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Systematic Review

Systematic Review of the Effectiveness of Thermal Annular Procedures in Treating Discogenic Low Back Pain

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Background: Chronic discogenic low back pain is a common problem with significant personal and societal costs. Thermal annular procedures (TAPs) have been developed in an effort to provide a minimally invasive treatment for this disorder. Multiple techniques utilized are intradiscal electrothermal therapy (IDET), radiofrequency annuloplasty, and intradiscal biacuplasty (IDB). However, these treatments continue to be controversial, coupled with a paucity of evidence.

Study Design: A systematic review of the literature evaluating the efficacy or effectiveness of TAPs.

Objective: To determine the effectiveness of TAPs in reducing low back pain in patients with intradiscal disorders.

Methods: A comprehensive evaluation of the literature relating to TAPs was performed. The literature was evaluated according to Cochrane Review criteria for randomized controlled trials (RCTs) and according to the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies.

The level of evidence was classified as Level I, II, or III based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF). Pain relief was the primary outcome measure. Other outcome measures were functional improvement, improvement of psychological status, and return to work.

Data sources included relevant literature of the English language identified through searches of PubMed, EMBASE, the Cochrane Library, and the Database of Reviews of Effectiveness (DARE).

Outcome Measures: Short-term effectiveness was defined as one-year or less and long-term effectiveness was defined as greater than one-year.

Results: Systematic review of IDET identified 2 RCTs and 16 observational studies with an indicated evidence of Level II-2.

Systematic review of radiofrequency annuloplasty identified no RCTs but 2 observational studies with an uncertain evidence of Level II-3.

Systematic review of IDB identified one pilot study. The level of evidence is lacking with Level III.

Limitations: The limitations of this review include paucity of the literature and lack of evidence with internal validity and generalizability.

Conclusion: IDET offers functionally significant relief in approximately one-half of appropriately chosen chronic discogenic low back pain patients. There is minimal evidence supporting the use of radiofrequency annuloplasty and IDB.

Key words: Chronic low back pain, degenerative disc disease, internal disc disruption, intervertebral disc, thermal annular procedures, intradiscal electrothermal therapy, radiofrequency ablation, intradiscal biacuplasty, radiofrequency annuloplasty

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Chronic low back pain is a common problem with a prevalence ranging from 35% to 75% at 12 months after the initial attack of pain (1,2). The widely held myth that 90% of low back pain is short-lived and that most patients get better on their own has been dispelled in multiple studies (3-7). The anatomical sources of persistent low back pain have been defined and include the lumbar intervertebral discs, facet or zygapophysial joints, and the sacroiliac joint (8-12). Disorders of the intervertebral disc have been estimated to be the cause of persistent low back pain in 7%, 39%, and 26% of patients in various studies (9-11). Valuable information pertaining to the diagnosis of discogenic low back pain could be achieved by performing provocation discography (12). However, treatment of discogenic low back pain can be frustrating, with neither conservative treatment nor fusion reliably resolving the problem (13,14).

To provide an alternative between failed conservative therapy and fusion, several technologies have been developed to apply heat to the posterior lumbar annulus. The rationale is that the degenerated disc has the ability to generate pain and that the application of heat can resolve this pain. The lumbar intervertebral disc consists of a central nucleus pulposus, a surrounding annulus fibrosis, and the endplates. The annulus is composed of ordered collagen fibers (15,16). With aging, the disc undergoes degeneration in the form of delamination of the annular layers like tearing, along with endplate changes which reduce diffusion. These changes are age related and have the ability to generate pain (17-19).

This degeneration is ubiquitous and begins to occur as early as age 11 (20). Degeneration appears to cause pain because of the development of granulation tissue and nerve endings in the fissures (21). The normal annulus and posterior longitudinal ligament are innervated and nerve growth in normal discs is limited to the superficial 3.5 mm of the disc (22-26). Degenerated discs have increased innervation compared to normal discs and are a source of back pain (27,28). Substance P is found in degenerated discs, providing an anatomic basis for pain perception from the disc (29,30). Mechanoreceptors are also present. Nerve supply from either the sinuvertebral nerves or the paravertebral sympathetic trunks entering the dorsal root ganglia at L2 or above has been demonstrated (27,31-35). Aoki et al (36) found that gene-related peptide-immunoreceptive neurons proliferated in inflamed discs, suggesting these neurons were responsible for pain from intradiscal disorders. These receptors appear to be sensitized by the production of proinflammatory cytokines and mediators such as prostaglandin E2, and interleukin (IL)-6 and (IL)-8, so that pressure directly stimulates the nociceptors (21,37). Painful discs also show evidence of injury and repair not found in aged, non-painful discs (38).

The current hypothesis, therefore, is that the inflammatory response associated with the onset of annular fissures sensitizes the nerves that innervate the fissures, leading to pain. Intradiscally applied heat has been used to treat this pain. Despite the ongoing clarification as to the mechanisms by which intradiscal pain occurs, the mechanisms by which heat relieves pain emanating from the disc are unclear. Derby et al (39) have reviewed the proposed mechanisms of action, including changes in disc biomechanics, annular contraction, thermally induced healing response, sealing of annular tears, annular denervation, and decreased intradiscal disorder, with the conclusion that the mechanism of pain relief is unclear. Derby et al (39) hypothesize that if patients with no or a minimal (< 1 week) flare of pain after the procedure do better, then that finding would be consistent with a denervation mechanism. Kapural et al (40) have shown that intradiscal biacuplasty (IDB) generates sufficient annular temperatures for neuroablation, suggesting that the pain relief is caused by denervation.

The first technology to apply heat was IDET, using convection heating, first applied in 1996 (41). IDET utilizes a 5 cm active tip catheter placed in the nuclear-annular junction or in the posterior annulus. Finch et al (42) developed a technique using monopolar radiofrequency energy to apply ionic heating to the posterior annulus. Recently, bipolar cooled radiofrequency, with electrodes placed on both sides, has been used to treat the posterior annulus (40).

Percutaneous intradiscal treatment of low back pain has been the subject of several reviews (43-50). The Centers for Medicare and Medicaid Services (CMS) has recently issued a non-certification for these procedures (50). CMS refers to them collectively as thermal intradiscal procedures, including intradiscal electrothermal therapy (IDET), percutaneous intradiscal radiofrequency thermocoagulation (PIRFT), radiofrequency annuloplasty, intradiscal biacuplasty (IDB), percutaneous (or plasma) disc decompression (PDD) or coblation, or targeted disc decompression (TDD).

This systematic review is undertaken to evaluate the current evidence of thermal annular procedures (TAPs). The current review focuses on heat treatment

of the annulus. Accordingly, only IDET, radiofrequency annuloplasty, and IDB are covered here. Since we are referring to heat treatment of the annulus rather than any heat treatment within the disc, these procedures are collectively referred to as TAPs.

Methods

Literature Search

Databases reviewed were PubMed, EMBASE, the Cochrane Library, and the Database of Reviews of Effectiveness (DARE). Bibliographies of reviewed papers were also examined. In addition, authors known to be active in the field were contacted. The time frame covered was 1966 to November 2008.

Inclusion criteria were:

1. Lumbar intradiscal pain of at least 6 months duration;
2. Treatment with an annuloplasty procedure using IDET, radiofrequency annuloplasty, or IDB;
3. Minimum of 6 month follow-up.

Search terms included intervertebral disc, degenerative disc disease, intradiscal electrothermal therapy (IDET), radiofrequency ablation, annuloplasty, internal disc disruption, and thermal intradiscal procedures.

Only articles in English or with English abstracts, systematic reviews, randomized controlled trials (RCTs), and observational studies were reviewed. All data extraction was performed by one author (SH). Each article was reviewed by 2 reviewers. Discrepancies in rating were resolved by adjudication by a third reviewer. If there was a conflict of interest with the reviewed manuscripts such as authorship or any other type of conflict, the involved authors did not review the manuscripts for quality assessment, clinical relevance, evidence synthesis, or grading of evidence.

Methodologic Quality Assessment

The method of quality assessment was a function of the type of study. For RCTs, the Cochrane review criteria were used (Table 1) (51). Assessment of study quality for observational studies was done according

Table 1. *Modified and weighted Cochrane methodologic quality assessment criteria.*

CRITERION		Weighted Score (points)
1. Study population		**35**
A	Homogeneity	2
B	Comparability of relevant baseline characteristics	5
C	Randomization procedure adequate	4
D	Drop-outs described for each study group separately	3
E	< 20% loss for follow-up	2
	< 10% loss for follow-up	2
F	> 50 subject in the smallest group	8
	> 100 subjects in the smallest group	9
2. Interventions		**25**
G	Interventions included in protocol and described	10
H	Pragmatic study	5
I	Co-interventions avoided or similar	5
J	Placebo-controlled	5
3. Effect		**30**
K	Patients blinded	5
L	Outcome measures relevant	10
M	Blinded outcome assessments	10
N	Follow-up period adequate	5
4. Data-presentation and analysis		**10**
O	Intention-to-treat analysis	5
P	Frequencies of most important outcomes presented for each treatment group	5
	TOTAL SCORE	100

Adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288 (51).

to the Agency for Healthcare Research and Quality (AHRQ) criteria (Table 2) (52). Both the RCTs and observational forms provide a maximum of 100 points; only studies with scores of over 50 points were included.

Table 2. *Modified AHRQ quality assessment criteria for observational studies.*

CRITERION	Weighted Score (points)
1. Study Question	2
• Clearly focused and appropriate question	
2. Study Population	8
• Description of study population	5
• Sample size justification	3
3. Comparability of Subjects	22
• Specific inclusion/exclusion criteria for all groups	5
• Criteria applied equally to all groups	3
• Comparability of groups at baseline with regard to disease status and prognostic factors	3
• Study groups comparable to non-participants with regard to confounding factors	3
• Use of concurrent controls	5
• Comparability of follow-up among groups at each assessment	3
4. Exposure or Intervention	11
• Clear definition of exposure	5
• Measurement method standard, valid and reliable	3
• Exposure measured equally in all study groups	3
5. Outcome measures	20
• Primary/secondary outcomes clearly defined	5
• Outcomes assessed blind to exposure or intervention	5
• Method of outcome assessment standard, valid and reliable	5
• Length of follow-up adequate for question	5
6. Statistical Analysis	19
• Statistical tests appropriate	5
• Multiple comparisons taken into consideration	3
• Modeling and multivariate techniques appropriate	2
• Power calculation provided	2
• Assessment of confounding	5
• Dose-response assessment if appropriate	2
7. Results	8
• Measure of effect for outcomes and appropriate measure of precision	5
• Adequacy of follow-up for each study group	3
8. Discussion	5
• Conclusions supported by results with possible biases and limitations taken into consideration	
9. Funding or Sponsorship	5
• Type and sources of support for study	
TOTAL SCORE	**100**

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (52).

Consensus-based weighted scoring developed by the Guidelines Committee of the American Society of Interventional Pain Physicians (ASIPP) was utilized. The same scoring system has been used in multiple evaluations (49,53-57).

Clinical Relevance

Clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (58,59).

Table 3 shows the clinical relevance questions. 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.

In the Cochrane review of "Injection Therapy for Subacute and Chronic Low Back Pain" (59) the authors considered a 20% improvement in pain scores (60) and a 10% improvement in functioning outcomes (61) to be clinically important.

Both RCTs and observational studies were included in the review to improve generalizability and application of the TAPs (62-68).

Outcome Measures

Pain relief was the primary outcome measure. Other outcome measures were functional improvement, improvement of psychological status, and return to work.

A decrease of either 2 points or 30% of pain scores provides a useful benchmark of clinical importance to assess effectiveness (60,69). Similarly, a 10% improvement in functioning outcomes provides an accepted benchmark of clinically useful benefit (61). However, in interventional pain management settings, a significant improvement has been defined as 50% or more relief, whereas significant improvement in disability has been defined as a 40% or more decrease in disability scores in multiple publications (62-68,70-76).

Analysis of Evidence

Level of evidence was determined based on the United States Preventive Services Task Force (USPSTF) criteria using 5 levels of evidence, ranging from Level I to III with 3 subcategories in Level II, as illustrated in Table 4 (77).

Table 3. *Clinical relevance questions*.

A) Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?
B) Are the interventions and treatment settings described well enough so that you can provide the same for your patients?
C) Were all clinically relevant outcomes measured and reported?
D) Is the size of the effect clinically important?
E) Are the likely treatment benefits worth the potential harms?

Source: Staal JB et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (59).

Table 4. *Quality of evidence developed by USPSTF.*

I:	Evidence obtained from at least one properly randomized controlled trial
II-1:	Evidence obtained from well-designed controlled trials without randomization
II-2:	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group
II-3:	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III:	Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees

Adapted from the U.S. Preventive Services Task Force (USPSTF) (77).

Recommendations

Recommendations for effectiveness were made according to Guyatt et al's criteria (78) (Table 5).

Data will be analyzed for both short-term (1 year or less) and long-term (longer than 1 year).

Results

The results of literature search for thermal annular procedures (TAPs) are illustrated in Fig. 1.

A total of 67 articles were located in the literature search. Of these, 36 were RCTs or observational studies.

Methodologic Quality Assessment

Randomized Controlled Trials

Of the RCTs, 2 studies met inclusion criteria with methodologic quality assessment scores illustrated in Table 6. The scores were 61 of 100 for Freeman et al (79) and 68 of 100 for Pauza et al (80).

Clinical Relevance Assessment

Both studies (79,80) met clinical relevance criteria as shown in Table 7. Both studies have been criticized (81,82). Despite these criticisms, both describe patients in sufficient detail for a practitioner to identify them in a clinical setting. Both describe IDET sufficiently that the procedure can be provided outside of the academic setting. Both measured and reported clinically relevant effects. Pauza et al (80) did meet all the criteria for clinically important improvement, including a greater than 30% improvement in pain scores, a 2-point reduction in visual analog score (VAS) in about 50% of patients, and a greater than 10% improvement in functioning scores, although the functioning score improvement was not clinically significant. According to Pauza et al (80), but not according to Freeman et al (79), the benefits of TAP are worth the potential harms.

Observational Studies

Overall 34 observational studies met the inclusion criteria for methodologic quality assessment (41,42,83-115). However, of these, methodologic quality assessment was performed on 31 studies after combining duplicate studies. Methodologic quality scores are described in Table 8, ranging from 35 to 85. Of these, 20 studies scored 50 or above (41,42,83-92,94-101,103,114,115), meeting

Table 5. *Grading recommendations*.

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181 (78).

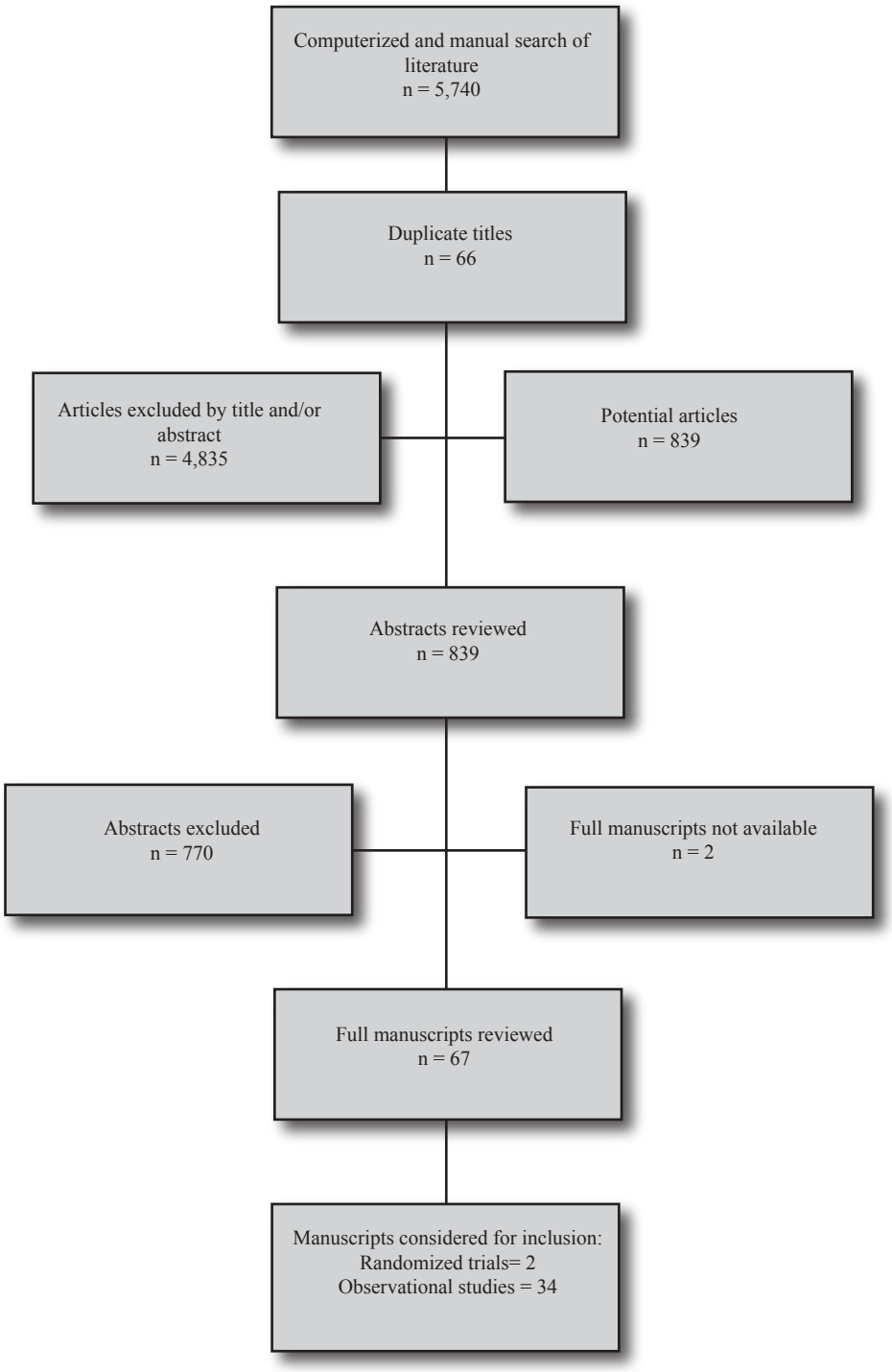

Fig. 1. *The flow diagram illustrating literature evaluating thermal annular procedures (TAPs).*

Table 6. *Methodological assessment of randomized clinical trials evaluating the effectiveness of TAPS.*

CRITERION		Weighted Score (points)	Pauza et al (80)	Freeman et al (79)
Study population				
A	Homogeneity	2	2	0
B	Comparability of relevant baseline characteristics	5	5	0
C	Randomization procedure adequate	4	4	2
D	Drop-outs described for each study group separately	3	3	3
E	< 20% loss for follow-up	2	2	2
	< 10% loss for follow-up	2	0	2
F	> 50 subject in the smallest group	8	0	0
	> 100 subjects in the smallest group	9	0	0
Interventions				
G	Interventions included in protocol and described	10	10	10
H	Pragmatic study	5	0	5
I	Co-interventions avoided or similar	5	5	5
J	Placebo-controlled	5	5	0
Effect				
K	Patients blinded	5	5	5
L	Outcome measures relevant	10	10	10
M	Blinded outcome assessments	10	10	10
N	Follow-up period adequate	5	2	2
Data-presentation and analysis				
O	Intention-to-treat analysis	5	0	0
P	Frequencies of most important outcomes presented for each treatment group	5	5	5
TOTAL SCORE		**100**	**68**	**61**

Table 7. *Clinical relevance of randomized clinical trials evaluating the effectiveness of IDET.*

	Freeman et al (79)	Pauza et al (80)
A) Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?	+	+
B) Are the interventions and treatment settings described well enough so that you can provide the same for your patients?	+	+
C) Were all clinically relevant outcomes measured and reported?	+	+
D) Is the size of the effect clinically important?	-	-
E) Are the likely treatment benefits worth the potential harms?	-	+
TOTAL CRITERIA MET	3/5	4/5

+ = 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 (59).

Table 8. *Methodological assessment of observational studies evaluating the effectiveness of TAPS.*

CRITERION	Weighted Score (points)	Assietti (105)	Bogduk and Karasek (90,115)	Bryce et al (84)	Cohen et al (85)	Davis et al (114)	Derby et al (102)	Derby et al (86)	Derby et al (87)	Derby et al (109)
1. Study Question	2	2	2	2	2	2	2	2	2	2
• Clearly focused and appropriate question		2	2	2	2	2	2	2	2	2
2. Study Population	8	5	5	5	5	4	5	4	5	5
• Description of study population	5	5	5	5	5	4	5	4	5	5
• Sample size justification	3	0	0	0	0	0	0	0	0	0
3. Comparability of Subjects for All Observational Studies	22	3	19	5	11	5	5	13	5	5
• Specific inclusion/exclusion criteria for all groups	5	3	5	5	5	0	5	5	5	5
• Criteria applied equally to all groups	3	0	3	0	3	0	0	2	0	0
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	0	3	0	0	0	0	3	0	0
• Study groups comparable to non-participants with regard to confounding factors	3	0	3	0	0	0	0	0	0	0
• Use of concurrent controls	5	0	3	0	0	0	0	0	0	0
• Comparability of follow-up among groups at each assessment	3	0	2	0	3	0	0	3	0	0
4. Exposure or Intervention	11	8	11	8	8	8	8	11	8	8
• Clear definition of exposure	5	5	5	5	5	5	5	5	5	5
• Measurement method standard, valid and reliable	3	3	3	3	3	3	3	3	3	3
• Exposure measured equally in all study groups	3	0	3	0	0	0	0	3	0	0
5. Outcome measures	20	15	15	15	13	20	13	13	13	9
• Primary/secondary outcomes clearly defined	5	5	5	5	5	5	5	5	5	5
• Outcomes assessed blind to exposure or intervention	5	0	1	0	0	5	0	0	0	0
• Method of outcome assessment standard, valid and reliable	5	5	4	5	5	5	5	5	3	4
• Length of follow-up adequate for question	5	5	5	5	3	5	3	3	5	0
6. Statistical Analysis	19	3	15	11	8	5	9	6	7	7
• Statistical tests appropriate	5	3	5	5	5	5	5	3	5	5
• Multiple comparisons taken into consideration	3	0	3	3	3	0	3	3	2	2
• Modeling and multivariate techniques appropriate	2	0	2	0	0	0	1	0	0	0
• Power calculation provided	2	0	2	0	0	0	0	0	0	0
• Assessment of confounding	5	0	3	3	0	0	0	0	0	0
• Dose-response assessment if appropriate	2	0	0	0	0	0	0	0	0	0
7. Results	8	8	8	7	6	5	5	7	8	8
• Measure of effect for outcomes and appropriate measure of precision	5	5	5	4	4	2	5	5	5	5
• Adequacy of follow-up for each study group	3	3	3	3	2	3	0	2	3	3
8. Discussion	5	5	5	5	5	3	2	5	4	5
• Conclusions supported by results with possible biases and limitations taken into consideration		5	5	5	5	3	2	5	4	5
9. Funding or Sponsorship	5	0	5	0	5	0	0	0	0	0
• Type and sources of support for study		0	5	0	5	0	0	0	0	0
TOTAL SCORE=	100	49	85	58	63	52	49	61	52	49

Table 8 cont.. *Methodological assessment of observational studies evaluating the effectiveness of TAPS.*

CRITERION	Weighted Score (points)	Endres et al (106)	Ergun et al (101)	Finch et al (42)	Freedman et al (88)	Gerszten et al (83)	Kapural et al (95)	Kapural et al (96)	Kapural et al (99)	Kapural (100)
1. Study Question	2	2	2	2	2	2	2	2	2	2
• Clearly focused and appropriate question		2	2	2	2	2	2	2	2	2
2. Study Population	8	4	5	5	5	5	5	5	6	6
• Description of study population	5	4	5	5	5	5	5	5	5	5
• Sample size justification	3	0	0	0	0	0	0	0	1	1
3. Comparability of Subjects for All Observational Studies	22	5	5	19	5	4	17	21	5	5
• Specific inclusion/exclusion criteria for all groups	5	0	0	5	0	4	5	4	5	5
• Criteria applied equally to all groups	3	0	0	3	0	0	3	3	0	0
• Study groups comparable to non-participants with regard to confounding factors	3	0	0	0	0	0	0	3	0	0
• Use of concurrent controls	5	0	0	5	0	0	3	5	0	0
4. Exposure or Intervention	11	8	8	11	8	8	11	10	8	8
• Clear definition of exposure	5	5	5	5	5	5	5	5	5	5
• Measurement method standard, valid and reliable	3	3	3	3	3	3	3	2	3	3
• Exposure measured equally in all study groups	3	0	0	3	0	0	3	3	0	0
5. Outcome measures	20	8	15	15	15	13	14	15	11	11
• Primary/secondary outcomes clearly defined	5	5	5	5	5	3	5	5	5	5
• Outcomes assessed blind to exposure or intervention	5	0	0	0	0	0	0	2	0	0
• Method of outcome assessment standard, valid and reliable	5	3	5	5	5	5	5	5	5	3
• Length of follow-up adequate for question	5	0	5	5	5	5	4	3	1	3
6. Statistical Analysis	19	5	9	4	13	5	13	16	8	8
• Statistical tests appropriate	5	0	5	0	5	2	5	5	5	5
• Multiple comparisons taken into consideration	3	0	2	0	3	3	3	2	3	3
• Modeling and multivariate techniques appropriate	2	0	2	0	0	0	0	2	0	0
• Power calculation provided	2	0	0	0	0	0	0	2	0	0
• Assessment of confounding	5	0	0	0	5	0	5	5	0	0
• Dose-response assessment if appropriate	2	0	0	0	0	0	0	0	0	0
7. Results	8	5	8	8	8	5	7	7	6	8
• Measure of effect for outcomes and appropriate measure of precision	5	5	5	5	5	3	25	5	5	5
• Adequacy of follow-up for each study group	3	0	3	3	3	2	2	2	1	3
8. Discussion	5	5	4	5	5	3	5	5	5	5
• Conclusions supported by results with possible biases and limitations taken into consideration		5	4	0	5	3	5	5	5	5
9. Funding or Sponsorship	5	0	0	0	5	5	0	0	5	5
• Type and sources of support for study		0	0	0	5	5	5	0	5	5
TOTAL SCORE=	100	42	56	69	66	50	74	81	56	58

Table 8 cont. *Methodological assessment of observational studies evaluating the effectiveness of TAPS.*

CRITERION	Weighted Score (points)	Lee et al (92)	Lutz et al (91)	Maurer and Squillante (104)	Maurer et al (97)	Mekhail and Kapural (94)	Nunley et al (98)	Park et al (113)	Saal and Saal (41,89,103)
1. Study Question	2	2	2	2	2	2	2	2	2
• Clearly focused and appropriate question		2	2	2	2	2	2	2	2
2. Study Population	8	5	5	5	5	5	5	5	5
• Description of study population	5	5	5	5	5	5	5	5	5
• Sample size justification	3	0	0	0	0	0	0	0	0
3. Comparability of Subjects for All Observational Studies	22	5	5	5	5	5	5	4	5
• Specific inclusion/exclusion criteria for all groups	5	0	5	5	5	5	5	0	5
• Criteria applied equally to all groups	3	0	0	0	0	0	0	0	0
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	0	0	0	0	0	0	0	0
• Study groups comparable to non-participants with regard to confounding factors	3	0	0	0	0	0	0	0	0
• Use of concurrent controls	5	0	0	0	0	0	0	0	0
• Comparability of follow-up among groups at each assessment	3	0	0	0	0	0	0	0	0
4. Exposure or Intervention	11	8	8	7	8	8	8	7	8
• Clear definition of exposure	5	5	5	4	5	5	5	5	5
• Measurement method standard, valid and reliable	3	3	3	3	3	3	3	2	3
• Exposure measured equally in all study groups	3	0	0	0	0	0	0	0	0
5. Outcome measures	20	15	14	13	15	13	13	13	15
• Primary/secondary outcomes clearly defined	5	5	5	4	5	5	5	5	5
• Outcomes assessed blind to exposure or intervention	5	0	0	0	0	0	0	0	0
• Method of outcome assessment standard, valid and reliable	5	5	5	5	5	5	5	5	5
• Length of follow-up adequate for question	5	5	4	4	5	3	3	3	5
6. Statistical Analysis	19	8	11	3	9	13	15	0	5
• Statistical tests appropriate	5	5	5	3	5	5	5	0	5
• Multiple comparisons taken into consideration	3	3	3	0	3	3	3	0	0
• Modeling and multivariate techniques appropriate	2	0	0	0	1	0	2	0	0
• Power calculation provided	2	0	0	0	0	0	0	0	0
• Assessment of confounding	5	0	3	0	0	5	5	0	0
• Dose-response assessment if appropriate	2	0	0	0	0	0	0	0	0
7. Results	8	5	8	7	8	7	7	6	8
• Measure of effect for outcomes and appropriate measure of precision	5	5	5	5	5	5	5	4	5
• Adequacy of follow-up for each study group	3	0	3	2	3	2	2	2	3
8. Discussion	5	5	5	3	5	5	5	3	4
• Conclusions supported by results with possible biases and limitations taken into consideration		5	5	3	5	5	5	3	4
9. Funding or Sponsorship	5	0	0	0	5	0	0	0	0
• Type and sources of support for study		0	0	0	5	0	0	0	0
TOTAL SCORE=	100	53	58	45	62	58	60	40	52

Table 8 cont.. *Methodological assessment of observational studies evaluating the effectiveness of TAPS.*

CRITERION	Weighted Score (points)	Singh (110)	Spruit and Jacobs (111)	Thompson and Eckel (112)	Webster et al (93)	Welch et al (107)
1. Study Question	2	2	2	2	2	2
• Clearly focused and appropriate question		2	2	2	2	2
2. Study Population	8	5	5	5	3	3
• Description of study population	5	5	4	5	3	3
• Sample size justification	3	0	1	0	0	0
3. Comparability of Subjects for All Observational Studies	22	5	3	0	3	4
• Specific inclusion/exclusion criteria for all groups	5	5	3	0	3	4
• Criteria applied equally to all groups	3	0	0	0	0	0
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	0	0	0	0	0
• Study groups comparable to non-participants with regard to confounding factors	3	0	0	0	0	0
• Use of concurrent controls	5	0	0	0	0	0
• Comparability of follow-up among groups at each assessment	3	0	0	0	0	0
4. Exposure or Intervention	11	8	8	3	3	8
• Clear definition of exposure	5	5	5	3	1	5
• Measurement method standard, valid and reliable	3	3	3	0	2	3
• Exposure measured equally in all study groups	3	0	0	0	0	0
5. Outcome measures	20	10	11	12	8	9
• Primary/secondary outcomes clearly defined	5	5	3	5	2	4
• Outcomes assessed blind to exposure or intervention	5	0	0	0	0	0
• Method of outcome assessment standard, valid and reliable	5	3	5	5	1	5
• Length of follow-up adequate for question	5	2	3	2	5	0
6. Statistical Analysis	19	5	5	3	10	3
• Statistical tests appropriate	5	0	5	3	5	3
• Multiple comparisons taken into consideration	3	0	0	0	3	0
• Modeling and multivariate techniques appropriate	2	0	0	0	0	0
• Power calculation provided	2	0	0	0	0	0
• Assessment of confounding	5	0	0	0	2	0
• Dose-response assessment if appropriate	2	0	0	0	0	0
7. Results	8	7	4	5	5	3
• Measure of effect for outcomes and appropriate measure of precision	5	5	4	2	2	0
• Adequacy of follow-up for each study group	3	2	0	3	3	0
8. Discussion	5	5	3	2	5	3
• Conclusions supported by results with possible biases and limitations taken into consideration		5	3	2	5	0
9. Funding or Sponsorship	5	0	0	5	0	0
• Type and sources of support for study		0	0	5	0	0
TOTAL SCORE=	100	47	41	37	39	35

the methodologic quality assessment criteria for evidence synthesis and 11 studies scored below 50 (93,102,104-107,109-113), thus, they were not included in evidence synthesis.

Study Characteristics

Study characteristics for RCTs are illustrated in Table 9, whereas study characteristics of observational studies are illustrated in Table 10.

Table 9. *Description of randomized controlled trials.*

Study/Methods	Participants	Inclusion/Exclusion	Interventions	Outcomes	Results	Conclusion Short-term ≤ 12 mos. Long-term > 12 mos.
Pauza et al 2004 (80) Randomized, placebo-controlled, double-blind, prospective trial. Study sponsored by device manufacturer.	64 patients Evaluated 1360 patients between September 2000 and April 2002; 260 potentially met the criteria. Study was done in a private practice setting. Of the 37 treated patients, 32 were included in the analysis; of the 27 sham patients, 24 were included in the analysis. Pauza et al were unable to enroll enough patients to fully power his study at 80%,study was statistically significant at 60%.	Inclusion: age 18-65 years; low back pain > leg pain of > 6 months duration; failure to improve after nonoperative therapy; no surgery within the last three months; less than 20% loss of disc height. Exclusion: abnormal neurological exam; Workers' Compensation; personal injury litigation or receiving disability. Positive discography and posterior annular tears on CT scan.	IDET 37 had IDET; 27 had a sham procedure in which the introducer needle was advanced to the outer annulus, but no catheter placed. Sham patients were exposed to a fluoroscopic monitor showing passage of the electrode, with appropriate sounds during the putative procedure.	SF-36 and VAS Unblinded at 6-months	56% of the IDET group had a greater than 2.0 improvement in the VAS; 38% of the sham group did. 24% of the treated group had greater than 75% pain relief; 4% of the sham group did. The improvement in the IDET group was significantly better than the sham. 40% of patients treated with IDET obtained 50% relief at 6 months.	Positive short-term. A needed-to-treat value of 5 for achieving 75% relief indicates that it is a worthwhile intervention for some highly select patients.
Freeman et al 2005 (79) Randomized, placebo- controlled, double-blind, prospective trial. Study sponsored by device manufacturer.	57 subjects from 3 spine practices in Australia. Unable to enroll the 75 patients required to power study at 80%. Number of patients screened to enroll the 57 was not given. Patients enrolled from November 1999 to December 2001. Between 84% and 89% of enrollees had abnormal reflexes. 13% of the treated and 5 percent of the sham patients had positive Waddell signs. Ten percent of the treated group was on disability. Duration of low back pain was up to 20 years	Inclusion: symptoms of degenerative lumbar disc disease > 3 months; failure to improve with at least 6 weeks of conservative treatment; MRI documented degenerative disease; one or 2 positive levels on discography; dye spread on post discography CT scan to or beyond the outer annulus; age > 18. Exclusion: loss of more than 50% disc height; severely disrupted disc; 3 or more symptomatic lumbar discs; previous back surgery; current injury litigation.	IDET Treated group had IDET, with catheter covering at least 75% of the annular tear. The control had a catheter placed in the annulus and the cable attached to it. The cable was then passed to an independent technician who would either attach or not attach the cable to the IDET generator. 100 mg of cefazolin injected at end of procedure.	VAS, Low Back Pain Outcome Score, Oswestry Disability Index, SF-36, Zung Depression Index and the Modified Somatic Perception Questionnaire.	At six months, neither group showed any benefit in any parameter.	Negative short-term

Table 10. *Description of observational studies of TAPs.*

Study/Methods	Participants	Inclusion/Exclusion	Interventions	Outcomes	Results	Conclusion Short-term ≤ 12 mos. Long-term > 12 mos.
Bogduk and Karasek 2000, 2002 (90,115) Prospective observational study, with controls	53 consecutive patients seen in private pain practice between May 1998 and November 1998	Inclusion: Positive discography at one to two levels, intact annulus. Disc height ≥ 80% of normal. Exclusion: Disc prolapsed, neurologic disease, tumor, or infection.	Patients assigned to treatment or control by whether insurance authorized procedure. Catheter placed around entire posterior annulus. 1 mg of cefazolin injected intradiscally after procedure Control group given PT.	Visual Analogue Scale (VAS), return to work and opioid use	Mean treated VAS decreased from 8.0 to 3.0 at 2 years; 57% of treated group had 50% relief.	Positive for short- and long-term relief. Powered at 76% at 2 years.
Gerszten at al 2002 (83) Prospective observational study	23 consecutive patients 19 patients were on Workers' Compensation.	Inclusion criteria: back pain > 6 months duration. Low back pain > leg pain; pain with axial loading and relief with recumbency; discogenic disease on MRI or positive discography; failure of conservative treatment.	IDET with catheter covering symptomatic side. No antibiotics given. Co-interventions were limited to therapies given prior to the IDET.	Oswestry Low Back Pain Disability and the Short Form (SF)-36	47% of patients had significant (> 7 points) improvement in SF-36 scales. 75% had improvement in Oswestry. Workers' Compensation did not influence outcome.	Positive for short- and long-term relief.
Saal and Saal 2000 & 2002 (41,89,103) Prospective observational study	53 patients selected from 1,162 low back pain patients. 34% Workers' Compensation.	Inclusion: Low back pain > 6 months duration; Failure to improve with non-operative care; positive discography; normal neurological exam; no compressive lesion on MRI; positive discography at < 1.25 mL of dye, maximum 3 levels with negative control.	IDET passed "as far as possible around posterior annulus. 2-20 mg of cefazolin injected. No other medications injected into the disc.	VAS, sitting tolerance and SF-36	At 24 months, at least 72% experienced at least a 2 point decrease in VAS and 50% had a 4 point reduction. 78% had at least a 7 point reduction in the bodily pain scale of the SF-36. Sitting tolerance increased from a mean of 32 to 85 minutes. 97% of the private pay and 83% of the Workers' Compensation returned to work.	Positive for short- and long-term results. Patients with chronic discogenic low back pain show sustained improvement in VAS, sitting tolerance and SF-36.
Cohen et al 2003 (85) Retrospective observational pilot study	70 patients with discogenic low back pain.	Inclusion criteria: Abnormal MRI and positive discography. Annular tears were permitted. Low back pain> 6 months duration; age < 60; loss of disc height < 50%; failure to respond to conservative therapy; absence of prominent radicular signs and symptoms.	IDET limited to 1 or 2 discs. Coverage of at least 70% of the posterior annulus. Cefazolin and bupivacaine, dose not recorded, injected.	50% reduction in pain at 6-months.	48% had > 50% relief. 54% of the nonobese vs. 10% of the obese had a good outcome; 50% of 1-level vs. 38% of 2-level patients had good outcomes. No difference with smoking, diabetes, non-dermatomal leg pain, and previous surgery.	Positive short-term results. Long-term results not available.
Freedman et al 2002 (88) Retrospective observational study, no control	41 active duty soldiers seen at Walter Reed between 1999 and 2001.	Inclusion: Low back pain > 6 months duration; positive discography with at least one normal disc; MRI absence of nerve root compression, tumor, infection or trauma; no radicular symptoms; failed nonoperative treatment	IDET "using the protocol described by Saal and Saal."	50% reduction in pain	29% reported symptoms as improved at last follow-up. Overall satisfaction was 16%. 52% had a 2 point reduction in VAS.	Positive short-term and negative long-term outcomes.
Lee et al 2003 (92) Prospective observational study	62 consecutive patients. 51 patients were available for follow-up at 2 years 20 patients were Workers' Compensation or no fault insurance.	Inclusion criteria: Low back pain > 6 months; sitting> standing pain; normal neurologic exam; failure of conservative care; no compressive lesion on imaging; positive discogram with annular tear; < 50% disc height.	VAS, Roland Morris, and NASS patient satisfaction index. 2-year follow-up	IDET catheter passed "past midline." No mention of intradiscal antibiotics	53% had VAS and RM improvements > 2 points. No difference with age, insurance (including Workers' Compensation), pre-IDET VAS, number of levels, or microdiscectomy.	Positive short- and long-term results.

Table 10 cont. *Description of observational studies of TAPs.*

Study/Methods	Participants	Inclusion/Exclusion	Interventions	Outcomes	Results	Conclusion Short-term ≤ 12 mos. Long-term > 12 mos.
Lutz et al 2003 (91) Prospective observational study	33 patients in an academic-affiliated private physiatry practice. Dates of recruitment not given.	Inclusion criteria: Low back pain > 6 months duration; positive discography; non-responsive to conservative care. Exclusion: > 50% loss of disc height; > 5 mm disc extrusion or sequestration; severe stenosis; spondylolisthesis; previous spinal surgery; segmental instability; infection	VAS, Roland Morris, and NASS patient satisfaction index. Success was a 2 point improvement in VAS or RM and a positive NASS satisfaction response. Follow-up at 15 months	IDET Catheter "into the posterior annular wall past the midline."	Mean change in VAS was 3.9. 77% indicated they would repeat the procedure. Complete relief in 24% of patients and partial relief in 46%. 15% of patients required an epidural steroid injection for flare-up of leg pain.	Positive short- and long-term results.
Davis et al 2004 (114) Retrospective observational study	60 patients referred from 17 spine specialists. IDET performed by 4 physicians. 73% of patients responded to questionnaire.	Inclusion criteria: diagnosis of discogenic low back pain > 6 months; positive discogram with provocation discography using < 2.5 ml of contrast, with annular fissure; disc height >50%; failed conservative therapy.	Short and long questionnaires from the National Low Back Pain Study. Core questions were pain intensity, functional limitation, work status, analgesic use, other treatment for low back pain, overall satisfaction.	IDET. Technique not described.	37% of patients had a successful outcome. 14% had further surgery at one year. At two years, 4 more patients had had surgery. One patient developed discitis and one developed a Grade I spondylolisthesis requiring surgery.	Negative short- and long-term relief.
Derby et al 2004 (86) Retrospective pilot study	35 patients for restorative injection therapy and 74 for IDET. "Retrospectively performed through the analysis of a prospectively collected data base." Patients seen between January 2000 and October 2002.	Inclusion criteria: Chronic low back pain not responsive to conservative therapy; being considered for additional surgery; positive discography. Prior surgery and, for the injection group, prior IDET at the treated level, was allowed. For IDET, no focal neurological signs; single level; disc height > 50%.	Compared effectiveness of restorative injection therapy and IDET. VAS Follow-up 15.5 months in IDET and 7.7 months for injection group.	For injection, chondroitin sulfate, glucosamine, DMSO, bupivacaine, 1-2 mL injected. For IDET, coverage of entire posterior annulus. Cefazolin (dose not recorded) injected at end of procedure.	Mean improvement for IDET was 1.27 on VAS, versus 2.2 for injection group. 47.8% of IDET group felt better; 65.5% of injection group did. Pain relief was statistically significant for both groups. 81% of injection group had flare-up compared to 60% of IDET. Duration of flare was 8.6 days for injection group and 33.1 days for IDET.	Positive short-term relief. Both IDET and injection therapy provided benefit. Results subsumed under Derby et al (87) as same patient population presumed to be evaluated.
Derby et al 2004 (87) Retrospective observational study	99 patients seen in a single practice between January 1999 and December 2000 who did not have subsequent surgery and who met inclusion criteria. Study assessed changes in referred leg pain.	Inclusion criteria: low back or low back and leg pain > 6 months duration unresponsive to conservative treatment; negative straight leg raising; non-focal neurological signs; no compressive lesions on MRI; disc protrusion < 2 mm; positive discogram with annular tear: no previous surgery; disc height > 50%.	IDET with catheter coverage of the entire posterior annulus. 18-month follow-up.	VAS and 5-point pain scale from the NASS low back pain assessment instrument. Patients divided into groups of leg pain dominant; back pain dominant; leg and back pain the same.	52% had an improvement in leg pain, with a mean improvement of 1.9 (5 point scale). Back pain decreased from 3.37 to 2.59 (5 point scale = Δ1.56/10). Relief of back pain correlated with relief of leg pain.	Positive short- and long-term relief. IDET can relieve associated limb pain.
Mekhail and Kapural 2004 (94) Prospective observational study	34 consecutive patients in an academic pain practice. 32 followed for 1 year. 10 patients Workers' Compensation.	Inclusion criteria: Disc height > 50%; no lumbar stenosis; 1-or 2-level DDD; no disc herniation on MRI; positive discography; no psychological issues.	IDET Catheter position not described.	Pain disability index (7 different activities of daily living plus VAS) Follow-up 1 year.	Non-Workers' Compensation had a 78% decrease in VAS versus 53% for Workers' Compensation. No significant difference in gender, smoking or age.	Positive short- and long-term relief. .

Table 10 cont. *Description of observational studies of TAPs.*

Study/Methods	Participants	Inclusion/Exclusion	Interventions	Outcomes	Results	Conclusion Short-term ≤ 12 mos. Long-term > 12 mos.
Kapural et al 2004 (95) Prospective observational study	17 consecutive patients with multilevel disc disease matched with 17 of 22 consecutive patients with 1- or 2-level disc disease.	Inclusion criteria: Low back pain>6 months not responsive to conservative therapy; no compressive radiculopathy; no previous surgery at symptomatic levels; disc height>50%; no signs or symptoms of stenosis; positive discography.	IDET Catheter position not described.	Pain disability index (7 different activities of daily living plus VAS) Follow-up 1 year.	The 1- or 2 level group had a pretreatment VAS of 7.7 versus 2.5 at 12 months. The multi-level group decreased from 7.4 to 4.9.	Positive short- and long-term relief. IDET results are better in patients with 1- or 2-level disc disease.
Kapural et al 2005 (96) Prospective controlled non-randomized observational study	42 matched patients, 21 with IDET and 21 with radiofrequency annuloplasty in an academic pain practice.	Inclusion criteria: Low back pain > 6 months not responsive to conservative care; no compressive radiculopathy; positive discography; no prior surgery; disc height > 50%; not Workers' Compensation claimants	IDET and radiofrequency annuloplasty	Pain disability index questionnaire. 12 month follow-up	IDET VAS decreased from 7.4 to 1.4; radiofrequency annuloplasty VAS decreased from 6.6 to 4.4 PDI scores mirrored these changes.	Positive short-term for IDET. Negative long-term for radiofrequency annuloplasty
Finch et al 2005 (42) Prospective, controlled but not randomized, observational study	46 patients: 31 treated; 15 non-treated, because of insurance denial, served as control. About 2/3 of patients were Workers' Compensation	Inclusion criteria: low back pain > 6 months duration not responsive to conservative care; positive discography with annular tears; disc height > 70%.	Radiofrequency annuloplasty	VAS, Oswestry Disability Index, Medication Quantification Score 12-month follow-up	The treated group had a 37% average decrease in VAS. Oswestry had a significant decrease No difference in outcome based upon Workers' Compensation status.	Positive long-term for radiofrequency annuloplasty Negative short-term relief.
Bryce et al 2005 (84) Prospective observational study	86 consecutive patients in a rural Wisconsin pain practice.	Inclusion criteria: Low back pain > 6 months duration unresponsive to conservative treatment; back pain > 60% of other symptoms; normal neurological exam; positive discography; annular tears; 18-50 years.	IDET	VAS and Roland Morris Disability Questionnaire 24 months follow-up	Significant (> 20 point) improvement in RMDQ. VAS improved. Improvement best in females and in those aged 18-45 years.	Positive short- and long-term relief.
Maurer et al 2008 (97) Prospective observational study	56 consecutive patients 16% of patients on Workers' Compensation Industry sponsored study	Inclusion criteria: low back pain > 6 months duration; disc height > 50%; normal lower extremity neurological exam; 1-3 desiccated discs discography; and posterior annular tear. Exclusion: previous back surgery.	IDET	Back pain severity, physical function and quality of life Follow-up 24 months	VAS improved by 61%. There were also significant improvements in sitting, standing and walking tolerances. 61% improvement in SF-36. 75% treatment successes.	Positive short- and long-term improvement.
Nunley et al 2008 (98) Prospective observational study	53 consecutive Workers' Compensation patients with low back pain.	Inclusion criteria: persistent low back pain > 6 months with failure to respond to conservative therapy; prior spine surgery; abnormal neurological exam; disc height > 40%; positive discography with an annular tear; BMI between 20.1-44.2.	IDET	VAS, Oswestry and self-assessment questionnaires of pain and disability 12-month follow-up.	The mean reduction of VAS was 62.6%, while the mean reduction in Oswestry was 69.3%. There was no significant effect of age or BMI on outcome. Narcotic use dropped from 51% initially to 13.2% after treatment. 47% returned to work in a full or partial capacity	Positive short- and long-term improvement.

Table 10 cont. *Description of observational studies of TAPs.*

Study/Methods	Participants	Inclusion/Exclusion	Interventions	Outcomes	Results	Conclusion Short-term ≤ 12 mos. Long-term > 12 mos.
Ergun et al 2008 (101) Prospective observational study	39 consecutive patients in a Turkish pain practice.	Inclusion criteria: Low back pain > 6 months non-responsive to conservative therapy; 1- or 2-level disease; no evidence of nerve root compression; > 50% disc height.	IDET Catheter covered 75% of the annulus. No post procedure antibiotics.	Turkish version of the Oswestry Disability Index 18-month follow-up	At 18 months, the mean decrease in ODI was 24. 79.5% of patients benefited. No complications.	Positive short- and long-term improvement.
Kapural et al 2008 (99) and Kapural 2008 (100) Prospective pilot observational study	15 patients aged 22 to 55, with 13 available at 12 months	Inclusion criteria: low back pain of greater than 6 months duration, back pain greater than leg pain, positive discography, disc height greater than 50% of normal and one or two level disc disease only; normal weight; age 55 or less.	IDB	VAS, Oswestry, SF-36 12-month follow-up	Seven of 13 patients had more than 50% pain relief. The VAS decreased from 7 (6,8) to 4 (1,6) at 12-months. The Oswestry decreased from 23.3 to 17.5 and the SF-36 physical functioning scores increased from 51 to 67.	Positive short- and long-term improvement.

Intradiscal Electrothermal Therapy

Level of Evidence

Table 11 illustrates results of published studies of effectiveness of IDET.

Two RCTs meeting inclusion criteria exist for IDET (79,80). One was favorable, with a significant placebo effect, and one was non-responsive to the study question.

Sixteen observational studies meeting inclusion criteria evaluated IDET. Of these, 14 studies found the procedure to be effective (83-85,87,89,91,92,94-98,101,115). Three studies found it to be ineffective (86,88,114)

The indicated evidence for IDET is Level II-2 based on U.S. Preventive Services Task Force (USPSTF) criteria.

Recommendations

Based upon one positive RCT and one unfavorable RCT, which was not responsive to the study's null hypothesis, a recommendation of 2A/weak recommendation is provided.

The recommendation is supplemented based on observational evidence derived from multiple studies.

Radiofrequency Annuloplasty

Level of Evidence

Table 12 illustrates the results of published studies of effectiveness of radiofrequency annuloplasty.

Two studies dealt with radiofrequency annuloplasty (42,96). Finch et al (42), in a case series, found the procedure to be effective. Kapural et al (96), in an observational study, found radiofrequency annuloplasty to be less effective than IDET.

The level of evidence for radiofrequency annuloplasty is II-3 (uncertain).

Recommendations

The recommendation is 2C/weak.

Intradiscal Biacuplasty

Level of Evidence

Table 13 illustrates the results of published studies of effectiveness of IDB.

Only one pilot study is available for IDB (99,100) evaluating the effectiveness of the procedure. There is a randomized, placebo-controlled trial in progress.

The level of evidence for IDB is Level III.

Table 11. *Results of published studies of effectiveness of IDET.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief		Results	
				≤ 12 mos.	> 12 mos.	Short-term relief ≤ 12 mos.	Long-term relief > 12 mos.
Pauza et al 2004 (80)	RA	68	64	56% had 2 point decrease 40% had > 50 % decrease	NA	Yes	NA
Freeman et al 2005 (79)	RA	61	57	No change	NA	No	NA
Karasek and Bogduk 2000 and 2002 (90,115)	O	85	53	70%	57%	Yes	Yes
Gerszten et al 2002 (83)	O	50	27	75%	75%	Yes	Yes
Saal and Saal 2000 & 2002 (41,89,103)	O	52	53	SI	SI	Yes	Yes
Cohen et al 2003 (85)	O	80	70	48%	NA	Yes	NA
Freedman et al 2002 (88)	O	66	41	47%	16% > 50% decrease	Yes	No
Lee et al 2003 (92)	O	53	62	NA	53%	Yes	Yes
Lutz et al 2003 (91)	O	58	33	NA	70%	Yes	Yes
Davis et al 2004 (114)	O	52	60	NA	37%	No	No
Derby et al 2004 (86)	O	61	34 Injection 74 IDET	2.2 point decrease for injection 1.27 for IDET	NA	Yes	No
Derby et al 2004 (87)	O	52	99	NA	52% 1.56 point decrease back pain	Yes	Yes
Mekhail and Kapural 2004 (94)	O	58	34	SI	SI	Yes	Yes
Kapural et al 2004 (95)	O	74	34	SI	SI	Yes	Yes
Kapural et al 2005 (96)	O	81	21	SI	SI	Yes	Yes
Bryce et al 2005 (84)	O	58	86	SI	SI	Yes	Yes
Maurer et al 2008 (97)	O	62	56	SI	SI	Yes	Yes
Nunley et al 2008 (98)	O	60	53	SI	NA	Yes	NA
Ergun et al 2008 (101)	O	56	39	NA	79%	NA	Yes

O = observational; RA = randomized; VAS = visual analog scale; SI = significant improvement; NSI = no significant improvement; NA = not available

Table 12. *Results of published studies of effectiveness of radiofrequency annuloplasty.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief (VAS)		Results	
				≤ 12 mos.	> 12 mos.	Short-term relief ≤ 12 mos.	Long-term relief > 12 mos.
Finch et al 2005 (42)	O	69	46	37%	NA	No	NA
Kapural et al 2005 (96)	O	81	21	NSI	NA	No	NA

O = observational; RA = randomized; NSI = no significant improvement; NA = not available

Table 13. *Results of published studies of effectiveness of IDB.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief (VAS)		Results	
				≤ 12 mos.	> 12 mos	Short-term relief ≤ 12 mos.	Long-term relief > 12 mos.
Kapural et al 2008 (99) and Kapural 2008 (100)	O	56/58	15	SI	SI	Yes	Yes

O = observational; SI = significant improvement

Recommendations

The recommendation is 2C/very weak.

Discussion

Three thermal annular procedures (TAPs) are currently available — IDET, radiofrequency annuloplasty, and IDB. IDET is supported with an indicated evidence of Level II-2 with a 2A/weak recommendation. Radiofrequency annuloplasty and IDB have a evidence levels of II-3 and III with 2C/very weak recommendations.

A meta-analysis of IDET was performed by Appleby et al (44). The lead author was an employee of the device manufacturer. He reviewed 17 reports on IDET, finding a mean improvement in VAS of 2.9. The mean improvement of the physical functioning scale of the SF-36 was 21.1 points. The mean improvement of the Oswestry Disability Index was 7.0 points. The complication rate was 0.8%. Complications which resolved included burning pain in the legs, paresthesias, foot drop, headache, increased radicular pain, dural puncture, incontinence of bowel, and non-dermatomal leg pain. Discitis did appear in one patient. Patients did go on to fusion, although the incidence was not provided. Appleby et al (44) did note the importance of selection criteria. They reported that the pooled results of published studies provided compelling evidence of the relative efficacy and safety of IDET. Andersson et al (45) in a systematic review of spinal fusion and IDET concluded that the majority of patients reported improvement in symptoms following both spinal fusion and the IDET procedure. The IDET procedure appears to offer sufficiently similar symptom amelioration to spinal fusion without the attendant complications.

Two RCTs met the criteria for inclusion in this review, those of Freeman et al (79) and Pauza et al (80). Both evaluated IDET. Pauza et al's study (80) has been criticized for the extensive placebo effect. It has also been criticized for how highly selective it was in terms

of screening patients, raising questions as whether the results could be extrapolated to clinical practice. Another criticism is that it did not control for patients with multilevel degenerative disease, raising the question as to whether, despite the rigorous selection process, patients who have been shown to not respond well to IDET, those with multilevel degenerative disease, were provided the procedure, thereby decreasing the apparent efficacy of the procedure. Placebo effects are a major source of patient response in RCTs. The concern is that there is additional relief above and beyond the placebo effect in the treated group. Pauza et al (80) have shown such an incremental effect; this analysis showing the NNT to get 75% relief (an endpoint which is arbitrarily chosen) convincingly argues for the efficacy of the procedure.

Freeman et al's study (79) is interesting for a number of reasons. Despite having enrolled patients earlier than Pauza et al (80), the study did not publish until after Pauza et al's paper was published (although Freeman et al did present the study at a meeting prior to publication of Pauza et al's study). Freeman et al opines that the clinical significance of the results found by Pauza were uncertain, although this statement is presented as a matter of fact, with no supporting documentation. The quality of blinding in Freeman et al's study is unclear. In Freeman et al's study, after the IDET catheter was placed, the randomization was done by a technician either connecting or not connecting the cable to the generator. In performing an IDET procedure, the generator makes a noise every 5 seconds. If the catheter is not attached, then the characteristic noise is not made. Freeman et al (79) do not disclose how this conundrum was handled: it is not clear whether the treating physician was therefore blinded. Procedurally, the 100 mg of cefazolin is a very large dose and may have caused a chemical irritation to the disc. Further, despite the entrance criterion of a normal neurological examination, patients were admitted with an abnormal motor assessment and abnormal sensory exams and positive Waddell's findings. In addition, the inclusion criteria allowed patients with back pain of up to 20 years duration; it is not clear that patients with pain of so long standing would benefit from any procedure. Freeman et al also included Workers' Compensation patients. These are all potential confounding factors.

These criticisms pale, however, in light of the failure of any patients, either treated or placebo to respond. One review suggests that this finding is because of the physical therapy provided prior to the procedure. This explanation is unlikely because all TAP studies had as an inclusion criteria failure to respond to conservative treatment, which would include physical therapy. For example, Webster et al (93), in a study critical of IDET, found that 100% of patients had physical therapy prior to IDET.

The inability to demonstrate any positive response to IDET in either group, in contradistinction to all other published reports, raises questions regarding study methodology. The absence of placebo response would seem to suggest an undefined methodological error in the study. One potential answer is that the study was inadequately powered. We know that the desired power was not met, but Freeman et al (79) does not disclose the actual power achieved. The presence of a placebo effect has been well studied and has been attributed to multiple factors, including the observation (Hawthorne) effect, the natural course of disease, and regression of measured observations to the mean (116-118). In addition, observer bias can influence outcomes (Pygmalion effect), although the mechanism by which participants become aware of latent bias is unknown (119). The absence of placebo effect has not been well evaluated. However, given the extensive body of literature documenting its presence, the absence of placebo effect must be interpreted as a serious methodological flaw in how Freeman et al's study (79) was conducted, although, as documented by the Pygmalion effect, the nature of this flaw is unknown. As such, the strongest conclusion that one can draw from Freeman et al's study is that it is non-responsive in evaluating the null hypothesis that IDET is no more effective than placebo for the treatment of chronic discogenic low back pain.

Twelve of 16 observational studies favored IDET. None of these studies is without flaw. Bodguk and Karasek's (90,115) series does use a control group, but that control has a potential nocebo effect in that their insurance declined coverage of IDET. Regardless, they did find ITDA to provide significant relief in approximately one-half of the patients. Gerszten et al's (83) study was done in a neurosurgical setting, in which patients who were candidates for fusion were offered IDET if they could not or would not have a fusion. Seventy percent of their patients were Workers' Compensation. There is some question as to how the procedure performed with annular coverage limited to the symptomatic side(s) and one case of dural puncture. Using the Oswestry as an outcome measure, they

found improvement in 75% of their cases.

Saal and Saal's (89) study showed significant improvement in VAS and SF-36 scores at 2 years after IDET. A significant confounding factor was their role as the developers of the device. Cohen et al (85), in a retrospective pilot study, investigated the risk factors for a poor outcome after IDET, finding only obesity to be associated with an adverse outcome. They did note that 50% of patients had a successful outcome, defined as a 50% reduction in pain. Freedman et al (88), like Cohen et al (85), looked at the military population. With the definition of success at 50% relief, only 16% had a successful outcome. Further, only 29% reported sustained relief at the latest follow-up and only 16% were either somewhat or very satisfied with their outcome. Freedman et al's study (88) is therefore considered a negative regarding the efficacy of IDET. However, 50% of patients had a sustained 2 point reduction in their VAS, a reduction which is felt to be clinically significant. Given the military active duty nature of the study population, it would be useful to have more information regarding what the soldiers would have required for them to be satisfied with the procedure. While Freedman et al does discuss the success and complication rate of IDET, they do not present analogous information regarding the satisfaction rate amongst active duty military with fusion. Regardless, Freedman et al do state that they would continue to offer IDET.

Lee et al (92) and Lutz et al (91) published IDET studies in 2003, both out of the same practice. These appear to be separate patient groups, although the methodological parameters are the same. Both found the procedure to be effective. They did focus on function and noted that some patients, including a professional ballerina and a college athlete, were able to return to full activity.

Davis et al's retrospective study (114) of the outcomes of IDET patients in the Los Angeles area found that the study was less effective than suggested by others. Their study is clouded by the use of high volume, 2.5 mL, discography, suggesting that there may have been false positives on discography. They did include an undisclosed number of Workers' Compensation patients. A confounding factor is that of overuse of IDET; the absence of a Workers' Compensation fee schedule for IDET in the ambulatory setting during the period when patients were recruited created an incentive for over utilization. The outcome measure was the percentage of patients going on to fusion. Given that IDET is designed to prevent some, but not all, patients from going to fusion, the relevance of this measure is unclear.

Derby et al (86) compared IDET and restorative injection therapy, finding that both caused clinically significant decreases in pain. The IDET group had only a 1.27 decrease in VAS, a decrease which does not met the 2 point VAS decrease criterion. The study suggests either that IDET operates by enhancing the hypermetabolic repair response of chondrocytes or that a strong placebo response was present in the study. Because of the failure to meet the 2 point VAS decrease threshold, this study was rated negative.

Derby et al (87) published a second study in 2004 looking at the same personal data base (not the Oratec National Registry), assessing the efficacy of IDET in relieving leg pain. Derby et al's two studies (86,87), as they involve the same database, should be viewed as one when evaluating the effectiveness of IDET. The study is interesting in that it shows that non-dermatomal leg pain associated with disc disease can be relieved by IDET. Because it showed only a 1.56 point decrease in VAS, it is rated negative for IDET.

Kapural et al (95) in a 2004 prospective, controlled, but not randomized, study showed that IDET provided better results when patients had one or two level disease than when they had multilevel disease.

Mekhail and Kapural (94) published another prospective study in 2004 examining whether additional inclusion criteria improved outcomes. They found that while Workers' Compensation patients had less improvement in reported pain scores than patients covered under private insurance, there was no functional difference between the 2 groups. This finding raises the question as to whether the inclusion of Workers' Compensation patients in effectiveness studies biases the results.

Webster et al (93) performed an interesting review of a Workers' Compensation data base, finding that the inclusion criteria for IDET were not followed in 68% of the cases, suggesting poor patient selection. The study focused on the criteria that could be identified, including narcotic usage, whether the same provider did the discogram as did the procedure (provider self-referral), and return to work. The study did not have a vehicle for how many patients were able to avoid fusion; however, the study does highlight the role of Workers' Compensation status as being a confounding factor in evaluating IDET. The study is rated negative for IDET.

Bryce et al's study (84) of IDET in a rural population documented positive results from the procedure. Interestingly, Bryce et al's study showed a gender preference for females. Ergun et al (101) evaluated the effectiveness of IDET in a group of Turkish patients. They used 2.5 mL of dye for discography, raising the possibility of false-positive discography results. Nunley et al (98) looked at the effects of IDET in Workers' Compensation patients. This study, which did not have a control, showed good results in this population, in contradistinction to other studies. It also included patients with a BMI of up to 44; again, this is in contradistinction to other studies showing worse outcomes with increased weight. Regardless, Nunley et al did find good outcomes with their patient population. Maurer et al (97) looked at the efficacy of IDET in patients treated in an academic orthopedic practice. Interestingly, although the patients were treated between 1998 and 2002, the paper was not published until 2008. The study was industry supported. Maurer et al did find IDET effective.

Regarding radiofrequency annuloplasty, Finch et al (42), who developed the radiofrequency annuloplasty technique, published a pilot study showing improvement in VAS and Oswestry. Kapural et al (96) performed a nonrandomized prospective study comparing IDET and radiofrequency annuloplasty. In this study, the IDET group showed significant improvement whereas the radiofrequency annuloplasty group did not.

The only IDB studies are Kapural et al's 2 reports (99,100) on their pilot study. Although IDB appears to be an interesting technology, final assessment of this technology must be deferred until the IDB RCT is completed.

Complications of the procedure are uncommon and usually transient (120,121). Not all patients will get relief and some patients will go on to have further spinal procedures. However, being able to avoid surgery in approximately 50% of patients, at minimal risk and cost to the patients, is the significant advantage of TAPs. Careful patient selection is critical to obtain maximum benefit from the procedure. The current understanding of the inclusion criteria would be low back pain of greater than 6 months duration non-responsive to conservative treatment; back pain greater than leg pain; positive well-performed discography with a negative control; presence of an annular tear; disc disease limited to one or 2 levels; disc height at least 50% of normal; no evidence of compressive radiculopathy or abnormal lower extremity neurological exam other than diminished ankle reflexes; disc bulges $\leq$ 5 mm; no prior surgery at the treated level; no symptoms or signs of stenosis; no pending Workers' Compensation claims; and no significant depression or psychiatric issues on exam or history. Exclusion criteria would include tumor; systemic infection; localized infection at needle site; coagulopathy or unexplained bleeding; progressive neurological defects; history of substance abuse; manual labor; smoking; BMI > 30 or age > 55. By these criteria, those who are categorically related to Medicare based upon age would not be candidates for IDET for failure to meet the age criterion. Those who are eligible for Medicare benefits for other reasons, such as disability, would have to be evaluated by the other criteria to determine potential eligibility for the procedure.

The mode of action is unclear. A likely candidate is neuroablation of nociceptors in the annulus, although this hypothesis is not entirely satisfactory in that pain relief does not occur immediately after the procedure. Other hypotheses, including enhancement of chondrocytes activity, exist and have not been disproven.

TAP have been extensively criticized for a variety of reasons. The procedure seems to have been politicized. It is speculation as to why this has occurred. One argument seems to be the rapid, even indiscriminate acceptance of the procedure, with many payors not seeing benefit because of poor patient selection and many practitioners feeling that promotion of the product was self-serving. Another argument would be that the procedure does prevent some patients from going on to a fusion, thereby raising financial concerns in certain quarters.

The present systematic review is limited in that the authors do perform TAP in their clinical practices; as such, they can be expected to have a bias in favor of the procedure. This potential bias can be minimized only by acknowledging its existence and presenting a methodology-transparent review, so that all can compare the authors' evaluation of the literature with their own.

This systematic review highlights the strengths and weaknesses of an interesting body of literature dealing with TAP. It is unlikely that there will be any further RCTs dealing with either IDET or radiofrequency annuloplasty. The data base that we currently have will serve as the basis for any future discussion. However, further studies are in progress for IDB. This review will require an update.

Contemporary thought on clinical practice guidelines emphasize the need for consideration of patient preference (122,123). TAPs provide patients with chronic discogenic low back pain who also meet the other treatment criteria an option which is supported by evidence-based medicine and which might meet their personal values and preferences. Further, TAP does meet the criteria of clinical relevance as described by Staal et al (59).

Conclusion

TAPs provide clinical benefit in about one-half or more of carefully selected patients. Some patients who have a TAP go on to fusion. TAPs are not a substitute for fusion and a patient does not need to have been offered a fusion prior to proceeding with a TAP. TAPs offer carefully selected patients the potential to get relief of their otherwise refractory low back pain. A diligent review of the evidence supports the use of TAPs.

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