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Predictors of a Favorable Response to Transforaminal Injection of Steroids in Patients with Lumbar Radicular Pain due to Disc Herniation

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Abstract

Background. Transforaminal injection of steroids (TFIS) is effective for some patients with lumbar radicular pain caused by disc herniation. Factors associated with better outcomes are unknown.

Objective. To identify clinical and radiological features predictive of a favorable response to TFIS.

Methods. Seventy-one patients with lumbar radicular pain caused by disc herniation were treated with TFIS as part of a previously reported, randomized, clinical trial. The clinical features analyzed were the presence of neurologic symptom, neurologic signs, and the duration of sciatica. Radiological features evaluated using magnetic resonance imaging (MRI) were the segmental level of the pathology, the location and morphological features of the disc herniation, the cross-sectional area of the disc herniation and its ratio to the cross-sectional area of the spinal canal, and the grade of nerve root compression.

Results. None of the clinical features was associated with successful outcome from treatment. The only radiological feature associated with successful outcome was the grade of nerve root compression. Of patients with low-grade root compression, 75% responded favorably to TFIS. Only 26% of patients with high-grade nerve root compression responded.

Discussion. These results indicate that TFIS is more often successful in patients without significant compression of the nerve root and, therefore, in whom an inflammatory basis for radicular pain is most likely. In such patients, a success rate of 75% renders TFIS an attractive alternative to surgery. In patients with significant compression of the nerve root, the likelihood of benefiting from TFIS is low. The success rate may be no more than that of a placebo effect, and surgery may be a more appropriate consideration.

Key Words. Disc Herniation; Lumbar; Radiculopathy; Transforaminal; Injection; Predictor; MRI

Introduction

Transforaminal injections of steroids have been promoted as an alternative to surgical treatment for lumbar radicular pain caused by disc herniation. The evidence for their efficacy, however, is mixed. Whereas some studies found no evidence of efficacy [1–4], others found transforaminal injection of steroids to be more effective than interlaminar epidural injection of steroids [5], and more effective than sham therapy with intramuscular injections of normal saline [6]. Transforaminal injection of steroids, as well, has been shown to spare patients from the need for surgery [7,8], with outcomes remaining stable for 5 years [9].

A recent, randomized controlled trial found that transforaminal injection of steroids was more often effective than transforaminal injection of either local anesthetic or normal saline, and was more often effective than intramuscular injection of either steroids or normal saline for providing relief of pain at 1 month after treatment [10]. However, not all patients benefited. Only 54% of patients responded to transforaminal injection of steroids. This implies that, perhaps, only a certain subgroup of patients responds to this treatment; but the criteria that define that subgroup were not evident in the original study [10].

The present study was undertaken to explore possible determinants of response to transforaminal injection of steroids. The study was undertaken with no particular conjecture in mind. A variety of standard clinical and radiological features were explored in case one or more emerged as a predictor of response.

Methods

Data for the present study were drawn from those available from patients who participated in a controlled trial of transforaminal injection of steroids, which has been reported previously [10]. In that study, patients received transforaminal injection of steroids either as their allocated treatment or as a rescue treatment. A total of 79 patients were so treated. Adequate clinical and imaging data were available for 71 patients. Data were missing on seven patients either because imaging data were not accessible or because patients who had rescue treatment were lost to follow-up. One patient was excluded because the injection was technically inadequate for lack of delivery of contrast medium and steroids along the course of the roots of the target nerve.

All patients had been assessed by their treating neurosurgeon as eligible for surgery. Six patients were inpatients of the hospital, with intractable pain, not responding to analgesia, rendering safe discharge impossible. The other 65 patients had radicular pain that had persisted for over 6 weeks, and had not been relieved by analgesics.

The severity of pain was evaluated using a visual analogue scale (VAS), before and at 1 month after the injection. Favorable response was defined as a reduction of at least 50% in VAS lasting beyond the first month after treatment. The clinical parameters evaluated were the duration of symptoms, presence of neurologic symptoms, and abnormal neurologic findings on examination (sensory deficit, abnormality of reflex, motor deficit). Magnetic resonance imaging (MRI) films were reviewed independently by a specialist neurosurgeon and a pain specialist, accustomed to performing transforaminal injections for radicular pain, each blinded to the patient's response to treatment. The radiologic features assessed were the level and side of the nerve root affected, the location of the herniation, and the morphology of the disc displacement based on the classification system of Fardon and Milette [11] (Table 1). The presence of any degenerative changes, including endplate osteophytes, facet hypertrophy, ligamentum flavum hypertrophy, and spondylolisthesis, contributing to the nerve root compression, at the segment treated, was recorded.

The displaced disc material was measured for maximal thickness of herniation posterior to the normal posterior boundary of the disc, and the ratio of the cross-sectional area of the herniated disc to that of the canal area, using the axial slice showing the largest disc herniation. These areas were measured using the area measurement tool of the institution's radiology picture archiving and communication system.

From axial views, the location of the herniation was classified as central, paracentral, or foraminal, according to the direction of what appeared to be the average radial axis of the herniation. For paracentral disc herniation, the severity of nerve root compression was assessed using the modification of a system described by Pfirmann et al. [12], and validated by Lurie et al. [13]. In this system, Grade I applies when the disc simply contacts the nerve root, Grade II when the nerve root is displaced but with preservation of periradicular cerebrospinal fluid (CSF) or fat, Grade III when the periradicular CSF or fat is obliterated, and Grade IV when the nerve root is morphologically distorted (Figures 1 and 2).

MRI T2-weighted imaging was used to visualize CSF, which normally surrounds the nerve roots within the thecal sac and can sometimes be visualized where the nerve roots pass from the thecal sac to the inner zone of the intervertebral foramen. T1-weighted imaging was used to assess periradicular fat that is visualized more consistently around the root in the lateral recess and the foramen.

A system introduced by Lee et al. [14] was used to grade foraminal root compression caused by a far lateral disc herniation. Grade I was applied when perineural fat was obliterated in two opposing directions (vertical or transverse), Grade II was applied when perineural fat was obliterated in four directions without morphologic distortion of the nerve root, and Grade III was applied when distortion

Table 1 Classification of disc herniations according to the system introduced by Fardon and Milette [11]

Descriptor	Definition
Bulge	Generalized displacement of disc material (>50% or >180° of disc circumference) beyond the limits of the intervertebral disc space.
Herniation	Localized displacement of disc material (<50% or <180°) beyond the limits of the intervertebral disc space.
Broad-based	25–50% of the disc circumference.
Focal	<25% of the disc circumference.
Protrusion	The fragment does not have a neck that is narrower than the fragment in any dimension.
Extrusion	The fragment has a neck that is narrower than the fragment in at least one dimension.
Sequestration	A type of disc extrusion that has lost continuity with the disc origin.
Migration	The extruded disc fragment has migrated away from the origin. This fragment may or may not be in continuity with the origin.

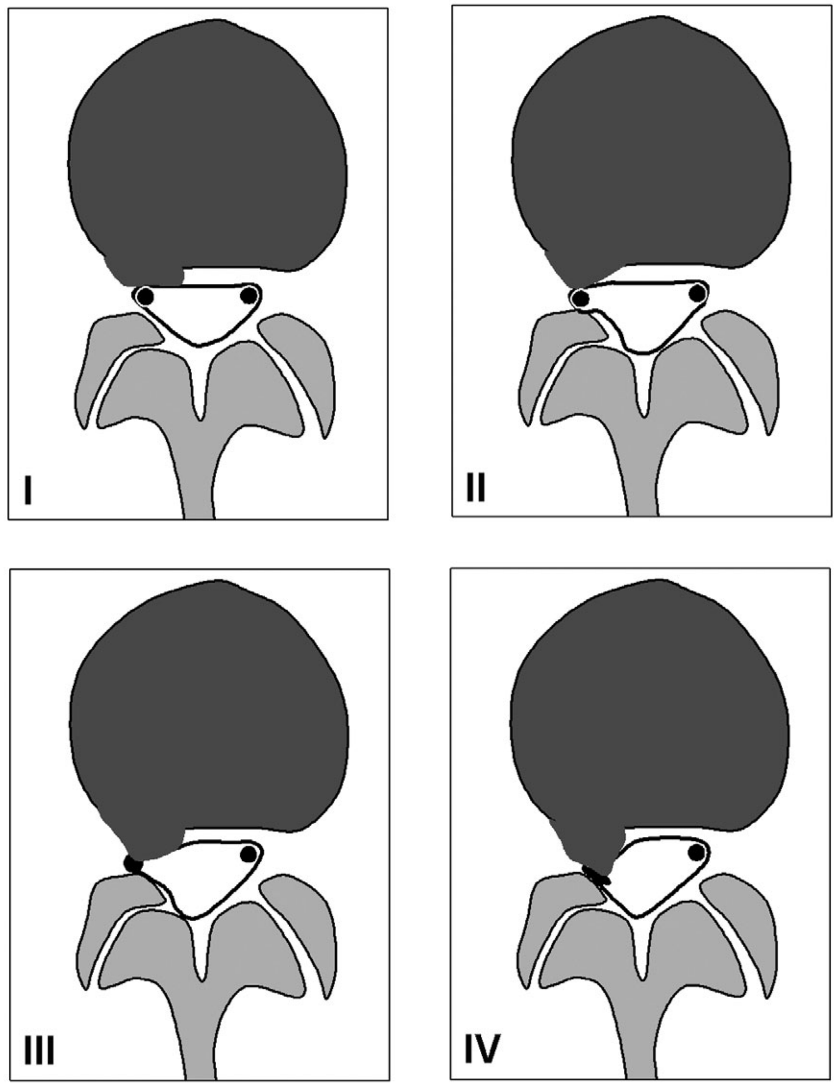

Figure 1 Sketches of axial scans of the lumbar spine showing the grading system used for compression of nerve roots by paracentral disc herniations. Grade I: the disc simply contacts the nerve root. Grade II: the nerve root is displaced but periradicular CSF or fat is preserved. Grade III: periradicular CSF or fat is obliterated. Grade IV: the nerve root is morphologically distorted. CSF = cerebrospinal fluid.

or other morphologic change in the nerve root was evident (Figures 3 and 4).

For degenerative changes at the segment affected by herniation, an ad hoc system of grading was used. Features not related to the nerve roots, such as disc dehydration and subchondral sclerosis, were disregarded. Only those changes that might impact the spinal nerve or its roots were considered. Images were scored as 0 for no changes, or 1 each for the presence of disc narrowing, osteophytes from the disc, facet enlargement, or bulging ligamentum flavum, for a total score of up to 4. Images were classified as having degenerative changes if their total score was 2 or more.

For continuous data on disc thickness and area, a two-sample *t*-test was used to compare values in those patients who did and did not respond to treatment. For categorical data, associations between response to treatment and individual clinical features or imaging features were assessed using contingency tables and a chi-squared test. When positive associations were encountered, the strength of association was assessed by calculating the sensitivity, specificity, and positive likelihood ratio of the feature as a predictor of favorable outcome.

For the analysis of nerve root compression, in order to compensate for small numbers in certain categories, categories were collapsed into either low-grade compression or high-grade compression. In the case of paracentral disc herniations, patients with Grades I or II compressions were classified as having low-grade compression, and all others were classified as high grade. Foraminal herniations with Grade I compression were classified as low grade, and all others were classified as high grade.

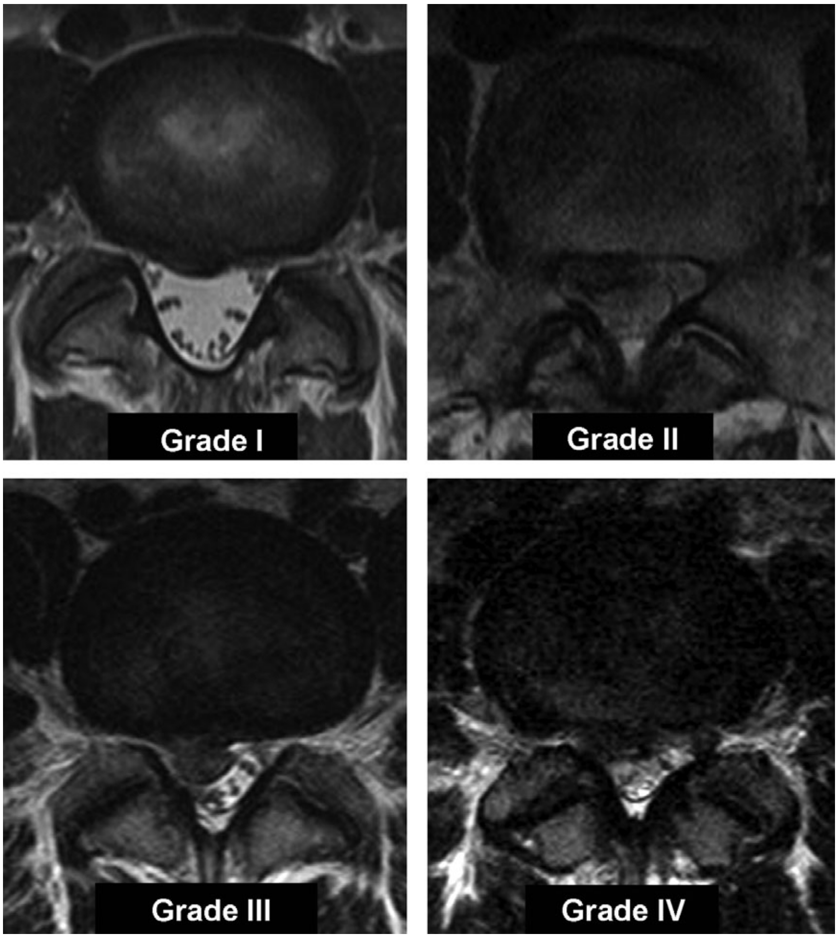

Figure 2 Axial magnetic resonance images showing examples of different grades of nerve root compression, as seen and as interpreted in the present study.

For imaging features found to be associated with outcome, observer agreement was checked by having the second author read all the available films while blinded as to outcome. A kappa score for agreement was calculated according to the method of Cohen [15].

Results

The sample consisted of 38 male and 33 female patients, with mean age of 48.2 years, of whom 38 (53.5%) had a favorable response to transforaminal injection of steroids; the remainder obtained no relief of pain from the treatment. Across both groups, clinical features and imaging variables were sufficiently well distributed to allow for contingency analysis.

There was no association between response to treatment and any of the clinical variables examined (Tables 2 and 3). There was no association with the location of the disc herniation (Table 4) or its morphology (Table 5) nor was there any association with the dimensions or relative size of the herniation (Table 6). Disc area tended to be smaller in those patients who responded ($P = 0.057$), but that tendency dissipated when corrected for canal size. Response to treatment was not associated with the presence of degenerative changes at the affected segment (Table 7).

The grade of nerve compression was a strong predictor of response for both paracentral and foraminal disc herniations (Table 8). In the presence of a paracentral disc herniation, 74% (95% confidence interval [CI]: 59–89%) of patients with low-grade nerve compression had a favorable response to treatment, whereas only 26% (95% CI: 11–41%) of those with high-grade nerve root compression responded ($P < 0.000$). In those with foraminal herniations, five of six patients with low-grade herniation responded, whereas only one of the four patients with a high-grade herniation responded. This latter association did not reach statistical significance ($P = 0.065$) because of the small sample size but was concordant with the association found for paracentral herniations. When all patients were pooled, favorable responses to treatment occurred in 75% (95% CI: 62–88%) of patients with low-grade compression, but only in 26% (95% CI: 12–38%) of those with high-grade compression.

In patients with paracentral herniation, low-grade compression, as a predictor of favorable outcome, had a sensitivity of 0.73, a specificity of 0.74, and a positive

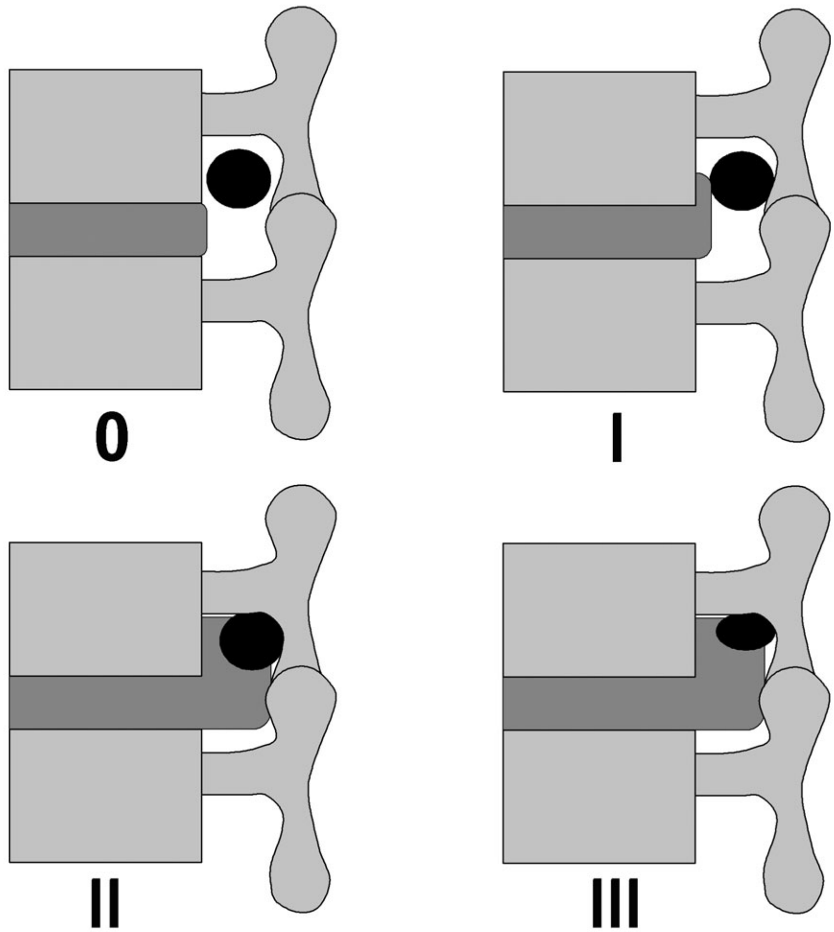

Figure 3 Sketches of sagittal scans of the lumbar spine showing the grading system used to compression of nerve roots by far lateral disc herniations. Grade I: perineural fat obliterated in two opposing directions (vertical or transverse). Grade II: perineural fat obliterated in four directions without morphologic distortion of the nerve. Grade III distortion or other morphologic change in the nerve root evident.

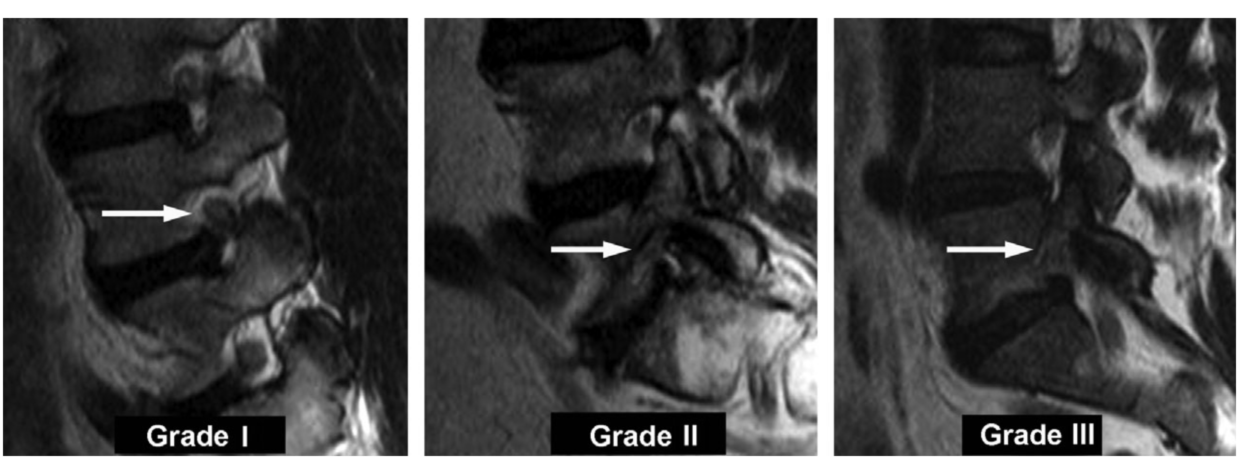

Figure 4 Sagittal magnetic resonance images showing examples of different grades of foraminal stenosis caused by far lateral disc herniations, as seen and as interpreted in the present study. The arrow points to the affected nerve.

Table 2 Contingency table for response to transforaminal injection of steroids and duration of symptoms

Duration of Symptoms (Months)	Response to Treatment		
	Favorable	None	*P*
0–2	19	15	
2–4	6	4	
4–6	3	3	
>6	10	11	0.979

Table 3 Contingency table for presence of neurologic features and response to transforaminal injection of steroids

	Response to Treatment		
Neurologic Feature	Favorable	None	*P*
Sensory change			
Present	10	6	
Absent	28	27	0.413
Total	38	33	
Neurologic sign			
Present	12	9	
Absent	26	24	0.692
Total	38	33	

Neurologic signs encompass motor weakness or depressed reflex.

likelihood ratio of 2.8. For patients with foraminal herniations, the numbers were too small to allow meaningful calculations of corresponding values.

For the grading of nerve root compression using four grades, the two observers achieved agreement that was good (kappa = 0.60) but was less than optimal (Table 9). However, disagreements arose largely between Grades I and II, or III and IV. When the grades were collapsed into low grade and high grade, agreement improved to more than acceptable levels (kappa = 0.87) (Table 10).

Discussion

The rationale for transforaminal injection of steroids is that lumbar radicular pain is caused by inflammation of the nerve roots as a result of an inflammatory response to the herniated disc material. This rationale is supported by circumstantial evidence from laboratory studies [16–22]. While not refuting this rationale, the results of the present study call for an amendment of it.

Transforaminal injection of steroids was successful in relieving pain in 75% of patients with low-grade compression of the affected nerve roots. In these patients, MRI explicitly showed no substantial, mechanical component to their pathology. That leaves chemical, i.e., inflammatory,

Table 4 Contingency table for response to transforaminal injection of steroids and location of herniation and segment affected

	Response to Treatment		
Location of Herniation	Favorable	None	*P*
Central and paracentral			
L2-3	1	0	
L3-4	0	3	
L4-5	18	12	
L5-S1	13	14	0.164
Foraminal			
L2-3	1	0	
L3-4	2	0	
L4-5	1	0	
L5-S1	2	4	0.217
All			
L2-3	2	0	
L3-4	2	3	
L4-5	19	12	
L5-S1	15	18	0.293

Sensory changes pertain to objective sensory loss. Neurologic signs encompass motor weakness or depressed reflex.

Table 5 Contingency table for response to transforaminal injection of steroids and type of herniation

	Response to Treatment		
Morphology of Herniation	Favorable	None	*P*
Central and paracentral			
Broad-based bulge	6	6	
Focal protrusion	17	16	
Extrusion	5	2	
Sequestration	4	5	0.346
Foraminal			
Broad-based bulge	1	3	
Focal protrusion	3	1	
Extrusion	1	0	
Sequestration	1	0	0.290
All			
Broad-based bulge	7	9	
Focal protrusion	20	17	
Extrusion	6	2	
Sequestration	5	5	0.542

Table 6 Contingency table between for response to transforaminal injection of steroids and dimensions of the herniation

Dimensions of Herniation	Response to Treatment Favorable	None	*P*
Thickness of herniation (mm)			
Mean	6.9	6.9	
SD	1.9	3.7	0.959
Cross-sectional area of herniation (mm^2)			
Mean	60.7	78.3	
SD	4.9	7.5	0.057
Cross sectional area of vertebral canal (mm^2)			
Mean	262	257	
SD	99	101	0.859
Ratio area of herniation and spinal canal			
Mean	0.24	0.31	
SD	0.13	0.18	0.105

SD = standard deviation.

processes as the cardinal mechanism of their pain. In such cases, transforaminal injection of steroids should, theoretically, be effective, and it proved to be so in the present study.

In patients with overt mechanical distortion of the nerve roots, there is little reason to expect transforaminal injection of steroids to work. In some patients, inflammation might still be a factor, which would explain why one in four benefited, but a placebo effect cannot be excluded, and should not be ignored. In the remaining majority of patients, it appears that mechanical compression is the cardinal pathology, and this is not relieved by the injection of steroids. In such cases, physical therapy, analgesics, or electrical therapies cannot remove the mechanical compression, and surgery emerges as the only rational option.

These deductions, and the results of the present study, serve to inform decisions and choices in the management of lumbar radicular pain. In the present study, two cardinal features were used to select patients for treatment. Firstly,

Table 7 Contingency table for response to transforaminal injection of steroids and presence of degenerative changes at the segment affected for patients with paracentral disc herniation

Degenerative Changes at the Segment Treated	Response to Treatment Favorable	None	*P*
Present	6	9	
Absent	26	20	0.266

Table 8 Contingency table for response to transforaminal injection of steroids and grade of compression of the nerve root affected

Grade of Nerve Root Compression	Response to Treatment Favorable	None	*P*
Paracentral herniations			
Grade I	13	1	
Grade II	12	8	
Grade III	4	13	
Grade IV	3	7	0.001
Low-grade (I, II)	25	9	
High-grade (III, IV)	7	20	0.000
Foraminal herniations			
Grade I	5	1	
Grade II	1	0	
Grade III	0	3	
Low-grade (0, I)	5	1	
High-grade (II, III)	1	3	0.065
Combined			
Low-grade	30	10	
High-grade	8	23	0.000

Table 9 Agreement between two observers on the grading of nerve compression using four grades

		Observer 1 Grade I	Grade II	Grade III	Grade IV
Observer 2	Grade I	18	2		
	Grade II	7	13	1	
	Grade III	1	2	10	2
	Grade IV			6	3

Kappa = 0.60.

Table 10 Agreement between two observers on the grading of nerve compression using two grades

		Observer 1 Low-Grade (I, II)	High-Grade (III, IV)
Observer 2	Low-grade (I–II)	40	1
	High-grade (III–IV)	3	21

Kappa = 0.87.

they had to have pain of a lancinating nature radiating into the lower limb, which is the essential clinical feature of lumbar radicular pain [23]. Therefore, it is only for such patients that the ensuing recommendations apply. Secondly, patients had to exhibit on MRI, a disc herniation at a segment that reasonably matched the distribution of their pain. It is in this regard that the results of the present study can inform future practice. If MRI shows low-grade compression, patients and those who treat them can expect a success rate of 75% if transforaminal injection of steroids is undertaken. Reciprocally, if MRI shows high-grade compression, the expected success rate falls to 26%.

A success rate of 75%, in appropriately selected patients, should render transforaminal injection of steroids, an entertainable option as an alternative to surgery. More contentious is a success rate of only 26% in those patients with high-grade compression. Some surgeons might prefer to bypass such a low chance of success, and logically proceed directly to surgery. Others might care to indulge a one in four chance of avoiding surgery, provided that transforaminal injections are performed carefully in order to protect patients from potential complications.

Pivotal to these considerations is being able to distinguish low-grade from high-grade compressions, but radiologists do not customarily report precisely on grades of compression. Treating surgeons or interventional pain specialists are more likely to be interested in the predictive utility of grading compression. So, it falls to them to be able to grade compressions reliably. In that regard, the results of the present study are more than reassuring. Two observers were able to achieve very good agreement when distinguishing low-grade and high-grade compression. The few cases in which disagreement arose involved instances where one observer, but not the other, felt that perineural fat persisted around a nerve that was otherwise engulfed by a disc herniation; or when one observer failed to identify a sequestrated fragment that engulfed a nerve but which was remote from the principal herniation, which only displaced the nerve. Such disagreements can be resolved, and agreement improved beyond the levels achieved in the present study, by closer attention to T1-weighted axial and sagittal images as well as T2-weighted images, in order to map accurately the boundaries and complete distribution of disc material and its relationships to nerves.

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