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Prospective Study

Prospective Clinical Study on Natural History of Discogenic Low Back Pain at 4 Years of Follow-up

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Background: To accurately assess the effect of any therapy for treating discogenic low back pain, the natural history of such pain should be known beforehand. However, until now, no pathological characteristic could be used to predict the disease course of low back pain.

Objective: To better instruct the clinical treatment of discogenic low back pain, a prospective clinical study was performed to observe the natural history of the disease.

Study Design: A prospective clinical study during a 4-year follow-up period.

Setting: The study was performed at a spinal center in China.

Methods: A total of 279 patients with chronic low back pain were included from June 2006 through October 2007. Using discography, 156 patients (56%) were diagnosed to have discogenic back pain. A 101-point numerical rating scale (NRS) was used to assess the back pain symptoms and the Oswestry Disability Index (ODI) was used to assess lumbar function.

Results: Of the 156 patients, 131 (84%) completed the study at 4-year follow-up. At the end of follow-up, 17 patients (13.0%) had their low back pain symptoms alleviated and lumbar function improved; 10 patients (7.6%) were slightly improved; 16 patients (12.2%) had their symptoms aggravated; and 88 patients (67.2%) experienced the same pain and disability as before. Although the average NRS and ODI scores obtained during the 4-year follow-up study gradually decreased, statistical significances were found in such changes ($P < 0.05$,and $P < 0.05$, respectively); however, the improvement rates of both pain (7.6%) and disability (5.2%) were very low.

Limitations: The shortcoming of this study is its relatively small sample size.

Conclusion: The present study indicated that the natural history of discogenic low back pain was chronic but persistent, and that the pain and disability in most patients did not improve over time.

Key words: Discogenic low back pain, chronic low back pain, lumbar discography, painful disc, black disc, disc degeneration, internal disc disruption, natural history, prognosis.

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Chronic low back pain is a serious medical and social problem, and one of the most common causes responsible for disability. It is estimated that about 80% of all populations will experience low back pain at some period during their lifetime, and about 18% of the population is experiencing low back pain at any given moment (1,2).

Intervertebral disc degeneration is an age-related process that is asymptomatic in most individuals. For many, however, pathologic degeneration can be a major cause of pain and disability. Unfortunately, the etiologic factors that distinguish symptomatic from asymptomatic degeneration are obscure (2). Crock (3) first proposed the concept of internal disc disruption (IDD) as a condition marked by alteration in the internal structure and metabolic functions of the intervertebral disc. IDD is thought to be related to annular injury and subsequent repair of the annulus fibrosus (4). At present, the term "discogenic low back pain" is referred actually and specifically to the pain caused by IDD. Absent disc herniation and neurological deficits, it is unlikely to identify the cause of low back pain, specifically of discogenic origin, through magnetic resonance imaging (MRI), computed tomography, neurophysiological testing, and comprehensive physical examination (5). Utilizing controlled diagnostic blocks, the prevalence of pain due to IDD was reported to be 39% in patients suffering chronic low back pain (6), whereas primary discogenic pain was reported in 26% when no other cause was suspected (7). Discogenic low back pain has been classified as a separate clinical entity to be differentiated from other types of disc degenerative diseases, such as lumbar disc herniation, lumbar stenosis, and lumbar segment instability (8).

To accurately assess the effect of any therapy for treating discogenic low back pain, the natural history of such pain should be known beforehand. However, until now, no pathological characteristic could be used to predict the disease course of low back pain. Although a number of studies featuring the natural history of chronic nonspecific low back pain have been published, only Rhyne et al (9) and Peng et al (10) were concerned with the natural history of patients with discogenic low back pain. However, these 2 studies had flaws in their own way. In the present study, in order to better instruct the clinical therapeutics, a prospective clinical study was carried out to investigate the natural history of patients with discogenic low back pain.

Methods

Selection of Patients

A total of 279 consecutive patients were included in this study for the period from June 2006 through October 2007. The study was undertaken in the first author's hospital, which specializes in spinal surgery. The patients had low back pain as the main symptom for at least 6 months without radiculopathy but with evidence of lumbar disc degeneration on MRI. The preliminary diagnosis of discogenic low back pain was confirmed by lumbar discography. Lumbar lateral radiographs showed that the intervertebral spaces were normal or slightly narrowed. MRI showed disc degeneration in L4/5 or L5/S1, or both. Disc degeneration had to be restricted to the 2 lower levels. In addition, the extent of disc degeneration was restricted to grade 3 or 4 according to the Pfirrman et al (11) grading system. The diagnostic criteria for IDD established by the International Association for the Study of Pain in its taxonomy includes the emergence of a concordant pain response during discography, internal disc disruption shown by computed tomography after discography, and at least one adjacent disc without concordant pain (12). The patients here were chosen based on the diagnostic criteria for IDD.

Diseases, such as lumbar disc herniation, lumbar spinal stenosis, inflammatory diseases, and tumors, were ruled out as the possible pain generator by diagnoses formed from patient histories, and clinical, physical, and imaging examinations. Recipients of workers' compensation were excluded. The patients were aged 20-65 and did not have a history of lumbar surgery. Furthermore, as determined by a psychologist, these patients did not have psychological obstacles, depression, or psychiatric histories. Informed consent was obtained from the enrolled patients before discography, and the protocol was approved by the ethics committee of our hospital.

Discography

All discography was performed under fluoroscopy, using a standard posterolateral approach and a double-needle technique (6). If MRI showed L4/5 and L5/S1 disc degeneration, discographies were performed on 3 disc levels: L3/4, L4/5, and L5/S1. If MRI showed L4/5 or L5/S1 disc degeneration, discographies were performed commonly on 2 disc levels: L3/4 and L4/5 (for L4/5) or L4/5 and L5/S1 (for L5/S1). At least 2 disc levels were performed on each patient. Painless discs were used as con-

trols. Provocation discography was adopted as the test for discogenic pain according to the International Association for the Study of Pain criteria (12). Provocation of that disc should reproduce the patient's accustomed pain, provided that provocation of an adjacent disc did not reproduce the pain. The discographic needles were inserted on the contralateral side of the painful area. Once the needle was accurately inserted into the center of the disc, nonionic contrast medium iotrolan was slowly injected into the nucleus under low pressure. A positive discography was defined if the patient experienced exact reproduction of his or her usual pain response pattern, and the posterior annular disruption was shown to extend into the outer annulus or beyond the confines of the outer annulus by the contrast medium. In addition, at least one control disc adjacent to the painful disc must have been negative.

Outcome Measures

A 101-point numerical rating scale (NRS) pain score was taken before discography and 6, 12, 24, and 48 months after discography to analyze the low back pain symptoms for each patients. Oswestry Disability Index (ODI) scores (Version 1.0, 0-100) were taken at the time points as the NRS scores utilizing the Oswestry Disability Questionnaire (13,14). The NRS and ODI scores were assessed according to usual pain symptoms and functional disability in the last month at any follow-up point. Subjective improvement or aggravation of low back pain symptoms and lumbar function were evaluated as: obvious improvement in symptoms of low back pain and restriction of physical activities; slight improvement; no improvement; and pain aggravation and more severe restriction of activities.

Statistical Analysis

The SAS 9.1 statistical package (SAS Institute, Inc., Cary, NC) was used to analyze the statistical significances of NRS and ODI score variations. Variance analysis of repeated measurement data (mixed linear mode) was used to analyze NRS and ODI scores collected at different time points before and after discography, and to analyze the differences of NRS and ODI scores at baseline and different follow-up time points between patients with pain at a single segment and at double segments. The significance level was 0.05.

Results

Of the 279 patients, 156 (56%) were diagnosed to have discogenic back pain using discography. In total, 131 completed the study at 4-year follow-up (84%). Of the 25 patients that were lost to follow-up at 4-years, 23 had changed address or could not be contacted, and 2 were discovered to have other, new diseases. Of the 156 patients, 75 were men and 81 were women; their ages ranged from 20 to 65 years, with an average age of 41 years. At the end of the follow-up survey, the average age of these patients was 45 years. In total, 112 patients had single intervertebral disc pain, of which 51 had pain at L4/5, and 61 had pain at L5/S1; 44 had pain in 2 intervertebral discs: L4/5 and L5/S1. Table 1 shows the baseline characteristics of the study patients.

All patients received conservative treatments for 2 months after discography including physical therapy, drug therapy, and exercise. From then on, the patients only could use nonsteroidal anti-inflammatory drugs and/or opioids if low back pain occurred. According to subjective improvement or aggravation of low back pain symptoms and lumbar function, among those 131 patients who completed 4-year follow-up, 17 of them (13.0%) had their low back pain symptoms alleviated and lumbar function improved; 10 (7.6%) were slightly improved; 16 (12.2%) were aggravated; and 88 (67.2%) experienced the same pain and disability as before. The NRS scores of 17 patients with obvious improvement were reduced with a mean of 38.59 points, and the

Table 1. *Baseline characteristics of the patients* (n = 156).*

Characteristics	
Age (y)	41 ± 11
Gender	
Male (%)	75 (48.1)
Female (%)	81 (51.9)
Married (%)	126 (80.1)
Smoker (%)	65 (41.7)
Employed (%)	120 (76.9)
Duration of Back Pain (y)	4.1 ± 3.3
Painful Disc Level	
L4/5 (%)	51 (31.7)
L5/S1 (%)	61 (39.1)
L4/5, L5/S1 (%)	44 (28.2)
Numerical Rating Scale (NRS)†	57.33 ± 7.51
Oswestry Disability Index (ODI)‡	46.43 ± 8.29

*Plus-minus values are means ± SD.
†NRS scores range from 0 to 100, with lower scores indicating less severe symptoms.
‡ODI scores range from 0 to 100, with lower scores indicating less severe functional disability.

ODI scores were reduced with a mean of 30.29 points; the NRS scores of 10 patients with minor improvement were reduced with a mean of 13.40 points, and the ODI scores were reduced with a mean of 7.90 points. On the contrary, the NRS scores of the 16 aggravated cases were increased with a mean of 17.94 points, and the ODI scores were increased with a mean of 13.75 points (Table 2).

According to NRS and ODI scores taken at different time points, these 2 scores gradually decreased over time (Table 3). At the final follow-up at 48 months, the mean NRS score was 52.97 compared with the baseline score of 57.33, with a mean reduction of 4.36 (t = 3.17, P = 0.002), an improvement rate of 7.6%. Although a statistical significance was found, the back pain improvement rate was very low. The mean ODI score at 48 months was 44.03 compared with the baseline score of 46.43, with a mean reduction of 2.40 (t = 3.06, P = 0.003), an improvement rate of 5.2%. Again, the difference was statistically significant, even though the improvement rate was very low.

In addition, NRS and ODI scores before and after discography were compared between patients with pain at a single segment and at 2 segments. The patients who had pain at a single segment were found not to have better outcomes compared with those who had pain at 2 segments (Table 4).

Discussion

Basic and clinical studies have overwhelmingly illustrated the nerve supply of the disc and pathomorphologic correlates (4,6,7,15-22). Based on controlled evaluations, the lumbar intervertebral discs have been shown to be sources of chronic low back pain without disc herniation in 26% to 39% (6,7). Because of the variety of anatomic and pathophysiologic causes of chronic low back pain, it is a difficult diagnosis for clinicians to make. Clinicians primarily use advanced imaging techniques, such as MRI, to diagnosis low back pain. The better understanding of each finding on MRI appears likely to be helpful in selecting patients for discography and to lessen the risks for the patients who have persistent low back pain without neurologic deterioration. The high-intensity zone and severe disc dehydration on MRI are relatively reliable predictors of concordant pain. The combination of severe loss of disc height with severe nuclear signal loss correlates strongly with a painful disc. The presence of the high-intensity zone

Table 2. *Patient subjective improvement or aggravation at 4-year follow-up (n = 131).**

	Obvious Improvement (n = 17)		Slight Improvement (n = 10)		Unchanged (n = 88)		Aggravated (n = 16)	
Time (mo)	Baseline	48	Baseline	48	Baseline	48	Baseline	48
NRS†	59.47 ± 8.65	20.88 ± 10.48	62.00 ± 6.65	48.60 ± 6.13	59.14 ± 6.65	57.55 ± 7.96	46.69 ± 3.38	64.63 ± 5.04
ODI‡	44.00 ± 13.68	13.71 ± 7.44	49.40 ± 6.48	41.50 ± 7.17	48.09 ± 6.64	48.03 ± 8.44	42.06 ± 12.03	55.81 ± 9.32

*Plus-minus values are means ± SD.
†NRS, numerical rating scale, scores range from 0 to 100.
‡ODI, Oswestry Disability Index, scores range from 0 to 100.

Table 3. *Scores of NRS and ODI at each time point.*

Time (mo)	Baseline (n = 156)	6 (n = 156)	12 (n = 153)	24 (n = 141)	48 (n = 131)	F	P
NRS†	57.33 ± 7.51	56.01 ± 10.22	54.76 ± 11.60	53.66 ± 13.01	52.97 ± 15.12	6.30	0.0001
ODI‡	46.43 ± 8.29	45.97 ± 8.73	44.56 ± 9.96	44.26 ± 11.96	44.03 ± 14.72	3.48	0.0094

*Plus-minus values are means ± SD.
†NRS, numerical rating scale, scores range from 0 to 100.
‡ODI, Oswestry Disability Index, scores range from 0 to 100.
Variance analysis of repeated measurement data were used to analyze NRS and ODI scores collected at different time points respectively. Comparison results of NRS scores between different follow-up time points and at baseline were as follows: at 6 months, t = 2.03, P = 0.04; at 12 months, t = 3.17, P = 0.002; at 24 months, t = 4.32, P < 0.001; at 48 months, t = 4.41, P < 0.001. Comparison results of ODI scores between different follow-up time points and at baseline were as follows: at 6 months, t = 0.68, P = 0.50; at 12 months, t = 2.85, P = 0.005; at 24 months, t = 3.28, P = 0.001; at 48 months, t = 3.06, P = 0.003.

Table 4. *Comparison of scores between patients with pain at a single segment and at double segments*

	Single Segment		Two Segments		t	*P*
	n	means ± SD	n	means ± SD		
NRS†						
Baseline	112	57.43 ± 7.76	44	57.09 ± 6.92	0.25	0.80
6 months	112	55.92 ± 10.81	44	56.27 ± 8.66	-0.19	0.85
12 months	109	54.91 ± 12.15	44	54.41 ± 10.25	0.12	0.91
24 months	101	53.82 ± 13.54	40	53.25 ± 11.74	0.41	0.68
48 months	96	53.84 ± 15.21	35	50.57 ± 14.80	1.39	0.17
ODI‡						
Baseline	112	46.25 ± 8.92	44	46.89 ± 6.48	-0.43	0.67
6 months	112	45.78 ± 9.40	44	46.48 ± 6.79	-0.45	0.65
12 months	109	44.48 ± 10.31	44	44.75 ± 9.13	-0.25	0.80
24 months	101	44.48 ± 12.25	40	43.73 ± 11.33	0.60	0.55
48 months	96	44.56 ± 14.82	35	42.57 ± 14.56	0.91	0.36

*Plus-minus values are means ± SD.
†NRS, numerical rating scale, scores range from 0 to 100.
‡ODI, Oswestry Disability Index, scores range from 0 to 100.
NRS and ODI scores at baseline and different follow-up time points between patients with pain at a single segment and at double segments were compared with variance analysis of repeated measurement data.

plus disc protrusion are strong predictors for a painful disc (18,23).

Lumbar provocation discography is a procedure that is used to characterize the pathoanatomy and architecture of the disc and to determine if the disc is a source of chronic low back pain. In our present study, the patients presented persistent low back pain with disc degeneration on MRI, but we still could not make a precise diagnosis. So, lumbar discography become our only option to determine whether the disc degeneration was responsible for the low back pain. Recently, the American Pain Society developed and published multiple guidelines (24,25) for managing low back pain. Those guidelines did not recommend discography as a diagnostic test because of poor evidence for its sensitivity, specificity, and predictive value. However, subsequently, these guidelines were severely criticized (15). There were deficiencies and inappropriate evaluation in almost all areas; inappropriate studies were included and appropriate studies were excluded. The basic deficiency of these guidelines by Chou and Huffman (24) was their failure to recognize that discography must not be performed in asymptomatic volunteers or patients with mild low back pain. They also utilized outdated guidelines from the Agency for Health Care Policy and Research and European Cooperation in Science and Technology guidelines (15). In the interim, questioning the validity of discography warrants questioning the role of the disc as a discrete pain generator, or more specifically, challenges the concept of symptomatic internal disc disruption. If one considers discography to be a useless test, then one may have to abandon the concept of the disc as a discrete pain generator and abandon the pursuit of intradiscal therapies, whether surgical or nonsurgical (26). Recent systematic reviews have concluded that there is strong evidence that lumbar discography can identify the subset of patients with chronic discogenic pain (26-28).

The present study is not intended to support or refute the validity or indications for discography. Although some controversies may still exist (29-31), at our current level of understanding lumbar discography is thought of as the best tool to evaluate disc-related low back pain (26-28). Our current study may have a limitation in the method of discography technique. More recent descriptions of the procedure using a pressure-controlled device with more control discs are thought to reduce the false positive rate. Derby et al (22) performed a prospective study to determine the prevalence of positive responses to lumbar discography in 13 asymptomatic volunteers. Although 44% of injected discs elicited pain, most required high pressures to reach the nociceptive threshold. And even then, they were only mildly painful. They concluded that if one takes into consideration pain intensity and the amount of pressure needed to provoke symptoms, the false-

positive rate is less than 10%. The false-positives may be very low in our current study because we completed discography under low pressure. In addition, the patients with normal psychometric profiles, without other chronic pain syndromes, and without prior lumbar spine surgery, were selected.

Sample sizes in most studies for discogenic low back pain have been small. In terms of patient selection, the methodology was poor for most papers and all papers could be criticized for selection bias. Nonetheless, ethical barriers prevent performing invasive tests on large patient samples that may or may not have a disease (26). To the best of our knowledge, the patient sample in our current study is one of the largest ones published in the literature to date for using discography to investigate discogenic low back pain.

Unlike the 68% follow-up improvement rate reported by Rhyne et al (9), we found that the back pain symptoms in 27 out of 131 patients who finished a 4-year follow-up study were improved, accounting for a 20.6% improvement rate. An analysis of the 17 patients with obvious improvement was undertaken to identify the relationships between their and other group variables. The NRS and ODI scores at baseline in the 17 patients with obvious improvement were identical to the patients that slightly improved and were the same. Furthermore, we did not find any differences in terms of age, gender, duration of symptoms, disc levels (L4/5 disc or L5/S1 disc; single or double segments) between the patients with obvious improvement and the patients that slightly improved and were the same. Further studies need to be performed so as to clarify its exact cause. In Rhyne et al's study (9), all of the patients refused to have lumbar spine fusion surgery. Compared with those who received such surgery, they might have had milder symptoms, predisposing them to improve. Although the average NRS and ODI scores obtained during the 4-year follow-up study gradually decreased with statistical significances, the improvement rates for both pain and disability were very low. This indicated that most patients with IDD would not have relieved back pain or improved function over time. In addition, this study suggests no correlation between the clinical course and the particular discs involved.

In the present study, we used a prospective method that ought to be more convincing than the retrospective method used by Rhyne et al (9). Although Peng et al's study (10) was prospective, the patients they used were control cases randomly chosen for their prospective study on the therapeutic effects of intradiscal methylene blue injection for treating discogenic low back pain (32). Because the patients did not know whether they were in the therapeutic group or in the control group, they would be psychologically different from the patients who had common conservative treatment, which would, consequently, have an effect on the follow-up result. In addition, a relatively small sample size (32 patients) also makes the result less convincing. Some may argue that natural history may not be true in our current study because all patients were treated with a variety of modalities including physical therapy, drug therapy, and exercise. Certainly, the best way to study the natural history of a disease is to observe the natural progression of the disease without any intervention. However, this is hard to achieve in clinical practice, especially for patients with disabling low back pain. In our 4-year follow-up study, of the 131 patients in our group, 89 had occasionally or frequently taken anti-inflammatory painkiller drugs, and 21 with uncontrollable low back pain had taken additional opioid painkillers. However, we must keep in mind that the evidence for pharmacologic treatment for chronic low back pain is not compelling. In randomized trials, the differences in pain after a patient has taken nonsteroidal anti-inflammatory agents compared with placebo have generally been in the minimally detectable range (33). A meta-analysis revealed that opioids seem to have a small effect in improving function and relieving pain for patients with chronic low back pain (34). Long-term treatment with opioids is generally discouraged, given the associated risks of tolerance and side effects.

Here we found that the natural history of chronic discogenic low back pain was similar to that of nonspecific chronic low back pain (35-40). Deyo and Weinstein (41) considered that chronic low back pain will deteriorate periodically. It is more like asthma, rather than any acute diseases that can be cured. Despite the inherent challenge in elucidating the specific etiology of chronic low back pain, diagnostic procedures can reveal its source in 90% of patients. DePalma et al (42) published a very good clinical study report. They found that pain prevalence due to zygapophysial joints was 31%, for sacroiliac joints it was 18%, and for lumbar discs it was 42% (42,43). They confirmed the disc as the most common etiology for chronic low back pain in adults. The younger the patient, the more likely low back pain is discogenic in origin. Facetogenic or sacroiliac joint pain is more likely in older patients (42). This is an interesting new finding. Previous studies have indicated that chronic low back pain originating from zygapophysial

joints and sacroiliac joints were persistent (44). Our study suggests that the natural histories of 3 types of common chronic low back pain are similar. According to the results of our study, from the viewpoint of conservative treatment, the process of elucidating chronic low back pain etiology may not yield significant benefit. On the other hand, discography may prevent patients from undergoing unnecessary fusion surgery (45).

A wide range of factors have been linked with the poor prognosis of low back pain, including pain intensity or high levels of disability, recurrent or long-lasting back pain, lower education, and psychological factors (46-50). Patients with persistent back pain may have emotional and psychological problems which can influence future outcomes such as response to therapy and the development of disability due to chronic back pain. In our current study, in order to better observe the natural history of discogenic low back pain related to its pathology, we excluded patients with psychological problems.

In the present study, we found that the natural history of discogenic low back pain was continuous and chronic. The results indicate that most patients are expected to experience low back pain after a longer time interval, and their pain severity is expected to remain nearly the same. The exact cause of chronic back pain can be related to persistent inflammation in a painful disc (4,51,52).

The elucidation of the natural history of discogenic low back pain has important clinical significances for decision-making concerning treatments. When non-surgical treatments fail, fusion surgery or artificial disc replacement may have to be considered on highly selected patients, with the aim of reducing pain and decreasing disability (53-56).

Conclusion

In our current study, among all 279 patients with both symptoms of chronic low back pain and disc degeneration on MRI, only 156 (56%) were discogenic low back pain. So, when contemplating any invasive treatment for discogenic back pain, painful disc levels first must be determined.

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