

PERSPECTIVE & COMMENTARY

Commentary

Diagnostic Value, Prognostic Value, and Safety of Provocation Discography

Introduction

The use of provocation discography (discography) as a diagnostic tool is a source of debate. Literature has both confirmed and called into question the diagnostic value, prognostic value, and safety of this procedure. The following commentary provides an updated, evidence-based discussion of these topics within the context of the modern standards for performance of discography and the interpretation of the resulting data.

Background

The intervertebral disc is a common source of chronic low back pain in adults, with a prevalence of approximately 40% [1,2]. Patient history and physical examination provide inadequate sensitivity and specificity to accurately diagnose discogenic pain [2,3]. Similarly, because disc degeneration and disruption are common findings in asymptomatic individuals [4,5], advanced imaging cannot definitively distinguish a painful disc from a nonpainful disc [6,7].

Provocation discography (discography) is a diagnostic test meant to confirm or exclude the intervertebral disc(s) as a source of back pain. This technique involves puncture of the disc with a fine-gauge needle under fluoroscopic guidance and pressurization of the disc via the injection of contrast media. The pressurization process seeks to provoke pain of a concordant nature to the patient's index pain. Postdiscography CT scanning may then be performed to examine the disc for annular fissure presence, configuration, epidural extravasation, and communication between fissure and herniation. Concordant pain production, in the presence of fissures reaching the outer annulus, in a framework of strict diagnostic criteria, can allow the diagnosis of painful internal disc disruption [6,8].

Discography should be performed for chronic low back pain (≥ 3 months) only if adequate attempts at conservative therapy have been unsuccessful and noninvasive diagnostic tests have failed to reveal the etiology of back pain. It is used to confirm or exclude a suspected disc as a source of pain in a patient with severe, persistent symptoms, but is only advised if the results of the test will influence future care. Most commonly, discography

is used to inform the decision to perform or avoid an invasive therapeutic procedure such as disc thermocoagulation, discectomy, or a spinal fusion. However, discography is also useful to diagnose discogenic pain, such that if confirmed, further diagnostic testing does not need to be pursued (i.e., decrease unnecessary health care costs).

Since its introduction in the early 1940s [9], the standards for technique and interpretation of this diagnostic test have changed in order to improve the accuracy and safety of this procedure. While clinicians and investigators over the years have used a variety of definitions of a “positive” vs “negative” study, as well as pressurization and volume limits, current clinical guidelines require the following for the unequivocal diagnosis of discogenic pain [10]:

1. Concordant pain response of $\geq 6/10$
2. Volume limit of 3 mL
3. Pressurization of the disc to no greater than 50 psi above the opening pressure
4. Adjacent disc(s) provide controls
 - a. For one control disc:
 - i. Painless response
OR
 - ii. Nonconcordant pain that occurs at a pressure greater than 15 psi over opening pressure
 - b. For two adjacent control discs:
 - i. Painless response at both levels
OR
 - ii. One painless disc AND one disc with nonconcordant pain that occurs at a pressure greater than 15 psi over opening pressure

More detailed operational criteria for lumbar discography are described in the Spine Intervention Society (SIS) practice guidelines [10].

Diagnostic Value

The functional nature of discography is appealing due to the inability of advanced imaging to discern a painful disc from a painless disc [11,12] as disc degeneration and disruption are common findings in asymptomatic individuals [4,5]. In a cross-sectional study of asymptomatic

individuals who received lumbosacral magnetic resonance imaging (MRI), one study found that 35% of individuals age 20 to 59 years, and nearly all of those age 60 to 80 years, had at least one level of disc degeneration or bulging [5]. Twenty percent of individuals younger than age 60 years had a herniated nucleus pulposus, whereas this finding was present in 36% of those older than 60 years of age [5]. In a similar cross-sectional analysis of asymptomatic individuals who received lumbosacral MRI, with a mean age of 42 years, 61% of subjects had disc abnormalities in one lumbar level or more [4]. A high-intensity zone (HIZ) was present in 14% of individuals, and 60% of those age 60 years or older had at least one lumbar disc protrusion [4].

Due to methodological variability in the technique and interpretation of discography in the early literature, a lack of consensus exists with regard to the false positive rate and, thus, the diagnostic value of this procedure [6,8,13–29]. Early techniques implemented a high-pressure discography technique, with various definitions of a “positive” vs a “negative” response to disc provocation with regard to pain intensity, concordance of pain, and the use of control levels. However, systematic review and meta-analysis have revealed a low false positive rate of 9.3% per patient and 6.0% per disc when applying the later-developed SIS/IASP (International Association for the Study of Pain) technique and criteria for appropriate performance and interpretation of this procedure [28].

Prognostic Value

While the diagnostic value of discography is now well established, there has been less investigation into the prognostic value of this procedure. One retrospective matched cohort study found no difference in the success rate of lumbar spinal fusion surgery when comparing patients who were selected using discography with clinical assessment and imaging alone [30]. Notably, these investigators used a high-pressure discography technique and did not use pain scores to interpret the results of disc provocation. Because this technique is not in accordance with the standards discussed above, application of these study findings is limited. Based on these data, inferences regarding the accuracy of discography findings and their resultant prognostic value cannot be made. Alternatively, a prospective cohort study of individuals with an MRI suggestive of discogenic pain showed an 89% success rate following lumbar spinal fusion when the level treated was directed by a positive response to discography, as opposed to a 52% success rate with a negative response to discography [31]. However, description of the discography technique and interpretation is inadequate to determine what standard was applied, again limiting interpretation of these results. One prospective study demonstrated that, if performed according to SIS/IASP guidelines, the use of discography is associated with a threefold greater rate of clinically significant improvement in pain and

function following spine surgery compared with clinical assessment and imaging alone [32].

The negative predictive value of discography has not been directly studied due to ethical issues of operating on a disc that had a negative response to discography. However, the presence of a negative response to discography or indeterminate results due to the inability to identify a negative control disc, on principle, represents an important finding that guides the patient away from a poorly indicated discectomy and fusion surgery.

Safety

Acute/Subacute

Acute and subacute adverse events associated with discography are rare, and very few have been reported in the past four decades. These include bacterial discitis, meningitis, spinal headache/cerebral spinal fluid leakage, retroperitoneal bleeding, intrathecal hemorrhage, arachnoiditis, allergic reaction, acute disc herniation, epidural abscess, pulmonary embolism from nucleus pulposus material, and seizure [33–39]. A systematic review estimated an incidence of discitis of less than 0.25% per patient and less than 0.14% per disc exposed to discography [40].

Since the implementation of routine fluoroscopic guidance during spinal interventions, as well as improved discography technique and safety measures during the modern use of this technique, the only adverse events reported in the past 15 years include discitis [41,42], acute disc herniation [43,44], development of an acute Schmorl’s node [45], and intravascular injection [46]. Discitis following cervical discography has not been reported in over 15 years [47]. Five cases of acute lumbar disc herniations were reported, with maximal pressures reaching 40 and 44 psi in two patients, 93 psi in one patient, and unreported pressures in two patients during discography [43]. One patient experienced self-limited foot drop, and three patients required spine surgery due to persistently exacerbated radicular pain and/or thecal sac compression. A case of Cauda Equina Syndrome requiring spinal decompression was reported following discography [44]. No procedure details were reported, so the maximal disc pressure reached is unknown. Similarly, in a case of acute Schmorl’s node formation associated with discography, procedure details, including disc pressure, were not reported [45].

Chronic

Concern has been raised in the scientific community regarding possible long-term complications of discography. This apprehension stems from two publications assessing a single cohort of patients. In 2009, prospective longitudinal cohort data (mean follow-up of 8.7 years) were published that sought to investigate the long-term impact of discography on intervertebral discs by comparing MRI indices of disc degeneration and

Table 1 Comparison of imaging and health care utilization outcomes at remote follow-up after lumbar discography with overlapping 95% confidence intervals of proportions

Imaging and health care utilization outcomes [25,26]	Discography	Control
Grade III/IV Pfirrmann changes	8% (4–13%)	3% (0–5%)
Grade V Pfirrmann changes	18% (12–24%)	9% (4–13%)
New high-intensity zone	6% (3–10%)	3% (0–5%)
Spine surgery	19% (9–30%)	6% (0–12%)
New advanced imaging	37% (24–49%)	21% (10–32%)

disruption in individuals who had undergone discography with matched controls [25]. Subsequently, in 2016, clinical and health care utilization outcomes were reported from the same matched cohort at 10-year follow-up [26]. From these two studies, the research group concluded that at long-term follow-up discography results in a higher rate of lumbar disc degeneration, lumbar disc herniation, spine surgery, repeat advanced imaging, significant low back pain episodes, work lost, and medical visits. However, review of the study methodology reveals alternative conclusions.

These studies excluded individuals who were appropriate discography candidates: individuals 1) with low back pain significant enough to have presented to a physician for treatment, 2) taking pain medications for low back symptoms, or 3) with activity restrictions due to low back pain. Thus, generalizability of this study with respect to a realistic discography population is limited. Further, questions arise regarding the appropriateness of the control cohort as the prevalence rates of Modic changes in this group were far lower (11%) than reported rates in the general population (36%) [4]. This discrepancy increases the likelihood of observing inappropriate intergroup differences. In addition, loss to follow-up was substantial. While loss to follow-up is nearly unavoidable in long-term clinical studies, the rates in this matched cohort reach a magnitude that impairs the ability to comment on true patient outcomes. The loss to follow-up was reported as 30% in the 2009 data set and 24% in the 2016 data set.

With regard to procedure technique, inappropriately high disc pressures were produced in a majority of subjects. The investigators used a threshold of 100 psi, exceeding the SIS/IASP-recommended limit. In 96% of subjects, at least one disc was subjected to a pressure of 80 psi or greater. This is notable as high disc pressure has been demonstrated to cause annular disruption in animal models [48]. Thus, excessive disc pressurization technique may have damaged the disc structure due to artificially high disc pressure that is inconsistent with the established standards.

With regard to the presented data, 95% confidence intervals overlap, indicating a lack of statistical significance

for several of the comparisons made (see Table 1). Because no subgroup stratification was performed, it is unknown if new disc herniations or Modic changes were overrepresented in individuals who had prior disc pressurization of 100 psi. In addition, it is unknown what other health care resources or imaging were utilized by the individual patient pools consisting of 1) subjects having documented cervical disc disease, 2) subjects having previous lumbar disc herniation with complete resolution of symptoms, and 3) subjects with no history of previous cervical or lumbar disc illness but who did have history of serious psychological distress consistent with somatization disorder. Notably, secondary analysis of these data reported in the 2009 study showed that subjects with normal psychometric test results did not report significant long-term back pain at a higher rate in the discography cohort than in the control cohort [17]. Lastly, if the majority of patients who proceeded to surgery or utilized further medical care had discography performed in discs with prior herniations, this carries different implications than if discography was performed on structurally “normal” discs.

Other cohort studies have not demonstrated a higher rate of disc degeneration associated with discography. In a small prospective study (N = 36), Pfirrmann scores in subjects with symptomatic low back pain who had undergone provocation discography with or without confirmation by intradiscal bupivacaine injection (“discoblock”) were compared with matched controls at long-term follow-up [49]. No significant difference in disc degeneration was observed on MRI between groups at three- to five-year follow-up. Notably, pressure manometry and control disc levels were not used and statistical power was limited. A cross-sectional cohort study found no evidence of degenerative disc changes 10 to 20 years after discography in individuals who had originally presented for care due to low back pain [50]. Only radiography was performed (not MRI), so this study was not sensitive to anything but the most drastic disc changes. The discography technique was not described.

Published animal data on disc degeneration following disc puncture also appear equivocal. While annular disc puncture has been used in animal models of disc degeneration [51–53], evidence suggests that annular

puncture with a small gauge needle does not cause disc degeneration [54,55]. The possibility of a small gauge needle not causing disc degeneration is striking in an animal model given that even a 27 gauge needle represents 52% of a rat's disc height [56], far greater relative to disc height in a human disc. Elliot et al. [56] reviewed 23 in vivo disc puncture studies in rat, rabbit, dog, and sheep models and found that significant disc changes were not produced when the needle gauge represented less than 40% of the disc height. Yet, it must be noted that disc changes were assessed at short-term interval follow-up.

Conclusions

When adhering to published SIS/IASP standards for appropriate provocation discography technique and data interpretation, this diagnostic procedure is associated with a low false positive rate. There is some evidence that including positive response to discography, defined by these standards, correlates with improved surgical outcomes when compared with selection by clinical and imaging assessment alone. The negative predictive value of discography has not been directly studied, but the presence of a negative response to discography, or indeterminate results due to the lack of ability to identify a negative control disc, guides the patient away from a poorly indicated discectomy and fusion surgery. There is no convincing evidence that provocation discography, performed in accordance with SIS/IASP standards, results in an increased incidence of clinically relevant future disc degeneration or disruption. However, failure to adhere to these standards is associated with an unacceptably high false positive rate [28]. Observation from one cohort of patients suggests a possible increase in the long-term risk of disc degeneration, disc disruption, and inferior clinical outcomes compared with those who do not undergo this procedure [25,26]; however, there is concern that these findings may relate to overpressurization of the disc during discography, and overlapping confidence intervals and study methodology limit the practical utility of these study findings. Notably, these findings have not been reproduced in other studies [49,50]. Additional investigation of possible long-term risks of discography in a realistic population, with well-matched controls and the use of appropriate procedure technique, is needed. The decision to perform discography and accept the possible long-term consequences must be viewed in the context of the potential for an inappropriate discectomy and fusion procedure.

Key Point

Discography, performed in accordance with current standards in appropriately selected patients, is a safe and useful diagnostic tool to inform treatment decisions.

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References

- 1 DePalma MJ, Ketchum JM, Saullo T. What is the source of chronic low back pain and does age play a role? *Pain Med* 2011;12:224–33.
- 2 Schwarzer AC, Aprill CN, Derby R, et al. The prevalence and clinical features of internal disc disruption in patients with chronic low back pain. *Spine* 1995; 20:1878–83.
- 3 Young S, Aprill C, Laslett M. Correlation of clinical examination characteristics with three sources of chronic low back pain. *Spine J* 2003;3:460–5.
- 4 Jensen MC, Brant-Zawadzki MN, Obuchowski N, et al. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med* 1994;331:69–73.
- 5 Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. *J Bone Joint Surg Am* 1990;72: 403–8.
- 6 Derby R, Kim BJ, Lee SH, et al. Comparison of discographic findings in asymptomatic subject discs and the negative discs of chronic LBP patients: Can discography distinguish asymptomatic discs among morphologically abnormal discs? *Spine J* 2005;5: 389–94.

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- 7 Kang CH, Kim YH, Lee SH, et al. Can magnetic resonance imaging accurately predict concordant pain provocation during provocative disc injection? *Skeletal Radiol* 2009;38:877–85.
- 8 Bogduk N, Aprill C, Derby R. Lumbar discogenic pain: State-of-the-art review. *Pain Med* 2013;14: 813–36.
- 9 Lindblom K. Diagnostic puncture of intervertebral disks in sciatica. *Acta Orthop Scand* 1948;17:213–39.
- 10 Bogduk N. Lumbar disc stimulation. In: Bogduk N, ed. *Practice Guidelines for Spinal Diagnostic and Treatment Procedures*, 2nd edition. San Francisco, CA: International Spine Intervention Society; 2013:420–33.
- 11 Horton WC, Daftari TK. Which disc as visualized by magnetic resonance imaging is actually a source of pain? A correlation between magnetic resonance imaging and discography. *Spine* 1992;17(suppl 6): S164–71.
- 12 Zucherman J, Derby R, Hsu K, et al. Normal magnetic resonance imaging with abnormal discography. *Spine* 1988;13:1355–9.
- 13 Massie WK, Stevens DB. A critical evaluation of discography. *J Bone Joint Surg Am* 1967;49A:1243–4.
- 14 Holt EP. The question of lumbar discography. *J Bone Joint Surg Am* 1968;50:720–6.
- 15 Walsh TR, Weinstein JN, Spratt KF, et al. Lumbar discography in normal subjects. A controlled prospective study. *J Bone Joint Surg Am* 1990;72: 1081–8.
- 16 Carragee EJ, Tanner CM, Yang B, Brito JL, Truong T. False-positive findings on lumbar discography. Reliability of subjective concordance assessment during provocative disc injection. *Spine* 1999;24: 2542–7.
- 17 Carragee EJ, Chen Y, Tanner CM, et al. Can discography cause long-term back symptoms in previously asymptomatic subjects? *Spine* 2000;25:1803–8.
- 18 Carragee EJ, Paragioudakis SJ, Khurana S. Volvo Award winner in clinical studies: Lumbar high-intensity zone and discography in subjects without low back problems. *Spine* 2000;25:2987–92.
- 19 Carragee EJ, Chen Y, Tanner CM, et al. Provocative discography in patients after limited lumbar discectomy: A controlled, randomized study of pain response in symptomatic and asymptomatic subjects. *Spine* 2000;25:3065–71.
- 20 Carragee EJ, Tanner CM, Khurana S, et al. Rates of false-positive lumbar discography in select patients without low back symptoms. *Spine* 2000;25: 1373–81.
- 21 Carragee EJ, Alamin TF, Miller JL, Grafe M. Provocative discography in volunteer subjects with mild persistent low back pain. *Spine J* 2002;2: 25–34.
- 22 Carragee EJ, Barcohana B, Alamin T, van den Haak E. Prospective controlled study of the development of lower back pain in previously asymptomatic subjects undergoing experimental discography. *Spine* 2004;29:1112–7.
- 23 Carragee EJ, Alamin TF, Miller JL, Carragee JM. Discographic, MRI and psychosocial determinants of low back pain disability and remission: A prospective study in subjects with benign persistent back pain. *Spine J* 2005;5:24–35.
- 24 Carragee EJ, Alamin TF, Carragee JL. Low-pressure positive discography in subjects asymptomatic of significant low back pain illness. *Spine* 2006;31: 505–9.
- 25 Carragee EJ, Don AS, Hurwitz EL, et al. 2009 ISSLS prize winner: Does discography cause accelerated progression of degeneration changes in the lumbar disc: A ten-year matched cohort study. *Spine* 2009;34:2338–45.
- 26 Cuellar JM, Stauff MP, Herzog RJ, et al. Does provocative discography cause clinically important injury to the lumbar intervertebral disc? A 10-year matched cohort study. *Spine J* 2016;16: 273–80.
- 27 Derby R, Lee SH, Kim BJ, et al. Pressure-controlled lumbar discography in volunteers without low back symptoms. *Pain Med* 2005;6:213–21.
- 28 Wolfer LR, Derby R, Lee JE, Lee SH. Systematic review of lumbar provocation discography in asymptomatic subjects with a metaanalysis of false-positive rates. *Pain Physician* 2008;11:513–38.
- 29 Shin D, Kim H, Jung J, Sin D, Lee J. Diagnostic relevance of pressure-controlled discography. *J Korean Med Sci* 2006;21:911–6.
- 30 Madan S, Gundanna M, Harley JM, Boeree NR, Sampson M. Does provocative discography screening of discogenic back pain improve surgical outcome? *J Spinal Disord Tech* 2002;15:245–51.
- 31 Colhoun E, McCall IW, Williams L, Cassar Pullicino VN. Provocation discography as a guide to planning

- operations on the spine. *J Bone Joint Surg Br* 1988; 70:267–71.
- 32 Cooper G, Kahn S, Lutz GE, et al. Predictive value of provocative lumbar disc stimulation. International Spine Intervention Society Annual Meeting Abstracts. *Pain Med* 2008;9:968.
- 33 Tallroth K, Soini J, Antti-Poika I, et al. Premedication and short term complications in iohexol discography. *Ann Chir Gynical* 1991;80:49–53.
- 34 McCulloch JA, Waddell G. Lateral lumbar discography. *Br J Rad* 1978;51:498–502.
- 35 Bernard TN. Lumbar discography and post-discography computerized tomography: Refining the diagnosis of low-back pain. *Spine* 1990;15:690–707.
- 36 Grubb SA, Lipscomb HJ, Guilford WB. The relative value of lumbar roentgenograms, metrizamidemyelography, and discography in the assessment of patients with chronic low-back syndrome. *Spine* 1987; 12:282–6.
- 37 Smith MD, Kim SS. A herniated cervical disc resulting from discography: An unusual complication. *J Spinal Disord* 1990;3:392–5.
- 38 Junila J, Niinimäki T, Tervonen O. Epidural abscess after lumbar discography: A case report. *Spine* 1997;22:2191–3.
- 39 Schreck RI, Manion WL, Kambin P, Sohn M. Nucleus pulposus pulmonary embolism. A case report. *Spine* 1995;20:2463–6.
- 40 Guyer RD, Ohnmeiss DD. NASS. Lumbar discography. *Spine J* 2003;3(suppl 3):11S–27S.
- 41 Montes GC, Nava Granados LF. Evocative lumbar discography. *Acta Ortopedica Mexicana* 2007;21: 85–9.
- 42 Werner BC, Hogan MV, Shen FH. *Candida lusitanae* discitis after discogram in an immunocompetent patient. *Spine J* 2011;11:e1–6.
- 43 Poynton AR, Hinman A, Lutz G, Farmer JC. Discography-induced acute lumbar disc herniation: A report of five cases. *J Spinal Disord Tech* 2005;18: 188–92.
- 44 Phillips H, Glazebrook JJ, Timothy J. Cauda equina compression post lumbar discography. *Acta Neurochir (Wien)* 2012;154:1033–6.
- 45 Pilet B, Salgado R, Van Havenbergh T, Parizel PM. Development of acute schmorl nodes after discography. *J Comput Assist Tomogr* 2009;33:597–600.
- 46 Smuck M, Yoon T, Colwell M. Intravascular injection of contrast during lumbar discography: A previously unreported complication. *Pain Med* 2008;9: 1030–4.
- 47 Kapoor SG, Huff J, Cohen SP. Systematic review of the incidence of discitis after cervical discography. *Spine J* 2010;10:739–45.
- 48 Veres SP, Robertson PA, Broom ND. ISSLS prize winner: Microstructure and mechanical disruption of the lumbar disc annulus: Part II: How the annulus fails under hydrostatic pressure. *Spine* 2008;33: 2711–20.
- 49 Ohtori S, Inoue G, Orita S, et al. No acceleration of intervertebral disc degeneration after a single injection of bupivacaine in young age group with follow-up of 5 years. *Asian Spine J* 2013;7:212–7.
- 50 Flanagan MN, Chung BU. Roentgenographic changes in 188 patients 10–20 years after discography and chemonucleolysis. *Spine* 1986;11:444–8.
- 51 Kim KS, Yoon ST, Li J, Park JS, Hutton WC. Disc degeneration in the rabbit: A biochemical and radiological comparison between four disc injury models. *Spine* 2005;30:33–7.
- 52 Rousseau MA, Ulrich JA, Bass EC, et al. Stab incision for inducing intervertebral disc degeneration in the rat. *Spine* 2007;32:17–24.
- 53 Sobajima S, Kempel JF, Kim JS, et al. A slowly progressive and reproducible animal model of intervertebral disc degeneration characterized by MRI, X-ray, and histology. *Spine* 2005;30:15–24.
- 54 Kahanovitz N, Arnoczky SP, Sissons HA, Steiner GC, Schwarcz P. The effect of discography on the canine intervertebral disc. *Spine* 1986;11:26–7.
- 55 An HS, Takegami K, Kamada H, et al. Intradiscal administration of osteogenic protein-1 increases intervertebral disc height and proteoglycan content in the nucleus pulposus in normal adolescent rabbits. *Spine* 2005;30:25–31.
- 56 Elliott DM, Yerramalli CS, Beckstein JC, et al. The effect of relative needle diameter in puncture and sham injection animal models of degeneration. *Spine* 2008;33:588–96.