Current Management of Symptomatic Lumbar Disc Herniation

ABSTRACT

Lumbar disc herniation is a common cause of low back pain and radiculopathy (sciatica). Diagnosis is initially made based on history and physical examination and ruling out red flags, particularly surgical emergencies such as Cauda Equina Syndrome. A trial of conservative treatment consisting of physical rehabilitation and oral medication is usually successful for back dominant pain. When persistent radiculopathy indicates lumbar discectomy the diagnosis must be confirmed by imaging but, due to very high rates of asymptomatic disc herniation, imaging cannot replace clinical diagnosis. For disabling leg dominant pain discectomy results in faster recovery but has a similar long-term outcomes compared to conservative treatment.

KEYWORDS: lumbar disc herniation, lower back pain, sciatica, radiculopathy

CME Pre-test Quiz

Introduction

Degenerative spine conditions and lumbar disc herniation (LDH) have afflicted humanity since ancient time. Hippocrates described sciatica and antalgic posture as well as claudication and prescribed rest, massage, heat, dietary changes and music.[1] Although LDH was thought to be due to traumatic causes, studies have demonstrated a strong genetic susceptibility to both disc herniation and degeneration.[2,3] Back pain occurs spontaneously in over 60% of cases.[4]

The incidence of symptomatic LDH in the United States is 2% to 5% and the lifetime prevalence is nearly 80%.[5-7] LDH occurs most commonly between the ages of

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40 and 45 with the majority of the LDH occurring at the L4/L5 and L5/S1 levels.[8] When pain is present LDH usually results in two types of symptoms: 1) most commonly localized back dominant pain termed as mechanical back pain and 2) in a small number of case sciatica or radiculopathy when the herniation irritates one or more adjacent nerve roots. Symptoms of mechanical back pain and radicular leg pain can coexist.

Anatomy

The intervertebral disc is central to the functional spinal unit, which comprises the vertebrae, the disc, and the associated paired facet joints at that level.[9] Intervertebral discs are found throughout the vertebral column except between the first and second cervical vertebrae, and are classified as amphiarthrodial joints as they have no synovial fluid or synovial lining. The discs and vertebral bodies support more than 80% of the axial load transmitted through the lumbar spine. Their ability to resist axial loads is substantial but it decreases with age.[10,11]

Each disc is composed of a nucleus pulposus and annulus fibrosus that provide support, absorb shock, and allow and resist excessive movement.[12] The nucleus pulposus is a semifluid mass of mucoid proteoglycan material, 70% to 90% water. The annulus fibrosis consists of twelve concentric collagen lamellae with alternating orientation. The annulus is 60% to 70% water. The proportions of proteoglycan and water decrease as you grow older.

Axial load, flexion, extension, or lateral-bending force vectors can cause significant deformity of the disc and result in disc bulging and herniation.[13] Disc bulging, however, should not be confused with disc herniation. The former is caused by distortion of the annulus fibrosus and is associated with eccentric loading. The latter is caused by migration of the nucleus pulposus from its normal anatomical location.[12]

Pathophysiology

Pathophysiological studies have demonstrated that LDH generally results from injury to the annulus fibrosus with subsequent prolapse of the disc, however most disc herniations regress without surgical intervention.[14] Histopathology and immunochemical studies have revealed that migrated or extruded disc material can undergo phagocytosis by macrophages or epidural tissue resulting in a 70% or greater reduction in disc protrusion size.[15] Many patients' symptoms resolve without a regression.[16,17]

Multiple mechanisms contribute to pain generation associated with LDH. Some of these result in mechanical back pain; described by Francis Murphey in 1968.[18] Herniations can activate pain fib-

ers in the annulus and because the posterior longitudinal ligament is innervated it can be painful if torn.[19-21] Pain generators also exist in the facet synovium and the anterior longitudinal ligament. All can produce mechanical back dominant pain. Muscle pain is almost always a secondary, reactive response. Other mechanisms lead to nerve root irritation with radiculopathy or sciatica. Leaking of nucleus pulposus into the spinal canal causes an inflammatory response around pain sensitive nerves.[22,23] Mechanical pressure on the nerve roots and dorsal root ganglia can cause both direct and indirect nerve irritation through altered blood supply and nutritional transport.

It is important to distinguish between back dominant pain and constant leg dominant radiculopathy. Discogenic or mechanical back pain arises from structures such as the posterior longitudinal ligament or annulus while the much less frequent radiculopathy is caused by nerve root irritation. Surgical intervention is usually only indicated for radicular pain.

Diagnosis

The terms used in the diagnosis of LDH and radiculopathy has changed over the last 100 years. Assessment is still based on clinical history and physical examination but, when it is required to direct care, advanced imaging now allows physicians to confirm the suspected diagnosis with some accuracy.

History

Start by establishing the exact site of the worst pain, whether that pain is constant and intermittent and the effect of flexion on the typical pain.[24] Patient risk factors should be elicited which include: excessive stress on the lumbar spine, obesity, tobacco use, prolonged driving and a positive family history of lumbar disc disease.[7,25-27] Classically, patients with LDH will complain of lower back pain exacerbated by specific movements or positions and frequently associated with radiating pain. The back pain may be midline or extend to the flank or over the trochanters. In most but not all cases, pain is increased with flexion and decreased with extension.

It is important to differentiate radiating back dominant pain which can extend from the buttock to the foot, from true radicular pain, usually called sciatica. Sciatica is a constant, leg dominant pain often combined with paresthesias that radiates to a specific, although not exact, dermatome distribution beginning below the gluteal fold. When defined in such a manner, the symptoms of sciatica have a 95% specificity for diagnosis of LDH.[28]

As part of the differential diagnosis for LDH involving radiating

leg pain consider spinal stenosis, synovial cysts, tumour, abscess, peripheral nerve pathology and even unrelated visceral diseases such as endometriosis.[8]

Finally, it is important to rule out red flags. Question the patient about disproportionate night pain, fevers, unintended weight loss and a history of cancer. In particular consider the uncommon but potentially devastating diagnosis of Cauda Equina Syndrome with symptoms of bilateral lower limb pain, weakness, saddle anesthesia and bowel or bladder dysfunction in the form of urinary retention and bowl incontinence. It requires immediate surgical intervention.

Physical Examination

Using a systematic approach, physical examinations should start with inspection of posture, back movement, particularly determining if typical pain is produced on flexion. A lumbar shift (a lateral pelvic shift in relation to the lumbar spine) is suggestive of LDH.[29] Lower extremity motor and sensory examination including neural tension tests should be routine. If there is the suspicion of a cauda equina syndrome a rectal exam may be required to assess rectal sphincter function. The physical examination may include assessing the hips, abdomen and peripheral circulation.

Neural tension tests include the straight leg raise, "well-leg lift" cross-over and the slump sit test amongst others. Straight leg raise is done with the patient supine and the contralateral hip and knee flexed. It is considered positive if it reproduces or exacerbates the patient's typical leg dominant radicular pain. The production of back pain is not a positive test. Dorsiflexion of ankle and hip internal rotation can be used to add further stretch to the nerves. A positive well leg lift occurs when flexion of the asymptomatic hip by lifting the "well" leg results in radicular pain in the painful leg. This is thought to represent an extremely irritable nerve root and may be more specific than the straight leg raise on the affected side. Cross-over is pain produced in the apparently unaffected leg as well as in the leg with sciatica when raising the symptomatic limb. It is bilateral sciatica produced by lifting only one leg and is suggestive of a central disc herniation producing a cauda equina syndrome. The "slump sit test" where the symptomatic leg is extended while the patient sits slouched forward may be used to differentiate true positive straight leg raise from psychosomatic pain.[29,30]

In some cases the level of LDH can be determined from the dermatomal and myotomal patterns found on physical examination. The most common location for a disc herniation is posterolateral. Due to the local anatomy, this

Physical Examination to Assess Low Back Pain

1 Observation

Hip Abduction (Trendelenburg) Test (L5 Nerve Root Conduction)

2 Standing

Movement to Reproduce Pain

Gait

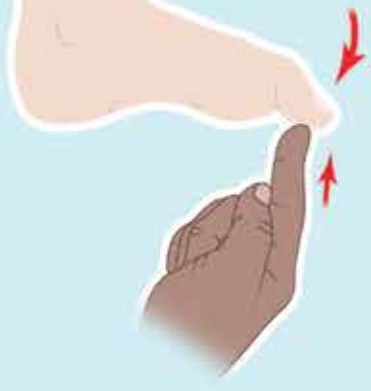
Toe Walking Test (S1 Nerve Root Conduction)

Heel Walking Test (L4-L5 Nerve Root Conduction)

* 5 steps at maximum elevation

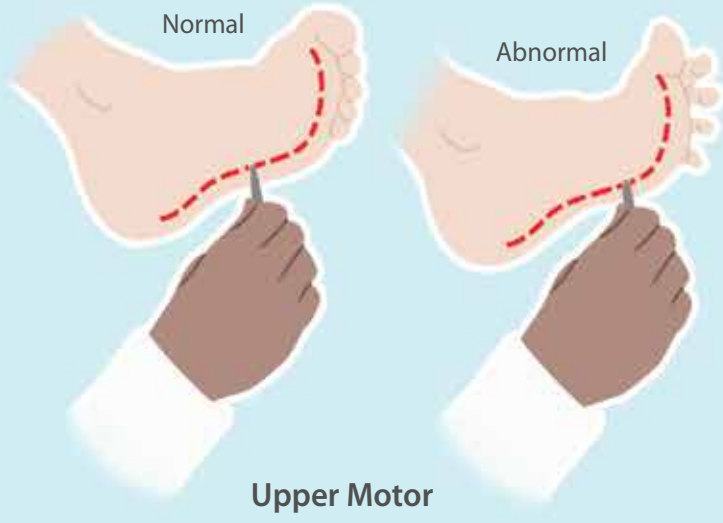
3 Sitting

Great Toe Flexion Test (S1 Nerve Root Conduction)

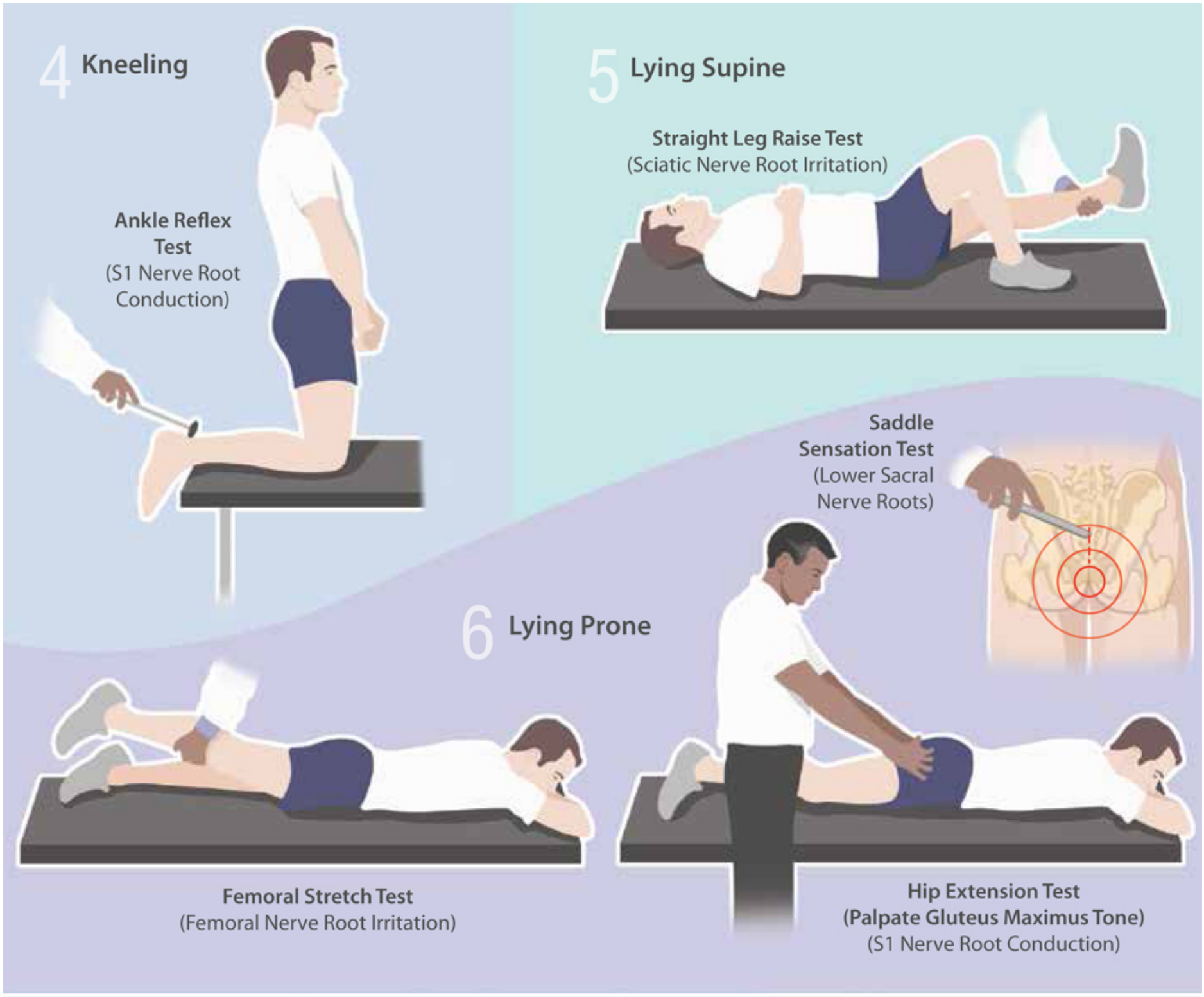


Great Toe Extension Test (L5 Nerve Root Conduction)

Ankle Dorsiflexion Test (L4 and L5 Nerve Root Conduction)



Upper Motor Test



Classification of Mechanical Patterns of Low Back Pain

	Reported Pain Location	Pain Constancy	Pain Improved	Pain Worsened	Neurological Findings	Pain Origin
1	Back, buttocks or around hips	Constant or intermittent	One of 2 cohorts will improve on extension	Forward flexion, one of the 2 cohorts' pain also worsens on extension	Normal	Most likely discogenic
2	Back dominant	Intermittent	Unaffected or may be improved on flexion	Worsens on extension	Normal	Most likely posterior spinal elements
3	Leg dominant	Constant	By immobility and recumbent rest	By all back movement, usually more by flexion	Positive irritative test and/or conduction loss	Sciatic (or occasionally femoral) nerve root irritation
4	Leg dominant	Intermittent	Relieved by rest in flexion (sitting)	Activity in extension (walking)	May have positive conduction test; no irritative test.	Neurogenic claudication, often mislabelled spinal stenosis

results in compression of the traversing nerve root. For example, a L4/L5 disc herniation will result in compression of the traversing L5 nerve root with possible weakness of the extensor hallucis longus and numbness over the dorsum of the foot.

For strength testing it is crucial to test the strength of the muscle with consideration of its normal function. For instance, the patients' planter flexion should be sufficiently strong enough to lift their own body weight several times.

Reflexes are objective findings and should not be neglected. The patellar reflex will assess L3/ L4 nerve root function while the ankle reflex represents S1 function.

The low back examination should include testing for upper motor findings such as sustained clonus or a positive plantar response. Spinal cord pathology can masquerade as a low back problem.

Imaging

X-ray imaging can show late stage degenerative changes, disc height collapse and alignment abnormalities. A more definitive imaging technique from the 1970s was CT scanning with myelography. Improvements in MRI in the 1990s offered an even more precise tool for evaluation of LDH.[15,31] In fact, MRI is sensitive enough that absence of abnormality on MRI can be considered a contraindication to surgery.[32] However, the sensitivity of MRI also results in large number of false positives. It soon became clear that a disc herniation seen on MRI was usually asymptomatic and MRI should only be used to confirm or reject a diagnosis made on history and physical examination.[32,33] Similarly discography may offer information of use to the surgeon but has no place in the initial assessment.[34]

It is important to note that the vast majority of LDH are asymptomatic. In postmortem studies 39% of individuals had asymptomatic LDH similar to the results of CT scans and myelograms.[35,36,37] With the advent of MRI, the frequency of finding asymptomatic LDH has again increased significantly. Abnormal MRI findings cannot predict future back pain.[38]

Natural History

Management

Conservative

In the early years of lumbar discectomy, surgeons were aggressive in managing radiculopathy from LDH with surgery. However, it became clear that many patients with leg dominant pain improve without surgical intervention. In 1996 John McCulloch, a microdiscectomy pioneer, wrote that "Long-term results of surgery are only slightly better than conservative measures".[32] It is now recognized that the majority of LDH will heal spontaneously or with conservative management.[39,40]

Effective conservative measures for management of LDH without radiculopathy include education, activity modification, mechanical therapy and OTC medications. High patient expectations prior to the initiation of conservative treatment may have a beneficial effect on outcome.[41]

Historically bed rest was recommended for back pain. Studies have shown this to actually be detrimental and patients with acute back pain treated with bed rest have increased likelihood of developing chronic pain.[42,43,44] This is very different than prescribing scheduled rest periods throughout the day in the most effective pain-reducing positions, which is an essential part of managing acute radicular pain.

Initial pain control for back dominant pain is often a matter of employing positions and/or progressive movement in the direction of that most reliably reduces the symptoms.[45,46] Patients without a directional preference pose more of a challenge and may be more likely to be considered for surgery.[47-50]

As the acute back pain subsides a physical therapy program can be initiated focusing on aerobic exercise, core muscle strengthening and flexibility training.[8] Studies have shown good to excellent outcomes associated therapeutic exercise to speed recovery.[39,51,52]

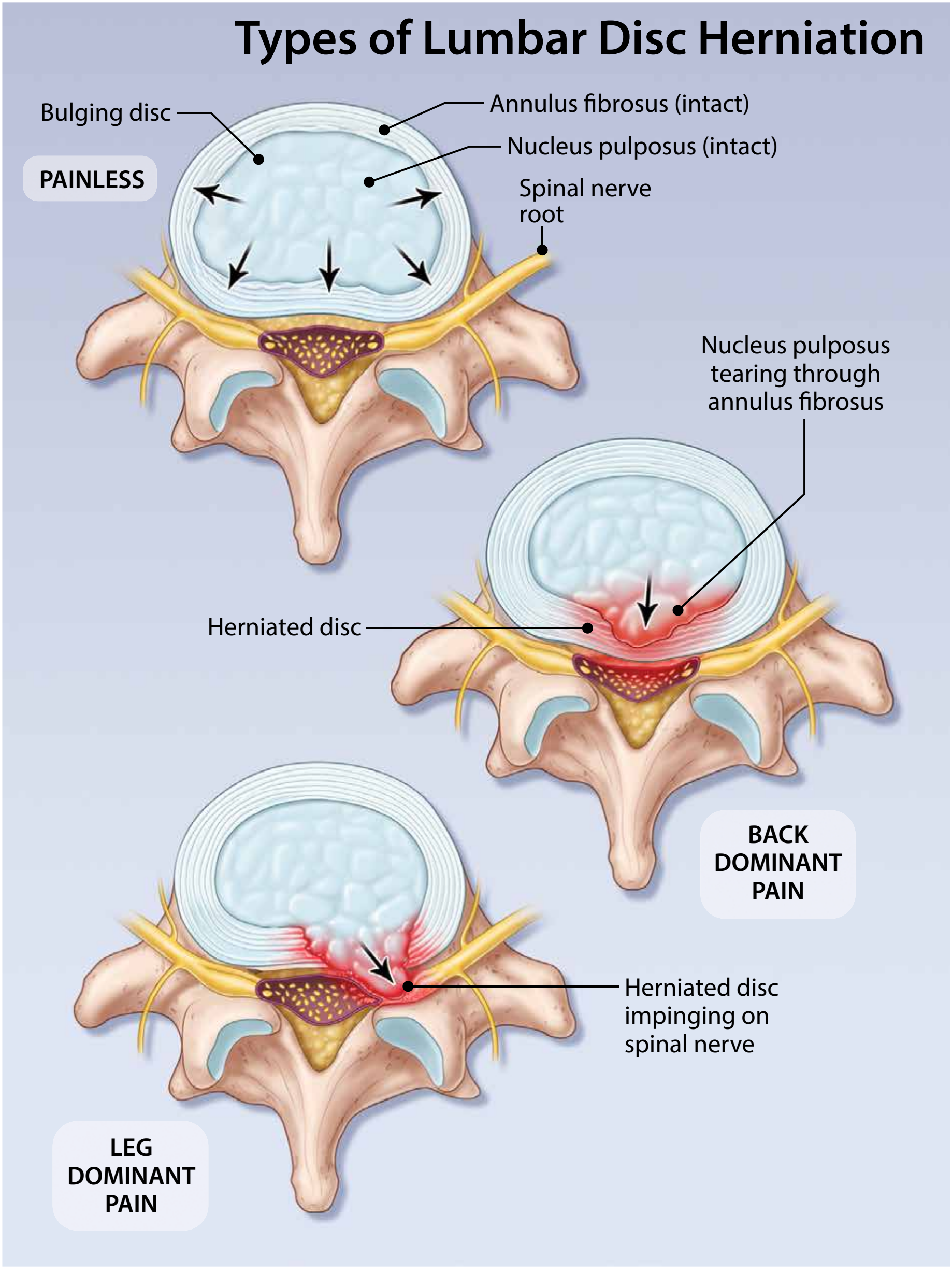
Oral medications should be utilized to allow the patient to remain active by controlling the pain. The classes of drugs best utilized in the management of mechanical back pain are acetaminophen, non-steroidal anti-inflammatories (NSAIDS) and muscle relaxants. When there is direct nerve root irritation the medicinal approach can be more aggressive and include oral steroids. Prescribing pain medication on an as-needed basis can result in poor pain control and greater medication requirement.[8]

Acetaminophen is a safe analgesic for most individuals. It is effective for mild pain and as long as a maximum adult dose is below 4 g per day liver failure is unlikely.[8] No major difference exists between the different types of NSAIDS and no benefit is seen beyond the maximum recommended dose.[53-55]

Opioids may be used for moderate to severe radicular pain but they pose a risk of dependence and long-term use is not recommended.[56] Tolerance results in the need to progressively increase the dose. Opioid use is not associated with surgical avoidance.

The mode of action of muscle relaxants is not fully understood however they can reduce pain and may work when combined with other oral analgesic. They are best employed at night and not when the patient is engaged in complex activities.[57,58]

Multiple modalities are utilized often without strong evidence for efficacy. These include cryo-


Types of Lumbar Disc Herniation
Bulging disc
Annulus fibrosus (intact)
Nucleus pulposus (intact)
PAINLESS
Spinal nerve root
Nucleus pulposus tearing through annulus fibrosus
Herniated disc
BACK DOMINANT PAIN
Herniated disc impinging on spinal nerve
LEG DOMINANT PAIN

therapy and ultrasound. Traction is a popular treatment modality for management of LDH and has been practiced since the Middle Ages. It is promoted to correct the truncal shift associated with radiculopathy and has been theorized to promote regression of LDH and improve disc nutrition and blood flow.[59,60] These claims have been widely discredited and a recent Cochrane review revealed that only low to moderate quality evidence exists that traction is even helpful in reducing pain.[61]

Finally, epidural cortisone injections can be used to manage the constant leg dominant pain associated with nerve root inflammation. Intramuscular dexamethasone injections given within 24 to 48 hour of onset of radicular pain have been reported as effective.[62,63] Studies show mixed results with a wide range in success rates for the use of corticosteroids.[64-68] The use of fluoroscopy may increase the success rate of epidural cortisone injections but there is no strong evidence for the use of epidural steroid injections and there are no good placebo-controlled studies to define the indications and the benefits.[69,70] In the face of such uncertainty the decision is left up to patients and their physicians and personal preference holds sway.[71,72]

Surgical

By the mid-1990s nearly 200,000 discectomies were performed annually in the United States alone.[73,74] It is now frequently performed in an outpatient setting and full activity after a short period of rest and healing is sufficient for postoperative recovery.[75-78] There have been minor alterations in the procedure. Attempts to totally remove the nucleus have been abandoned in favour of extracting only the loose fragments. The change resulted in little change in the recurrence rate which remains, at about 15%, the most common complication of disc surgery ahead of dural tear or post-operative infection.[58,79-81]

Adding fusion to discectomy in the surgical management of radicular pain associated with LDH is controversial. Most authors agree discectomy alone has the best benefit-to-cost ratio and that the additional risks associated with fusion even in revision cases are not justifiable.[82-85]

It is unlikely that any health care professional reading this article has not been asked the question, “Is laser surgery of any benefit?” The laser is primarily a cutting tool that can evaporate the protruded disc with less nerve retraction than standard instruments.[86] However there are no studies that confirm its theoretical benefits or improved results and it is marketing more than science that has created its popularity.

Studies show good to excellent results for simple discectomy in 70

SUMMARY OF KEY POINTS

1) Lumbar disc herniation is common and frequently asymptomatic.

2) Lumbar disc herniation may result in back pain. Much less frequently, when the adjacent nerve root is involved it can cause radiculopathy (sciatica).

3) Under most circumstances, the symptoms of lumbar disc herniation can be managed conservatively with physical rehabilitation and oral medications.

4) Red flags and surgical emergencies such as Cauda Equina Syndrome must be considered and should lead to urgent imaging and surgical referral.

5) Imaging, particularly MRI, has high rates of false positives and should only be used to confirm a diagnosis made based on history and physical examination.

6) For disabling persistent radiculopathy with good radiological correlation, surgical intervention in the form of a discectomy can be considered.

to 90% of patients with disabling leg dominant radicular pain. Patient selection is the primary indicator of a good surgical outcome.[31,87] Multiple publications equate less successful outcomes with surgery on patients receiving workers' compensation, in psychological distress, on long term opioids use, with long standing symptoms and a history of smoking and diabetes.[31,88-94] Additional considerations for determining the place for surgery include findings that non-contained or extruded disc fragments tend to have better results with surgery than with conservative treatment.[95] A study by Kerr *et al.* found that at four-year follow-up sequestered fragments identified on MRI and patients with higher levels of baseline back pain had a greater likelihood of getting benefit from surgery than from non-surgical care.[96] Obesity does not appear to have a negative impact on the surgical outcome for LDH.[97] In cases of constant leg dominant pain, general advice and education have been shown to be less effective than surgery in the short-term but equally as effective over time.[98]

Surgical vs. Conservative Comparison

The Spine Patient Outcomes Research Trial (SPORT) was a large randomized clinical trial that enrolled patients between March of 2000 and November of 2004 from 13 multidisciplinary spine centers in the United States. Patients enrolled in this study all had radiculopathy for a minimum of six weeks and a confirmed LDH on imaging. The results of the SPORT have been compared to other large national patient samples and found to be similar and relatively generalizable. Much has been published from the results of this

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Post-test Quiz

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study that help guide the current management of LDH producing constant leg dominant pain. Overall, the study demonstrated that both operative and non-operative groups showed significant but similar improvement over time in the intent-to-treat analyses. However, the surgical group demonstrated significantly better scores for bodily pain, physical function and the Oswestry disability index in the as-treated analysis. These differences were most significant early and narrowed by two years, a finding which has been shown by other trials.[99-102] Beneficial outcomes with surgical treatment for radicular pain have been reported from the SPORT trial for up to eight years follow-up.[103] The SPORT studies had a high cross-over between treatment groups, particularly from the conservative to the surgical group, which created a significant bias.[100-104] While the as-treated analysis provides a better assessment of the impact of the operative treatment, the study results have to be interpreted with caution since half the patients chose their own treatment. This emphasizes that patients' preference should play a central role when treating lumbar disk herniation causing leg dominant pain and that a shared decision making process is crucial.

Conclusion

The majority of patients suffering from back pain and or radicular symptoms secondary to LDH will improve on their own without surgical intervention. In the case of back dominant pain active rehabilitation should first focus on pain control

CLINICAL PEARLS

1) Lumbar disc herniation (LDH) is common and in most cases asymptomatic. Findings on MRI of lumbar disc herniation are not predictive of future back related disability. MRI findings should be interpreted along with history and physical exam findings to determine the appropriate diagnosis.

2) LDH can result in back pain and, when the adjacent nerve root is involved, radicular leg pain. The first line of treatment for back dominant pain should be education, lifestyle modification, mechanical therapy and oral medications in the form of acetaminophen, non-steroidal anti-inflammatories.

3) Radicular leg dominant pain may require opioids and/or epidural corticosteroid injections. The majority of patients will improve without further intervention.

4) For persistent symptoms of sciatica, surgical intervention can be considered. Lumbar discectomy is the most common procedure performed and has good to excellent outcomes.

through position and direction specific movements and oral medications should be added as needed to promote activity. For acute radiculopathy intermittent scheduled rest (not prolonged bed rest) in the best pain-reducing position accompanied by adequate medication is the correct initial management. When disabling leg dominant pain persists despite the use of mechanical therapy and medication, it is reasonable to consider surgical intervention. In our current Canadian health care system patients often wait more than six months to receive a first consultation so the results of trials, such as the SPORT trial, may not be applicable.

Multiple studies have been published on the outcome of surgical vs. nonsurgical management of radiculopathy secondary to LDH. Generally conservative treatment is safe and patients who refuse surgery often eventually improve to acceptable level of pain and function. But studies have also shown that surgery can improve symptoms faster with a low complication rate.

References

1. Marketos, S.G. & Skiadas, P. Hippocrates. The father of spine surgery. Spine (Phila Pa 1976) 24, 1381-1387 (1999).
2. Chedid, K.J. & Chedid, M.K. The "tract" of history in the treatment of lumbar degenerative disc disease. Neurosurg Focus 16, E7 (2004).
3. Matsui, H., et al. Familial predisposition for lumbar degenerative disc disease. A case-control study. Spine (Phila Pa 1976) 23, 1029-1034 (1998).
4. Hall H, McIntosh G, Wilson L, Melles T. The spontaneous onset of back pain. Clinical Journal of Pain 14(2), 129-33 (1998)
5. Deyo, R.A. & Tsui-Wu, Y.J. Descriptive epidemiology of low-back pain and its related medical care in the United States. Spine (Phila Pa 1976) 12, 264-268 (1987).
6. Herring SA, W.S. Assessment and nonsurgical management of athletic low back injury. in The Lower Extremity and Spine in Sports Medicine (ed. Nicholas JA, H.E.) 1117-1197 (Mosby, St. Louis, 1995).
7. Kaul M, H.S. Rehabilitation of lumbar spine injuries. in Functional Rehabilitation of Sport and Musculoskeletal Injures (ed. Kibler WB, H.S., Press JM et al.) 188-215 (Aspen Publishers, Gaithersburg, 1998).
8. Shahbandar, L. Diagnosis and nonoperative management of lumbar disk herniation Operative Techniques in Sports Medicine 13, 114-121 (2005).
9. Wood, G.W.I. Spinal anatomy and surgical approaches. in Campbell's operative orthopaedics, Vol. 2 (eds. Canale, S.T., Beaty, J.H. & Campbell, W.C.) 1524-1558 (Elsevier/Mosby, Philadelphia, PA, 2013).
10. Takeuchi, T., Abumi, K., Shono, Y., Oda, I. & Kaneda, K. Biomechanical role of the intervertebral disc and costovertebral joint in stability of the thoracic spine. A canine model study. Spine (Phila Pa 1976) 24, 1414-1420 (1999).
11. White, A.A., 3rd & Panjabi, M.M. The basic kinematics of the human spine. A review of past and current knowledge. Spine (Phila Pa 1976) 3, 12-20 (1978).
12. Benzel, E.C. Biomechanics of Spine Stabilization, (Thieme, New York, New York, 2015).
13. Hall, L.T., Esses, S.I., Noble, P.C. & Kamaric, E. Morphology of the lumbar vertebral endplates. Spine (Phila Pa 1976) 23, 1517-1522; discussion 1522-1513 (1998).
14. Adams, M.A. & Hutton, W.C. Gradual disc prolapse. Spine (Phila Pa 1976) 10, 524-531 (1985).
15. Postacchini, F. & Postacchini, R. Operative management of lumbar disc herniation : the evolution of knowledge and surgical techniques in the last century. Acta Neurochir Suppl 108, 17-21 (2011).
16. Maigne, J.Y., Rime, B. & Deligne, B. Computed tomographic follow-up study of forty-eight cases of nonoperatively treated lumbar intervertebral disc herniation. Spine (Phila Pa 1976) 17, 1071-1074 (1992).
17. Teplick, J.G. & Haskin, M.E. Spontaneous regression of herniated nucleus pulposus. AJR Am J Roentgenol 145, 371-375 (1985).
18. Murphey, F. Sources and patterns of pain in disc disease. Clin Neurosurg 15, 343-351 (1968).
19. Inman, V.T. & Saunders, J.B. Anatomicophysiological aspects of injuries to the intervertebral disc. J Bone Joint Surg Am 29, 461-475 (1947).
20. Konttinen, Y.T., et al. Neuroimmunohistochemical analysis of peridiscal nociceptive neural elements. Spine (Phila Pa 1976) 15, 383-386 (1990).
21. Olmarker, K. & Rydevik, B. Pathophysiology of sciatica. Orthop Clin North Am 22, 223-234 (1991).
22. Kawakami, M., et al. Experimental lumbar radiculopathy. Immunohistochemical and quantitative demonstrations of pain induced by lumbar nerve root irritation of the rat. Spine (Phila Pa 1976) 19, 1780-1794 (1994).

23. Marshall, L.L., Trethewie, E.R. & Curtain, C.C. Chemical radiculitis. A clinical, physiological and immunological study. Clin Orthop Relat Res, 61-67 (1977).
24. Wilson L, Hall H. McIntosh G. Melles. Intertester reliabiilty of a low back pain classification system. Spine (Phila Pa 1976) 24(3), 248-54 (1999)
25 Adams, M.A. & Hutton, W.C. Prolapsed intervertebral disc. A hyperflexion injury 1981 Volvo Award in Basic Science. Spine (Phila Pa 1976) 7, 184-191 (1982).
26. Akmal, M., et al. Effect of nicotine on spinal disc cells: a cellular mechanism for disc degeneration. Spine (Phila Pa 1976) 29, 568-575 (2004).
27. Farfan, H.F., Cossette, J.W., Robertson, G.H., Wells, R.V. & Kraus, H. The effects of torsion on the lumbar intervertebral joints: the role of torsion in the production of disc degeneration. J Bone Joint Surg Am 52, 468-497 (1970).
28. Deyo, R.A., Rainville, J. & Kent, D.L. What can the history and physical examination tell us about low back pain? Jama 268, 760-765 (1992).
29. Akuthota V, W.S., Harden RN. The adult spine: A practical approach to low back pain. in Low Back Pain, A Symptom-Based Approach to Diagnosis and Treatment (ed. Rucker KS, C.A., Weinstein SM) 15-39 (Butterworth-Heinemann, Boston, MA, 2000).
30. Vroomen, P.C., de Krom, M.C. & Knottnerus, J.A. Diagnostic value of history and physical examination in patients suspected of sciatica due to disc herniation: a systematic review. J Neurol 246, 899-906 (1999).
31. Padua, R. The history of the diagnosis and treatment of lumbar sciatic disc herniation. Chir Organi Mov 84, 367-373 (1999).
32. McCulloch, J.A. Focus issue on lumbar disc herniation: macro- and microdiscectomy. Spine (Phila Pa 1976) 21, 45S-56S (1996).
33. Boden, S.D., Davis, D.O., Dina, T.S., Patronas, N.J. & Wiesel, S.W. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 72, 403-408 (1990).
34. Anderson, M.W. Lumbar discography: an update. Semin Roentgenol 39, 52-67 (2004).
35. McRae, D.L. Asymptomatic intervertebral disc protrusions. Acta radiol 46, 9-27 (1956).
36. Hitselberger, W.E. & Witten, R.M. Abnormal myelograms in asymptomatic patients. J Neurosurg 28, 204-206 (1968).
37. Wiesel, S.W., Tsourmas, N., Feffer, H.L., Citrin, C.M. & Patronas, N. A study of computer-assisted tomography. I. The incidence of positive CAT scans in an asymptomatic group of patients. Spine (Phila Pa 1976) 9, 549-551 (1984).
38. Borenstein, D.G., et al. The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects : a seven-year follow-up study. J Bone Joint Surg Am 83-A, 1306-1311 (2001).
39. Benoist, M. The natural history of lumbar disc herniation and radiculopathy. Joint Bone Spine 69, 155-160 (2002).
40. Saal, J.A. Natural history and nonoperative treatment of lumbar disc herniation. Spine (Phila Pa 1976) 21, 2S-9S (1996).
41. Lurie, J.D., et al. Effect of Expectations on Treatment Outcome for Lumbar Intervertebral Disc Herniation. Spine (Phila Pa 1976) 41, 803-809 (2016).
42. Pearce J, M.J. Conservative treatment and natural history of acute lumbar disc leisons. J Neurol Neurosurg Psychiatry 30, 13-17 (1967).
43. Rozenberg, S., Allaert, F.A., Savarieau, B., Perahia, M. & Valat, J.P. Compliance among general practitioners in France with recommendations not to prescribe bed rest for acute low back pain. Joint Bone Spine 71, 56-59 (2004).
44. Deyo, R.A. Early diagnostic evaluation of low back pain. J Gen Intern Med 1, 328-338 (1986).
45. Donelson, R., Aprill, C., Medcalf, R. & Grant, W. A prospective study of centralization of lumbar and referred pain. A predictor of symptomatic discs and anular competence. Spine (Phila Pa 1976) 22, 1115-1122 (1997).
46. Donelson, R., Grant, W., Kamps, C. & Medcalf, R. Pain response to sagittal end-range spinal motion. A prospective, randomized, multicentered trial. Spine (Phila Pa 1976) 16, S206-212 (1991).
47. Sufka, A., et al. Centralization of low back pain and perceived functional outcome. J Orthop Sports Phys Ther 27, 205-212 (1998).
48. Werneke, M. & Hart, D.L. Centralization phenomenon as a prognostic factor for chronic low back pain and disability. Spine (Phila Pa 1976) 26, 758-764; discussion 765 (2001).
49. Werneke, M., Hart, D.L. & Cook, D. A descriptive study of the centralization phenomenon. A prospective analysis. Spine (Phila Pa 1976) 24, 676-683 (1999).
50. Wetzel, F.T. & Donelson, R. The role of repeated end-range/pain response assessment in the management of symptomatic lumbar discs. Spine J 3, 146-154 (2003).
51. Saal, J.A. & Saal, J.S. Nonoperative treatment of herniated lumbar intervertebral disc with radiculopathy. An outcome study. Spine (Phila Pa 1976) 14, 431-437 (1989).
52. Weber, H. Lumbar disc herniation. A controlled, prospective study with ten years of observation. Spine (Phila Pa 1976) 8, 131-140 (1983).
53. Piperno, M., et al. Phospholipase A2 activity in herniated lumbar discs. Clinical correlations and inhibition by piroxicam. Spine (Phila Pa 1976) 22, 2061-2065 (1997).
54. van Tulder, M.W., Scholten, R.J., Koes, B.W. & Deyo, R.A. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database Syst Rev, CD000396 (2000).
55. Roelofs, P.D., Deyo, R.A., Koes, B.W., Scholten, R.J. & van Tulder, M.W. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database Syst Rev, CD000396 (2008).
56. Radcliff, K., et al. Does opioid pain medication use affect the outcome of patients with lumbar disc herniation? Spine (Phila Pa 1976) 38, E849-860 (2013).
57. Basmajian, J.V. Acute back pain and spasm. A controlled multicenter trial of combined analgesic and antispasm agents. Spine (Phila Pa 1976) 14, 438-439 (1989).

58. Borenstein, D.G. & Korn, S. Efficacy of a low-dose regimen of cyclobenzaprine hydrochloride in acute skeletal muscle spasm: results of two placebo-controlled trials. Clin Ther 25, 1056-1073 (2003).
59. Ramos, G. & Martin, W. Effects of vertebral axial decompression on intradiscal pressure. J Neurosurg 81, 350-353 (1994).
60. Shterenshis, M.V. The history of modern spinal traction with particular reference to neural disorders. Spinal Cord 35, 139-146 (1997).
61. Wegner, I., et al. Traction for low-back pain with or without sciatica. Cochrane Database Syst Rev, CD003010 (2013).
62. Green, L.N. Dexamethasone in the management of symptoms due to herniated lumbar disc. Journal of neurology, neurosurgery, and psychiatry 38, 1211-1217 (1975).
63. Johansson, A., Hao, J. & Sjolund, B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand 34, 335-338 (1990).
64. Bush, K., Cowan, N., Katz, D.E. & Gishen, P. The natural history of sciatica associated with disc pathology. A prospective study with clinical and independent radiologic follow-up. Spine (Phila Pa 1976) 17, 1205-1212 (1992).
65. Bush, K. & Hillier, S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. Spine (Phila Pa 1976) 16, 572-575 (1991).
66. dreyer SJ, D.P., Cole A et al. Injection procedures. in The Low Back Pain Handbook (ed. Cole AJ, H.S.) 277-295 (Hanely and Belfus, Philadelphia, PA, 2003).
67. Manchikanti, L., Benyamin, R.M., Falco, F.J., Kaye, A.D. & Hirsch, J.A. Do Epidural Injections Provide Short- and Long-term Relief for Lumbar Disc Herniation? A Systematic Review. Clin Orthop Relat Res 473, 1940-1956 (2015).
68. Spijker-Huiges, A., Vermeulen, K., Winters, J.C., van Wijhe, M. & van der Meer, K. Costs and cost-effectiveness of epidural steroids for acute lumbosacral radicular syndrome in general practice: an economic evaluation alongside a pragmatic randomized control trial. Spine (Phila Pa 1976) 39, 2007-2012 (2014).
69. el-Khoury, G.Y., Ehara, S., Weinstein, J.N., Montgomery, W.J. & Kathol, M.H. Epidural steroid injection: a procedure ideally performed with fluoroscopic control. Radiology 168, 554-557 (1988).
70. Renfrew, D.L., et al. Correct placement of epidural steroid injections: fluoroscopic guidance and contrast administration. AJNR Am J Neuroradiol 12, 1003-1007 (1991).
71. Friedrich, J.M. & Harrast, M.A. Lumbar epidural steroid injections: indications, contraindications, risks, and benefits. Curr Sports Med Rep 9, 43-49 (2010).
72. Radcliff, K., et al. The impact of epidural steroid injections on the outcomes of patients treated for lumbar disc herniation: a subgroup analysis of the SPORT trial. J Bone Joint Surg Am 94, 1353-1358 (2012).
73. Truumees, E. A history of lumbar disc herniation from Hippocrates to the 1990s. Clin Orthop Relat Res 473, 1885-1895 (2015).
74. Taylor, V.M., Deyo, R.A., Cherkin, D.C. & Kreuter, W. Low back pain hospitalization. Recent United States trends and regional variations. Spine (Phila Pa 1976) 19, 1207-1212; discussion 1213 (1994).
75. An, H.S., Simpson, J.M. & Stein, R. Outpatient laminotomy and discectomy. J Spinal Disord 12, 192-196 (1999).
76. Cares, H.L., Steinberg, R.S., Robertson, E.T. & Caldini, P. Ambulatory microsurgery for ruptured lumbar discs: report of ten cases. Neurosurgery 22, 523-526 (1988).
77. Carragee, E.J., et al. Activity restrictions after posterior lumbar discectomy. A prospective study of outcomes in 152 cases with no postoperative restrictions. Spine (Phila Pa 1976) 24, 2346-2351 (1999).
78. Carragee, E.J., Helms, E. & O'Sullivan, G.S. Are postoperative activity restrictions necessary after posterior lumbar discectomy? A prospective study of outcomes in 50 consecutive cases. Spine (Phila Pa 1976) 21, 1893-1897 (1996).
79. Spengler, D.M. Lumbar discectomy. Results with limited disc excision and selective foraminotomy. Spine (Phila Pa 1976) 7, 604-607 (1982).
80. Williams, R.W. Microlumbar discectomy: a conservative surgical approach to the virgin herniated lumbar disc. Spine (Phila Pa 1976) 3, 175-182 (1978).
81. Lee, J.K., Amorosa, L., Cho, S.K., Weidenbaum, M. & Kim, Y. Recurrent lumbar disk herniation. J Am Acad Orthop Surg 18, 327-337 (2010).
82. Fritsch, E.W., Heisel, J. & Rupp, S. The failed back surgery syndrome: reasons, intraoperative findings, and long-term results: a report of 182 operative treatments. Spine (Phila Pa 1976) 21, 626-633 (1996).
83. Kotilainen, E. & Valtonen, S. Clinical instability of the lumbar spine after microdiscectomy. Acta Neurochir (Wien) 125, 120-126 (1993).
84. Dower, A., Chatterji, R., Swart, A. & Winder, M.J. Surgical management of recurrent lumbar disc herniation and the role of fusion. J Clin Neurosci 23, 44-50 (2016).
85. El Shazly, A.A., El Wardany, M.A. & Morsi, A.M. Recurrent lumbar disc herniation: A prospective comparative study of three surgical management procedures. Asian J Neurosurg 8, 139-146 (2013).
86. Colak, A., Bavbek, M., Aydin, N.E., Renda, N. & Acikgoz, B. Effect of CO2 laser on spinal epidural fibrosis. Acta Neurochir (Wien) 138, 162-166 (1996).
87. Junge, A., Dvorak, J. & Ahrens, S. Predictors of bad and good outcomes of lumbar disc surgery. A prospective clinical study with recommendations for screening to avoid bad outcomes. Spine (Phila Pa 1976) 20, 460-468 (1995).
88. Herron, L.D., Turner, J.A., Novell, L.A. & Kreif, S.L. Patient selection for lumbar discectomy with a revised objective rating system. Clin Orthop Relat Res, 148-155 (1996).
89. Kosteljanetz, M., Espersen, J.O., Halaburt, H. & Miletic, T. Predictive value of clinical and surgical findings in patients with lumbago-sciatica. A prospective study (Part I). Acta Neurochir (Wien) 73, 67-76 (1984).
90. Barrios, C., Ahmed, M., Arrotegui, J., Bjornsson, A. & Gillstrom, P. Microsurgery versus standard removal of the herniated lumbar disc. A 3-year comparison in 150 cases. Acta Orthop Scand 61, 399-403 (1990).

91. Kahanovitz, N., Viola, K. & Muculloch, J. Limited surgical discectomy and microdiscectomy. A clinical comparison. Spine (Phila Pa 1976) 14, 79-81 (1989).
92. Wilson, D.H. & Harbaugh, R. Microsurgical and standard removal of the protruded lumbar disc: a comparative study. Neurosurgery 8, 422-427 (1981).
93. Atlas, S.J., et al. The impact of workers' compensation on outcomes of surgical and nonoperative therapy for patients with a lumbar disc herniation: SPORT. Spine (Phila Pa 1976) 35, 89-97 (2010).
94. Dorow, M., et al. The Course of Pain Intensity in Patients Undergoing Herniated Disc Surgery: A 5-Year Longitudinal Observational Study. PLoS One 11, e0156647 (2016).
95. Folman, Y., Shabat, S., Catz, A. & Gepstein, R. Late results of surgery for herniated lumbar disk as related to duration of preoperative symptoms and type of herniation. Surg Neurol 70, 398-401; discussion 401-392 (2008).
96. Kerr, D., Zhao, W. & Lurie, J.D. What Are Long-term Predictors of Outcomes for Lumbar Disc Herniation? A Randomized and Observational Study. Clin Orthop Relat Res 473, 1920-1930 (2015).
97. Rihn, J.A., et al. The influence of obesity on the outcome of treatment of lumbar disc herniation: analysis of the Spine Patient Outcomes Research Trial (SPORT). J Bone Joint Surg Am 95, 1-8 (2013).
98. Hahne, A.J., Ford, J.J. & McMeeken, J.M. Conservative management of lumbar disc herniation with associated radiculopathy: a systematic review. Spine (Phila Pa 1976) 35, E488-504 (2010).
99. Gugliotta, M., et al. Surgical versus conservative treatment for lumbar disc herniation: a prospective cohort study. BMJ Open 6, e012938 (2016).
100. Weinstein, J.N., et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort. Jama 296, 2451-2459 (2006).
101. Weinstein, J.N., et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. Jama 296, 2441-2450 (2006).
102. Weinstein, J.N., et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976) 33, 2789-2800 (2008).
103. Lurie, J.D., et al. Surgical versus nonoperative treatment for lumbar disc herniation: eight-year results for the spine patient outcomes research trial. Spine (Phila Pa 1976) 39, 3-16 (2014).
104. Lurie, J.D., et al. Lumbar discectomy outcomes vary by herniation level in the Spine Patient Outcomes Research Trial. J Bone Joint Surg Am 90, 1811-1819 (2008).