applied to the general discogenic pain patient population.

Conclusion—There are few high quality studies evaluating non-operative treatments for reducing discogenic low back pain. Although conclusions from several studies favor intervention over sham, it is unclear whether these interventions confer stable long-term benefit. There is some promise in newer modalities such as biacuplasty; however, more inclusive studies need to be performed.

Keywords

discogenic; low back pain; steroid injection; methylene blue; nociceptive; analgesia; ablative therapy; intradiscal; electrothermal therapy; percutaneous intradiscal radiofrequency coagulation; ramus communicans; non-operative; provocative discography; biacuplasty

Introduction

Low back pain exacts a heavy socioeconomic burden on society with estimated healthcare and indirect costs at 100 billion dollars annually.^{1–3} Mechanical causes of low back pain include degenerative spine pathologies such as facet joint disease, spinal stenosis, disc herniations, spondylolysis or discogenic pain.⁴ Non-mechanical causes may be the result of spinal neoplasia, infection or an inflammatory disease that involves the spine or other structures of the lower back.⁴

According to one study, up to 39% of all low back pain is believed to be discogenic in origin.⁵ Degenerative disc changes are associated with inflammation, dehydration of the nucleus pulposus, decreased disc height, annular tears and impaired mechanical function of the disc.^{6–9} A possible mechanism for discogenic pain is that degeneration is accompanied by nociceptive nerve ingrowth into the intervertebral disc (IVD) and stimulation of these nerve endings with inflammatory mediators produce pain.^{7,8,10}

Physical examination maneuvers such as biphasic straightening and spinous process vibratory provocation were proposed as diagnostic maneuvers for disc pain but have never been validated.¹¹ The gold standard for diagnosing discogenic pain remains provocative discography whereby contrast is injected into a disc and concordant pain is reproduced with increasing intradiscal pressures.^{12,13} However, several studies have found that provocative discography may have a relatively high false positive rate and may also accelerate progression of degenerative changes in part due to morbidity associated with the needle puncture.^{11,12,14–17} While magnetic resonance imaging (MRI) may determine the severity of disc degeneration, these findings correlate poorly with patient-reported symptoms.^{11,18,19}

The clinical effectiveness of lumbar arthrodesis for alleviating discogenic pain is unclear.^{13,20,21} A randomized study found that only 63% of discogenic pain patients improved following surgery while another analysis found only 39% had good/excellent pain relief after fusion.^{22–24} Furthermore, successful surgical fusion does not necessarily translate into significant pain reduction.²⁵ It is also unclear whether lumbar arthrodesis confers superior clinical outcomes when compared to non-operative therapies for discogenic pain.²⁶ While lumbar arthroplasty offers a motion sparing alternative to fusion, a Cochrane Review failed to find clinically significant differences between lumbar arthroplasty and fusion surgery.²⁷

Psychological factors also influence the perception of discogenic pain.^{28,29} A prospective randomized study found that placebo analgesics tend to be more effective in subjects with more severe psychopathology.³⁰ Postoperative outcomes following lumbar fusion for discogenic pain are also influenced by emotional and psychological factors.^{30,31} Therefore,

studies evaluating treatments for discogenic pain should ideally include selection criteria that minimize the influence of psychological factors on pain perception.

In this review, we sought to answer the question, “For patients with discogenic low back pain, are there non-operative therapies that are effective compared to sham/placebo treatments for the reduction of pain and disability and improvement in function as assessed using patient-centered clinical outcome scores?” In order to answer this question, we reviewed prospective randomized controlled trials (RCTs) comparing active non-operative therapy with sham/placebo control in improving pain and disability (as assessed using patient-reported measures) in adults with discogenic pain.

Materials and Methods

Search Strategy

An ‘a priori’ search protocol was utilized. Pubmed, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) were searched using key terms (degenerative disc disease OR discogenic) AND low back pain AND treatment AND (Clinical Trial OR Randomized Controlled Trial). This search was limited to years (January 1, 2000–December 31, 2012), human subjects and English language.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were chosen in order to select randomized controlled trials that evaluated exclusively non-operative therapies for strictly discogenic low back pain using placebo or sham therapy as a control and patient centered questionnaires on pain, disability and functional status as outcomes. For the purposes of this review, a clinical trial was considered a study on discogenic pain if it included patients where the disc itself is considered the most likely and principle source of pain. The inclusion/exclusion criteria are listed in Table 1.

Risk of Bias

The articles were assessed for bias using the 12 criteria recommended by the Cochrane Back Review Group.³² Studies meeting fewer than 6 criteria were defined as having a high risk of bias while those that met 6 or more criteria were defined as having a low risk of bias.³² Each study was also assessed for level of evidence. The results of our assessment of the risk of bias are shown in Appendix A.³³

Selection of Studies

The initial database search identified 285 articles (n = 190 by Pubmed, n = 49 by Embase and n = 46 by CENTRAL) of which 226 citations were screened following the removal of duplicate citations. Of the 226 citations, review of the titles and abstracts excluded 195 articles that were not relevant to the subject matter (i.e. studies that did not evaluate discogenic pain, included subjects with non-discogenic low back pain or did not evaluate non-operative therapies).

The references from the remaining 31 potentially eligible articles were reviewed by the senior author in order to select studies that are important to the subject matter but were not retrieved in the initial database search. However, this review did not result in the inclusion of any additional studies.

Full texts of the 31 articles were reviewed and 20 articles were excluded with reasons for ineligibility provided in Appendix B. The remaining 11 prospective randomized controlled studies were included in the review and data regarding level of evidence, number of subjects, intervention type, outcomes assessed, significant findings, limitations and conclusions were extracted. (Figure 1)

The search algorithm and assessments of level of evidence, risk of bias were performed in duplicates by authors Y.L and J.G. Results were reviewed by senior author S.C. Any disagreements regarding the inclusion or exclusion of a study were also resolved by the senior author S.C.

Results

The 11 studies that met the inclusion/exclusion criteria evaluated traction, steroid therapy, methylene blue injection and ablative therapy. Nine of the eleven studies utilized discography to confirm the diagnosis of discogenic pain. In order to control for the psychopathologic aspects of pain, five of the eleven studies included psychopathology as an exclusion criteria (psychopathology was not uniformly defined across the included studies). Nine out of eleven studies were double-blinded. (Table 2)

All the studies were considered to have a low risk of bias as assessed in accordance to guidelines by the Cochrane Back Review Group. Any reported conflicts of interest can be found in Appendix C.

Physical Modalities

Traction therapy is a procedure that unloads the disc and facet joints through distraction and relaxation cycles. Animal models have shown potential benefits of traction on restoring disc disruption, and such distraction and relaxation cycles are theorized to promote disc health by increasing nutrient flow into the degenerated disc.³⁴⁻³⁷ The RCT on traction therapy by Schimmel et al³⁷ found no significant differences in any clinical outcomes between patients receiving traction therapy, according to the manufacturer's protocol, and a sham group using non-therapeutic weights.³⁷ (Table 3)

Steroid Therapy

Three RCTs investigated steroid injections for discogenic pain. (Table 4) Manchikanti et al³⁸ did not detect significant differences in any outcome scores between patients who received epidural steroid and lidocaine injections versus those who received only lidocaine. Patients receiving caudal epidural injection of lidocaine alone actually had significantly fewer annual procedures relative those who received lidocaine with steroids.³⁸ (Table 4)

Two randomized studies investigated the clinical effectiveness of intradiscal steroid injections. Khot et al³⁹ failed to detect significant differences in the change in percentage disability or VAS (Visual Analogue Score) scores from pretreatment values between patients receiving intradiscal steroid injections and those who received saline injections. In contrast, Cao et al⁴⁰ found that patients who received steroid or steroid plus Songmeile (Chinese Herbal Anti-Inflammatory Medication) injections had significantly improved VAS and ODI (Oswestry Disability Score) scores at 3 and 6 months post-treatment while those receiving saline did not experience significant clinical improvements.⁴⁰ (Table 4)

Epidural injections of steroids and lidocaine do not confer any significant additional benefits when compared to lidocaine injections alone. Intradiscal steroid injection therapy was supported by one study with a 6 month follow up but not by another study with one-year follow up.

Intradiscal Methylene Blue

Methylene blue has been demonstrated to chemically ablate nerve endings.^{41,42} Peng et al⁴³ evaluated the role of intradiscal injection of methylene blue in the treatment of discogenic pain. At 6, 12 and 24 months following the procedure, patients receiving methylene blue had significantly better outcome scores than the sham group, supporting the use of methylene blue injections as a clinically effective therapy for disc pain for up to 2 years. (Table 4)

Ablative therapy

Two randomized studies evaluated intradiscal electrothermal therapy (IDET). IDET is theorized to destroy intradiscal nociceptive nerve endings through thermal ablation thereby reducing pain.^{44,45} Thermal energy may also shrink collagen fibrils and effectively stiffen the biomechanical behaviors of the IVD. Pauza et al⁴⁴ found significantly greater improvements in VAS and ODI scores for IDET usage compared to sham therapy at 6 months. Furthermore, stratified analysis suggested that patients with low baseline pain scores, poor physical function and high disability were more likely to benefit from IDET.⁴⁴ (Table 5)

In contrast, Freeman et al⁴⁵ found that IDET did not confer any significant additional benefits over sham therapy. There were also no significant differences in any of the outcome scores between active therapy and sham at 6 months. Compared to Pauza et al⁴⁴, participants in Freeman et al⁴⁵ had greater baseline disability assessed with ODI and SF-36 (Short-Form 36) scores. There were also differences between the two studies regarding blinding and sham protocols.⁴⁵

Percutaneous Intradiscal Radiofrequency Thermocoagulation (PIRFT) uses radiofrequency current to heat the IVD in order to ablate the nociceptive nerve endings and coagulate collagen fibrils. Our review identified two RCTs comparing PIRFT versus sham control.^{46,47} (Table 5)

Recruitment for a PIRFT study by Kvarstein et al⁴⁶ was prematurely halted 6 months into the study due to lack of trend toward improvement for the PIRFT group thereby limiting the study to 20 subjects. There were no significant differences in any NRS (Numeric Rating

Scale) scores or changes in these scores from baseline between the two groups at 6 or 12 months. Furthermore, there were no significant differences in ODI and SF-36 scores or patients' categorical impression of pain at 6 or 12 months between the two groups.⁴⁶ A similar study by Barendse et al⁴⁷ also investigated PIRFT using a different protocol (90 seconds, 70 C lesion) also found no significant differences between sham and active group for any of the outcome scores at 8 weeks.⁴⁷ (Table 5)

The ramus communicans is hypothesized to be an important neural pathway for discogenic pain. A study by Oh et al⁴⁸ evaluated whether electrothermal ablation of this structure can alleviate disc pain. A study criterion required subjects to have at least 50% temporary pain reduction from analgesic blockade of the ramus communicans, which eliminated 22% (14/63) of candidates from the study. In this select population, there were significant differences in outcome scores at 4 months post-treatment favoring ablation over sham therapy.⁴⁸ (Table 5)

Intradiscal biacuplasty is a procedure where two radiofrequency probes, inserted into an affected IVD, deliver thermal energy that is intended to ablate nociceptive nerve endings. Kapural et al⁴⁹ showed that subjects receiving biacuplasty had significantly superior clinical outcomes as well as improvements in all outcome scores at 6 months relative to sham controls. However, the selection criteria used in this study excluded 93.5% (1771/1894) of patients initially screened including obese patients (Body Mass Index > 30 kg/m²) and smokers.

IDET and PIRFT are likely ineffective for the general discogenic pain patient population. Ablation of the ramus communicans and intradiscal biacuplasty offers some promise but their effectiveness for the general discogenic pain patient population is unclear.

Discussion

Our systematic review identified 11 RCTs that addressed non-operative strategies for treating discogenic pain. Six clinical studies failed to detect significant differences between active and sham/placebo therapies.^{37–39,45–47} Five studies (Peng et al⁴³, Cao et al⁴⁰, Pauza et al⁴⁴, Oh et al⁴⁸ and Kapural et al⁴⁹) which investigated intradiscal methylene blue injection, steroid therapy, IDET, ramus communicans ablation and intradiscal biacuplasty all demonstrated significant differences in clinical outcomes favoring intervention over sham treatment.

While Pauza et al⁴⁴ demonstrated results favoring IDET over sham control, stratified analysis suggested that IDET is only effective in patients who, at baseline, had lower pain and physical function scores and greater disability scores.⁴⁴ Another IDET study by Freeman et al⁴⁵ using a different study population did not show any significant differences between active therapy and control. Thus, IDET is likely not effective in providing relief for the general discogenic pain patient population.

Oh et al⁴⁸ demonstrated that ramus communicans ablation reduced discogenic pain in patients who previously responded to a diagnostic blockade of the ramus communicans. However, only 78% of the patients initially recruited met the inclusion criteria of a clinically

sufficient pain reduction following analgesic blockade of the ramus communicans and were included in the study. It is unclear whether this technique is effective for the general discogenic pain patient population. The study was also limited by lack of blinding.⁴⁸

Kapur et al⁴⁹ found that biacuplasty conferred significantly superior clinical outcomes compared to sham. However, the selection criteria in this RCT excluded patients with obesity as well as smokers. Studies have shown that obesity and smoking are important risk factors for disc degeneration.^{50–52} Thus, the selection criteria in this study potentially excluded an important subset of discogenic pain patients.⁴⁹ Biacuplasty may be an effective treatment for disc pain; however, it is unclear whether this therapy is effective for patients with comorbidities such as obesity and smoking that are associated with accelerated disc degeneration.

Peng et al⁴³ showed that intradiscal methylene blue injections significantly improved discogenic pain compared to sham controls.⁴³ However, additional literature searches did not reveal any other RCTs evaluating methylene blue injections. While this technique shows potential for the treatment of discogenic pain, more studies are needed to validate methylene blue injections prior to widespread clinical use. Importantly, there are reports that methylene blue may have neurotoxic effects and therefore epidural leakage of methylene blue through annular tears in a degenerated IVD can have deleterious effects on surrounding neural structures.^{53,54} These safety concerns should be addressed and thoroughly studied prior to widespread use of this technique.

While the 6 month follow up results from Cao et al⁴⁰ favored intradiscal steroid injections over sham controls, a similar study by Khot et al³⁹ on steroid injections with 1 year follow up failed to detect significant differences between steroid injections and sham groups.^{39,40} Therefore, it is unclear whether intradiscal steroid therapy can consistently confer clinical benefits for discogenic pain.

With the exception of Peng et al⁴³, which had a 24-month follow-up time point, the majority of the randomized studies that favored active therapy over the sham did not have any follow-up time points exceeding 6 months. Specifically, Pauza et al⁴⁴, Oh et al⁴⁸, Kapur et al⁴⁹ and Cao et al⁴⁰ had maximum follow-ups of six, four, six and six months, respectively. Additional literature search failed to identify prospective randomized controlled trials that evaluated these treatments with longer follow-up intervals and therefore it is uncertain whether these therapies are able to confer sustained long-term clinical improvements.

The other randomized clinical trials investigating traction therapy, epidural or intradiscal steroid injections or PIRFT failed to show differences favoring intervention over sham control.^{37–39,45–47} However, it is important to note that most of the studies in this review used provocative discography to confirm disc pain. There is ongoing debate regarding the accuracy of provocative discography with some studies raising concerns that this modality may have a high false positive rate (as high as 50–60% in one study).^{12,15,55} Although other analyses argued that discography is accurate and has a low false positive rate, there is still the distinct possibility that usage of this modality may potentially generate study populations

where a notable proportion of the patients do not have true discogenic pain, thereby unlikely to respond to the evaluated intervention.^{56,57}

It is also possible that the patients who are willing to undergo provocative discography and enroll in a clinical trial for low back pain tend to have more severe and persistent low back pain and therefore are less likely to respond to treatment. Therefore, the reduced clinical effectiveness of these treatment options seen in these studies may potentially be partially attributed to the characteristics of the patients examined.

Additionally, several of the studies that failed to demonstrate significant differences between active therapy and sham controls may have been statistically underpowered. Kvarstein et al⁴⁶ had a total of 20 subjects (10 patients in treatment and sham groups) and prematurely halted the study due to lack of trends towards significance. However, while the differences between treatment and sham groups were statistically non-significant, the results were still positive for the PIRFT group and therefore a larger study population could potentially lead to significant differences favoring the treatment group. Similarly, the study by Barendse et al⁴⁷, which also demonstrated lack of a significant difference between sham and active PIRFT groups but only having a total of 28 patients (13/15 in active and sham group respectively), may have also been statistically underpowered.

It is also possible that some of the intervention protocols utilized in these studies may be sub-therapeutic thereby reducing the effect size of the active therapy group. In Schimmel et al³⁷, it was unknown whether the most optimal traction protocol was utilized or whether the traction translated into actual disc distraction. Similarly, while Khot et al³⁹ failed to show that steroid therapy could successfully reduce disc pain, the patients in this study received only one injection of a low dosage of methylprednisolone (40 mg) and then were assessed after a year. Although the pharmacodynamic properties of steroids within the IVD are unknown, it may be possible that more frequent and higher dosage of intradiscal steroid injections may have been able to generate significant differences in clinical outcomes between patients receiving active therapy versus placebo. It is important to consider that increasing the frequency and dosage of intradiscal steroid injections may further accelerate disc degeneration through puncture injury, promote IVD calcification or cause iatrogenic infections.^{17,58}

A cadaveric study on IDET found that clinically effective temperatures were generated only in a 2 mm margin around the heated probe suggesting the posterior annulus, a site believed to be important for nociception, was insufficiently heated.⁵⁹ Another study found that thermal diffusivity of the disc varies dramatically between patients suggesting that usage of a fixed heating protocol may not be appropriate for all patients.⁶⁰ Optimizing IDET catheter position and probe temperature may result in more favorable outcomes. Lack of clinical success of PIRFT in the studies reviewed may also be due to sub-therapeutic heating.⁶⁰ However, increasing the thermal energy of these probes increases the risk of thermal damage to neighboring structures.

Appropriate identification of patients with discogenic pain is an important component in the design of clinical studies on disc pain. Although provocative discography is the gold

standard diagnostic modality for discogenic pain, the potentially harmful effects of discography complicate its usage. The difficulty in safely identifying discogenic pain patients for enrollment in a clinical study may be a key obstacle in the design of future randomized controlled trials.

A limitation of this literature review is the inconsistency of the outcome measures utilized in the studies, which makes it difficult to compare results between studies. The study criteria used in these randomized controlled trials were also inconsistent (specifically regarding inclusion/exclusion criteria on age, body mass index, duration of symptoms, modic changes, psychopathology, workman's compensation) thereby further complicating any comparisons between the studies. For purposes of brevity, we only discussed study criteria for the reviewed clinical trials where we felt that patient selection was an important source of bias and acknowledge that this may be a source of reporting bias.

We also limited our literature search to articles published in the English language and therefore may not have selected all the possible articles relevant to the subject matter. Furthermore, since there are numerous terms that can be used to describe discogenic low back pain, it is possible that the keywords used in the search algorithm did not fully retrieve all of the studies that were pertinent to our review. Our study is also limited by lack of quantitative data. Due to heterogeneity in intervention type, follow-up time-points and clinical outcome, we were unable to perform a meta-analysis.

Conclusion

Discogenic pain represents a significant health burden for both patients and society at large. Although many clinical studies have investigated various non-operative methods of managing discogenic pain, our review identified only eleven prospective randomized controlled studies with appropriate controls. While a small subset of these clinical trials investigating injection or ablative therapy favored active therapy over sham, it was uncertain whether these interventions would be able to confer long-term benefits to the general discogenic patient population. While the potential inaccuracy of provocative discography complicates research into discogenic low back pain, the high prevalence of this disease along with lack of successful non-operative treatments highlights the need for additional clinical investigations.

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Figure 1.
Methodology of included articles for study.

Table 1

Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Randomized Controlled Trials • Studies on patients with discogenic low back pain • Studies comparing non-operative treatments versus placebo or sham therapy • Studies with outcomes are patient-reported questionnaires quantifying pain, disability and/or functional status at baseline and post-intervention. 	<ul style="list-style-type: none"> • Studies based on preliminary data where later follow-up results were published. • Studies with patients whose low back pain can be attributed to non-discogenic etiologies (facet joint disease, spinal stenosis, disc herniations, spondylolysis or spondylolisthesis) • Studies on surgical interventions for discogenic pain (lumbar arthrodesis or arthroplasty).

Table 2

Results of the Systematic Review.

Study	Sample Size (Active/Sham)	Intervention	Randomization	Blinded	Psychopathology As Exclusion Criteria	Method of Determining Discogenic Pain	LOE
Schimmel <i>et al.</i> , 2009	24 (13/11)	Traction Therapy	Opaque Envelope	Yes	No	X-rays	II
Manchikanti <i>et al.</i> , 2012	120 (60/60)	Injection	Computer Randomization	Yes	Yes	Exclusion of disc herniations and facet joint pain	I
Cao <i>et al.</i> , 2011	40 (20/20)	Injection	Did not Specify	Yes	No	Provocative Discography	II
Peng <i>et al.</i> , 2010	72 (36/36)	Injection	Opaque Envelope	Yes	Yes	Provocative Discography	I
Khot <i>et al.</i> , 2004	120 (60/60)	Injection	Scaled Envelope	Yes	No	Provocative Discography	I
Freeman <i>et al.</i> , 2005	57 (38/19)	Ablation	Scaled Envelope	Yes	Yes	Provocative Discography	II
Pauza <i>et al.</i> , 2004	56 (32/24)	Ablation	Computer	Yes	No	Provocative Discography	I
Kvarstein <i>et al.</i> , 2009	20 (10/10)	Ablation	Random Numbers	Yes	Yes	Provocative Discography	II
Barendse <i>et al.</i> , 2001	28 (13/15)	Ablation	Computer Randomization	Yes	No	Analgesic Discography	II
Oh <i>et al.</i> , 2004	49 (23/26)	Ablation	Did Not Specify	No	Yes	Provocative Discography	I
Kapural <i>et al.</i> , 2012	59 (29/30)	Ablation	Computer Randomization	Yes	Yes	Provocative Discography	I

Abbreviations: (LOE) indicates Level of Evidence.

Table 3

Physical Modalities for Chronic Discogenic Low Back Pain.

Study	Intervention	Outcomes assessed	Time points when outcomes were assessed	Blinding	Study Design	Significant Findings
Schimmel <i>et al.</i> , 2009	Traction Therapy	VAS low back pain, VAS for leg pain, ODI, SF-36.	Baseline, 2, 6, 14 weeks.	Subjects and investigator assessing clinical outcomes were blinded. Therapists conducting the traction exercise were not blinded.	Active Therapy: Traction using AccuSPINA device (Steadfast Corporation Ltd, Essex, UK). One-half of subject's weight minus 10 lbs for day 1 and 2. Traction weight was increased until 50% of body weight plus 10 lbs was reached. Sham Therapy: Traction at non-therapeutic weights (10 lbs).	No significant differences in VAS scores (low back pain or leg pain), ODI or SF-36 scores between the two groups at any post-procedure time points.

Abbreviations: VAS (Visual Analogue Scale), ODI (Oswestry Disability Index), SF-36 (Short Form 36)

Table 4
Steroid and Methylene Blue Injection Therapy for Chronic Discogenic Low Back Pain.

Study	Intervention	Outcomes assessed	Time points when outcomes were assessed	Blinding	Study Design	Significant Findings
Manchikanti <i>et al.</i> , 2012	Epidural Steroid Injection	NRS pain scale, ODI, employment status and opioid usage	Baseline, 3, 6, 12, 24 months	Subjects and all Investigators were blinded.	Active Therapy: Epidural Steroid plus Lidocaine Injection. Sham Therapy: Lidocaine Injection Only.	No significant differences between the two groups. Patients receiving lidocaine alone had significantly fewer procedures than those who received lidocaine with steroids
Khot <i>et al.</i> , 2004	Intradiscal Steroid Injection	Change in pain score and disability from pretreatment baseline measured using VAS and ODI	Baseline and 1 year	Subjects were blinded. Outcomes were assessed through postal questionnaire. Investigator performing the intervention was not blinded.	Active Therapy: Intradiscal Steroid (depomedrone) Injections. Sham Therapy: Intradiscal Normal Saline Injections.	No significant differences between intervention and sham control.
Cao <i>et al.</i> , 2011	Intradiscal Steroid Injection	VAS and ODI	Baseline, 3 months and 6 months	Subjects, investigators performing the intervention and investigators assessing outcomes were all blinded.	Active Therapy: Intradiscal Steroid Injections with or without Songmeile (Chinese Herbal Anti-inflammatory Medication) Sham Therapy: Intradiscal Normal Saline Injection.	VAS and ODI scores were significantly better in patients receiving steroid therapy or steroid plus songmeile at 3 and 6 months. No significant differences between patients receiving steroids versus steroids plus songmeile
Peng <i>et al.</i> , 2010	Intradiscal Methylene Blue Injection	NRS (101 items), ODI, Post-treatment patient satisfaction, medication usage, complications	Baseline, 6, 12, and 24 months	Subjects and investigators assessing clinical outcomes were blinded. Investigator performing the intervention was not blinded.	Active Therapy: Intradiscal Methylene Blue Injections. Sham Therapy: Normal Saline Injections.	No postoperative complications. Significantly different NRS and ODI scores and analgesic medication usage favoring active group over to sham control at all time points.

Abbreviations: VAS (Visual Analogue Scale), ODI (Oswestry Disability Index), SF-36 (Short Form 36), NRS (Numeric Rating Scale)

Table 5

Ablative Therapies for Discogenic Low Back Pain.

Study	Intervention	Outcomes assessed	Time points of Outcomes	Blinding	Study Design	Significant Findings
Pauza <i>et al.</i> , 2004	IDET	VAS Pain, SF-36, ODI, relative changes in pain	Baseline, 6 months	Subjects and Investigator assessing clinical outcomes were blinded. Investigator performing the Intervention was not blinded.	Active Therapy: IDET catheter (SpineCath Catheters, Andover, MA, USA) is placed at boundary between AF and NP and heated to 90 C. Sham Therapy: Only the Introducer Needle was introduced.	Changes in VAS score and ODI between 6 months and baseline significantly favored IDET group over sham. Relative decreases in pain significantly favored IDET over sham.
Freeman <i>et al.</i> , 2005	IDET	VAS Pain, LBOS, ODI, SF-36, Zung Depression Index, Modified Somatic Perception Questionnaire, Sitting tolerance, work tolerance, medication, and any neurologic complications. Clinical success defined as improvement in LBOS by 7 points and SF-36 by 1 standard deviation.	Baseline, 6 months	Subjects, Investigator performing the Intervention and Investigator assessing clinical outcomes were all blinded.	Active Therapy: IDET catheter was introduced to cover 75% of the posterior annulus or annular tears and then heated from 65 C to 90 C. Sham Therapy: Catheter was introduced the same manner but never heated.	No post-procedure complications. No significant differences in change of outcome scores from baseline between sham and IDET groups at 6 months.
Kvarstein <i>et al.</i> , 2009	PIRFT	Change in pain intensity for worst pain, least pain, average pain and pain (NRS) Categorical impression of pain, Brief Pain Inventory, SF-36, ODI, and patient specific function scale (number of activities of daily living)	Baseline, 1, 3, 6, and 12 months	Subjects, operators and investigators assessing clinical outcomes were all blinded.	Active Therapy: discTRODE™ probe (Radionics RFG-3C Valleylab, Tyco Healthcare Group LP 5920 Colorado 80301-3299 USA) was inserted into the intervertebral disc. RF heating started at 50 C and increased by 5 C every second minute until 65 C and then as held at constant temperature for 4 minutes. Sham Therapy: Probe was inserted in the disc but no RF heating	No significant differences in any of the NRS pain intensity scores between sham and active therapy. No significant differences in categorical impression of pain, ODI, SF-36 scores at 6 or 12 months.
Barendse <i>et al.</i> , 2001	PIRFT	VAS Pain (10 point scale), Analgesic intake, ODI, Darnmouth COOP Functional Health Assessment Charts/World Organization of Primary Care Physicians, Global Perceived Effects, number of analgesics. Clinical Success defined as 2 in VAS and 50% pain reduction on Global Perceived Effects.	Baseline and 8 weeks	Subjects, investigators performing the intervention and investigators assessing outcomes were all blinded.	Active Therapy: RF probe (Radionics, Burlington, MA, USA) was placed in the center of the disc. A 90 second 70 C RF was used. Sham Therapy: RF probe was placed in center of the disc. No heating was applied.	No significant differences between sham and control for any of the outcomes.

Study	Intervention	Outcomes assessed	Time points of Outcomes	Blinding	Study Design	Significant Findings
Oh <i>et al.</i> , 2004	Ramus Ablation Communicas	VAS Pain and SF-36 Bodily Pain and Physical Function	Baseline and 4 months	No Blinding	Active Therapy: Ramus Communicas was ablated by RF probe (Stryker Leibinger GmbH & Co. KG, Freiburg, Germany) Sham Therapy: No ablation of Ramus Communicas	Significant improvements in VAS Pain scores and SF-36 Bodily pain and Physical Function at 4 months.
Kapur <i>et al.</i> 2012	Intradiscal Biacuplasty	SF-36, NRS, ODI, Health Care Utilization	Baseline, 1, 3 and 6 months	Patient, investigator assessing outcomes were blinded. Investigator performing intervention was not blinded	Active Therapy: Two transdiscal probes (Kimberly Clark Health Care, Rosewell, GA, USA) placed in the disc at a posterolateral oblique angle delivered RF energy at 45 C or 50 C. 15 patients also underwent monopolar lesioning at 50 C for 2.5 minutes. Sham Therapy: Mimic Active therapy except electrodes were positioned just outside the disc	No significant differences in outcomes or improvement in outcomes at 1 or 3 months between sham and active therapy. Significant differences in SF-36, NRS, ODI scores and improvements in these scores favoring active over sham therapy at 6 months.

Abbreviations: VAS (Visual Analogue Scale), ODI (Oswestry Disability Index), SF-36 (Short Form 36), NRS (Numeric Rating Scale), LBOS (Low Back Pain Outcome Score), IDET (Intradiscal Electrothermal Treatment), RF (Radiofrequency)