Disc Herniation and Radiculopathy

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Key Points

- Intervertebral discs are pads of fibrous cartilage located between the vertebrae of the spinal column designed to allow for complex range of motion and withstand mechanical loading.
- These discs undergo changes with aging, which may predispose the disc to prolapse beyond the limits of the intervertebral space.
- Disc herniation as a result of this degenerative process is the most common cause of radiculopathy, which refers to a condition that affects the function of one or more nerve roots as they exit the spinal column.
- Herniations commonly occur in the lower segments of the cervical and lumbar areas and can manifest as pain, paresthesia, sensory deficits, motor weakness, and muscle atrophy along the affected dermatome.
- Pain is generated from two distinct processes: mechanical compression of exiting nerve roots and chemical irritation as a result of the local inflammatory cascade in response to the nucleus pulposus itself.
- Prior episodes of back or neck pain, smoking, certain occupations or recreational activities, and genetics have been associated with an increased risk of developing neck and back radicular symptoms.
- Physical exam will often reveal a sensory deficit, motor deficit, or a combination of both in a dermatomal distribution, diminished deep tendon reflexes, and symptoms increased by provocative maneuvers. The supine straight leg raise (SLR) test has consistently shown the highest specificity for lumbar radiculitis/radiculopathy.
- Advanced imaging with CT or MRI has not been shown to improve outcomes if pain has been present for less than 6 weeks in the absence of red flag symptoms (fever, weight loss, severe or progressive deficits on exam, bowel and bladder dysfunction, etc.).
- Disc herniations have been shown to significantly diminish or fully resolve in almost 80% of patients. This resolution has a strong association with clinical improvement in pain over 6–12 weeks.
- Best evidence supports a stepwise approach to therapy beginning with physical therapy and non-opioid medication management in patients without concerning signs or symptoms.
- Epidural steroid injections have shown clear benefit to reduce acute-to-subacute radicular pain, with a transforaminal approach being superior in the case of unilateral symptoms.
- There is no clearly established consensus regarding surgical indications. However, progressive neurologic deficits, signs of myelopathy, fractures, or signs of instability may warrant surgical evaluation.

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Introduction

Intervertebral discs are pads of fibrous cartilage that rest between the vertebral bodies of the spine. With the exception of the articulation between the atlas (C1) and the axis (C2), as well as sacral vertebrae, each vertebra is separated from the others by a disc. Collectively, the intervertebral discs constitute 20–33% of the overall height of the normal vertebral col-

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umn. The function of the intervertebral disc is to provide articulation between the vertebral bodies and stability to the spine. In addition to allowing complex range of motion, the discs transmit and withstand mechanical loads such as axial loading, bending, and twisting. The discs have an overall similar structure throughout the spine with minor variation among the different regions. Three basic components comprise each intervertebral disc. The central nucleus pulposus (NP) is surrounded by the annulus fibrosus (AF). Both of these structures are bound on top and at the bottom by the cartilaginous end plates. The cells of these regions are morphologically distinct; however, major changes take place over time during the aging process. The anatomy of intervertebral discs is also briefly described in another chapter, and the following sections provide a more detailed description of the disc anatomy.

The outer annulus fibrosus is a highly organized cartilaginous structure, which contains elongated and fibroblast-like cells aligned parallel in discs of concentric lamellae [1]. These specialized cells produce both type I and type II collagen with the outer annulus consisting of primarily type I collagen and the inner annulus having a more balanced mixture of types I and II collagen [2]. Cells of the disc are responsive to all types of mechanical loading, including compression or strain, as well as the direction and magnitude of the load [3]. The nucleus pulposus is predominantly made up of cells that synthesize only type II collagen and tend to be more rounded or chondrocyte-like in morphology. Its ground substance is gelatinous and primarily made of proteoglycans in a loose network of collagen [4]. The cumulative hydrophilic nature of these proteins provides the nucleus pulposus with hydrostatic properties used to counteract compressive loading of the spine.

The state of the intervertebral disc is dynamic over its lifetime [5]. Changes in the vascularity, nutrition, and cellular and molecular structure vary from early youth through adulthood [6]. These changes correlate with age as the disc matures; however, early degeneration is frequently seen [7]. The nucleus pulposus is a homogeneous structure that serves a vital role in maintaining the mechanical function and structure of the disc. The healthy disc, with abundant hydration, largely hydrophilic proteoglycans, and a competent annulus, is ideal for absorbing complex loads early in life and in young adulthood (Fig. 12.1). Beginning in the second decade, however, as the nucleus begins to lose its strongly hydrophilic proteoglycans, the disc becomes more solid and less adept at absorbing these loads and dispersing them to its surrounding structures [8].

As a result of this degenerative process, the nucleus becomes heterogeneous and absorbs axial loads in a nonuniform manner, which alters load transfer to the annulus and vertebral end plate [9]. This uneven distribution of forces across the end plate increases as the degenerative process progresses. As a result, compressive and shear forces are increasingly transmitted to the annulus, stressing its fibers [10, 11]. Continued strain on the annular fibers results in fissuring within and rupture of the annular complex [12, 13]. Stress concentration in the posterior annulus may predispose this region to disc prolapse. Fissuring and concentration of stress to the posterolateral region permit the migration of nuclear fragments to the periphery of the disc and herald the herniation of disc material.

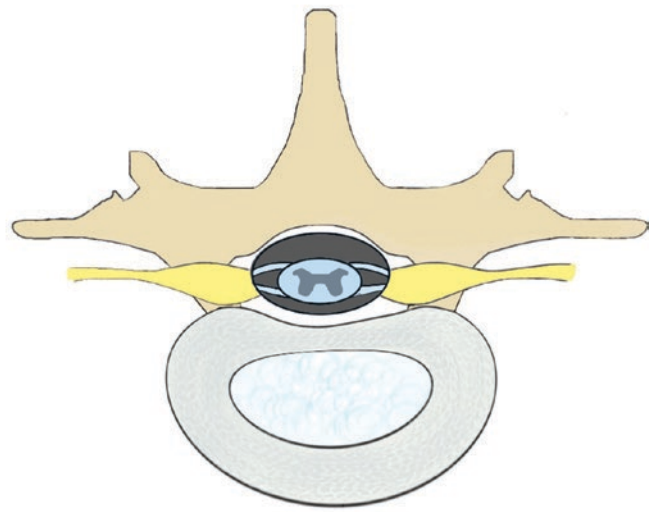

Fig. 12.1 Normal vertebral body and disc

Herniation is specifically defined as a "localized displacement of disc material beyond the limits of the intervertebral disc space." This classification encompasses all of the components of the disc (nucleus pulposus, annulus fibrosus, cartilaginous end plates). The disc space is defined by the end plates of the vertebral bodies and peripherally by the outer edge of the vertebral ring apophyses except osteophytes. Herniations are further classified as localized (<25% disc circumference), broad-based (25–50%), and circumferential (50–100%). The histology of herniated discs is quite variable, as is the degree of structural damage, ranging from protrusions (when the outer annular lamellae remain intact) (Fig. 12.2) to extrusions (when they are ruptured) (Figs. 12.3 and 12.5a) to sequestrations (in which the herniation is completely detached from the body of the disc) [14, 15] (Figs. 12.4 and 12.5b). The morphology of all of these herniations can be very heterogeneous and may include tissue that appears to be from any combination of the three materials that comprise the disc itself.

Radiculopathy refers to a disease process that affects the function of one or more nerve roots as they exit the spinal column. Structural lesions such as disc herniation or degenerative spondylosis are the most common cause; however, inflammatory, infectious or malignant disorders can exist. Radiculopathy can cause dysfunction in any of the three types of axons traveling in the spinal nerve roots. This

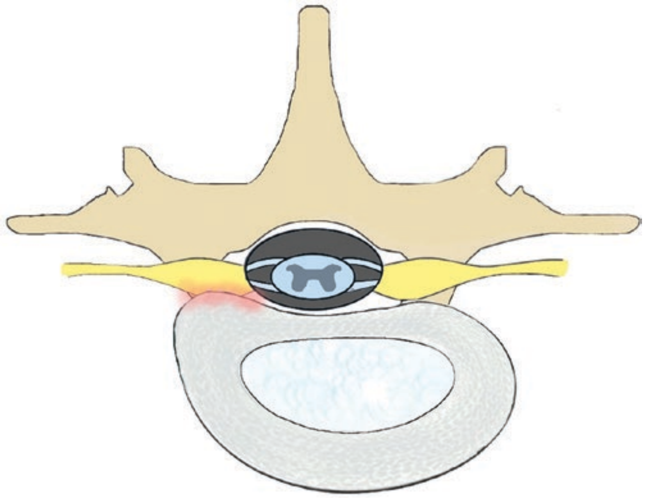

Fig. 12.2 Disc protrusion or “disc bulge”

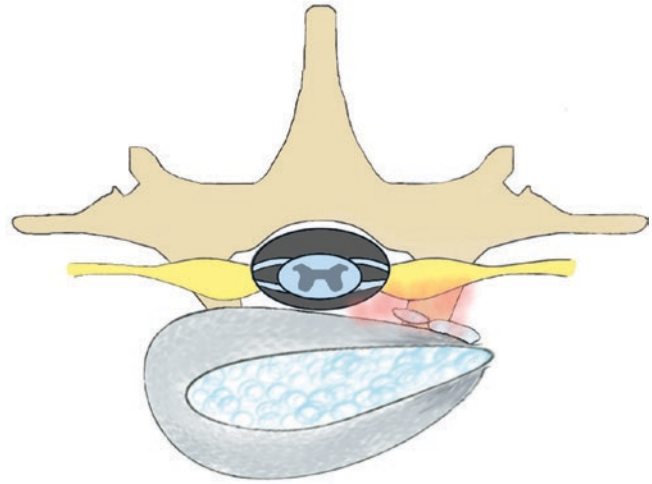

Fig. 12.4 Disc sequestration

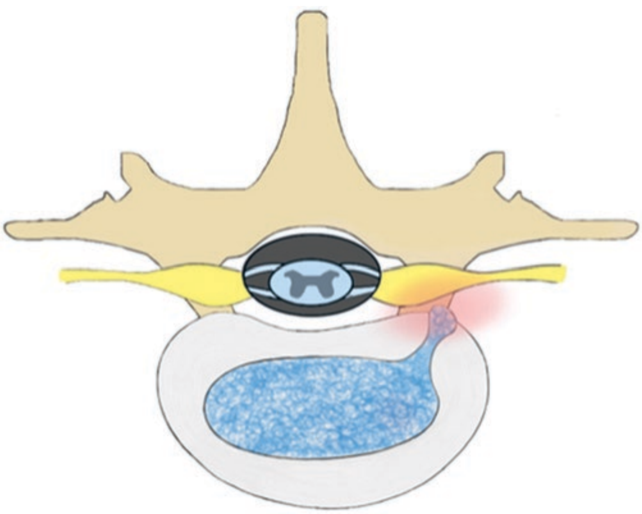

Fig. 12.3 Disc extrusion

includes somatosensory nerves, lower motor neuron nerves, or autonomic dysfunction. Somatosensory abnormality tends to be most prominent with radiculopathy and is described with a characteristic shooting pain along the dermatomal distribution of the affected spinal nerve root [16, 17].

Historic Perspective

While this condition has been described in medical literature dating back to Hippocrates, our understanding and treatment have grown much more sophisticated since the 1930s [18]. Mixer and Barr first introduced the concept of herniated disc material leading to radiculopathy in 1934, and the diagnosis of “ruptured disc” had gained favor in the medical community [19]. This team quickly pioneered a transdural approach for disc removal as the treatment of choice. Love, of Mayo Clinic (1937–1939) [20], introduced the extradural/interlaminar approach, which provides the basis of the standard open procedure performed even today. Caspar and Yasargil [21] applied the concepts of microsurgery to the procedure as early as 1977 through medial facetectomy and extradural dissection [22]. Advancements in lumbar radiculopathy treatment were paralleled by developments regarding cervical radiculopathy. In 1940, Stookey outlined three clinical manifestations that could occur following protrusion of cervical discs, namely, bilateral anterior pressure on the spinal cord, unilateral anterior pressure producing a Brown-Sequard syndrome, and nerve root pressure [23].

Due to the growing knowledge of disc herniations of the lumbar spine, surgeons began using decompression for treating cervical disc herniations [24]. Scaglietti, an Italian orthopedic surgeon, described one such surgery in 1949 for the treatment of cervical radiculopathy which like many of the early surgeries was performed through a posterior approach [25]. By the 1950s, surgeons had begun to shift to the anterior approach with the first being described by Smith and Robinson in 1955 [26]. By the mid-1990s, approximately 200,000 discectomies were performed annually in the United States alone [27]. New techniques are still being developed to reduce incision size, speed up recovery time, and improve long-term results [28–30].

Clinical Presentation

The clinical presentation of a herniated nucleus pulposus varies from no symptoms to rapid paralysis. Symptom severity often correlates with the acuity and degree of com-

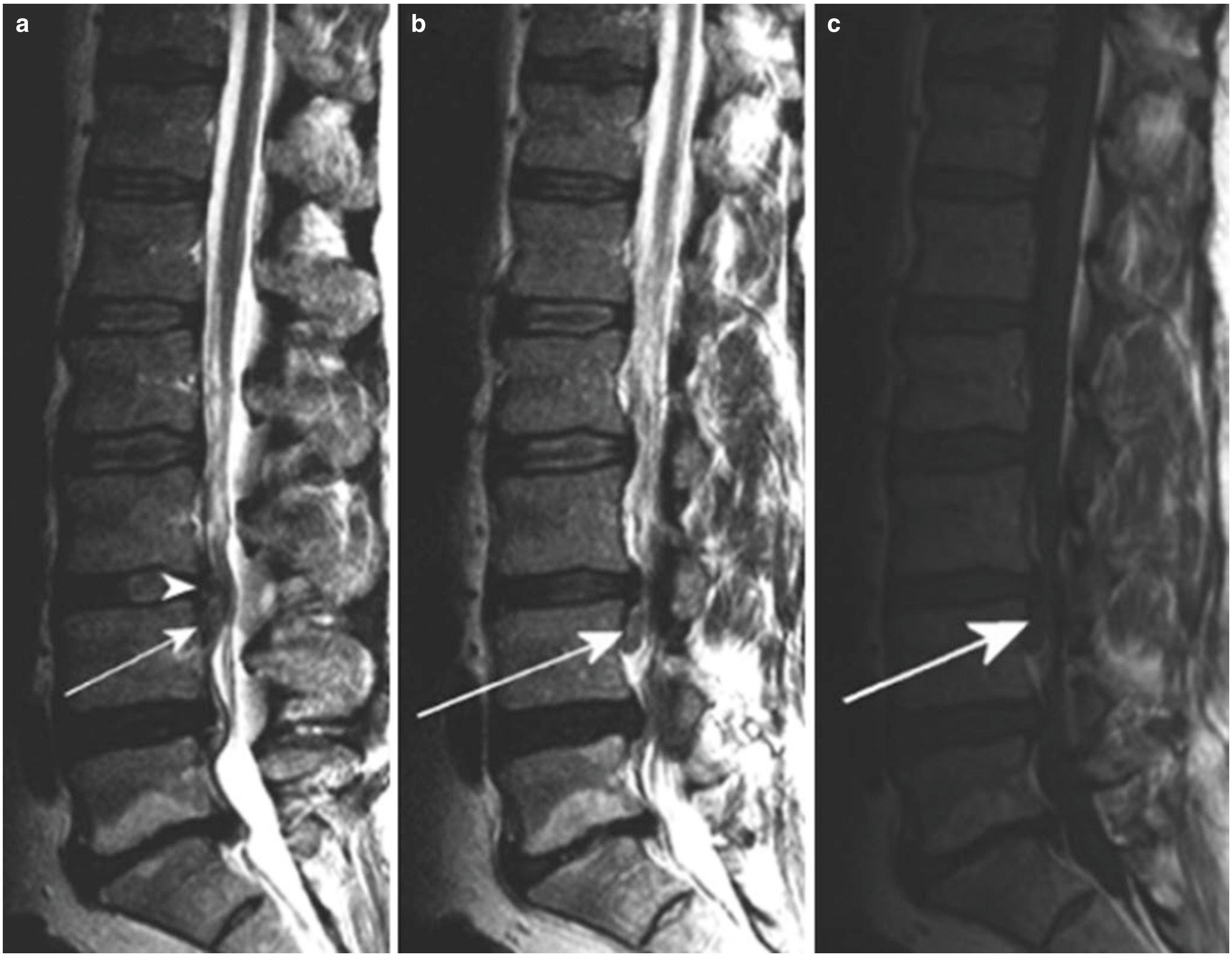

Fig. 12.5 MRI sagittal T2-weighted (**a**, **b**) and T1-weighted (**c**) image of herniated disc. In acute disc herniation, high signal intensity can be seen on T2-weighted MRI; however, with chronic intervertebral disc prolapse, low signal intensity is appreciated on T2-weighted MRI, which can be difficult to distinguish from osteophytes. Nerve root swelling and perineural enhancement can be seen after administration of a contrast agent. (Reprinted with permission from Hattingen et al. [140])

pression to the neural and vascular elements. In the lumbar spine, herniations are most common at L4–L5 and L5–S1. Manifestation of herniated discs ranges from progressive motor weakness along the affected nerve root(s) up to the bladder and bowel to sexual dysfunction from conditions such as conus medullaris and cauda equina syndrome. Fortunately, extreme presentations are rare, with incidence of about 1–2% in lumbar disc herniations and about 4 in 10,000 in all low back pain patients, but should connote immediate further evaluation [31]. Common presenting features of simple disc herniation include radicular pain and numbness, dysesthesias, motor weakness, and even muscle atrophy from prolonged compression or disuse. The lumbar spine is the most common location for symptomatic disc herniations accounting for 80% of all disc herniations. Common symptoms of symptomatic lumbar disc herniations are varied and include lower back and buttock pain, with or without radicular leg pain and sensory dysesthesias. These symptoms may be partially relieved with rest, activity modification, or change in position. Trunk flexion, prolonged standing or sitting, and straining maneuvers (i.e., Valsalva, cough) commonly increase the symptoms of disc herniation.

Risk Factors

Several factors have been investigated and associated with risk of developing neck and back radicular pain, including gender, prior episodes of neck or back pain, and occupational or recreational factors [32, 33]. Although some studies suggest that radiculopathy occurs more frequently in men, others have shown equal rates between genders. Previous history of axial low back pain is a well-established risk factor for lumbosacral radiculopathy, and a prior history of lumbosacral radiculopathy has been found in patients presenting with cervical radiculopathy [34]. Additionally, prior history of trauma was found in approximately 15% of cases of cervical radiculopathy, but this association has not been documented in the lumbar spine. Although there is a correlation between a higher body mass and low back pain, the same relationship does not appear to exist in radiculopathy [35]. Multiple studies have shown a genetic linkage for spinal canal size as well as occurrence of disc herniation and subsequent radiculopathy [36]. With regard to occupational factors, lumbosacral radiculopathy occurs more frequently in patients who have performed jobs requiring manual labor, who work in positions of sustained lumbar flexion or rotation, and who engage in prolonged driving [37, 38].

In a case-control study of juvenile disc herniation, the estimated risk of developing a herniated disc before the age of 21 was four to five times greater for patients who had a positive family history, as compared to those who did not [39]. Similarly, below 18 years old, the odds ratio of a patient with juvenile disc herniation to have a family history of disc surgery was 5.6 times that of a patient without disc herniation [40]. Clinicians should also consider risk factors for ankylosing spondylitis in this population. Symptoms of morning stiffness, improvement with exercise, alternating buttock pain, and awakening due to back pain during the second part of the night only should prompt immediate investigation [41].

While most factors focus on the risk of structural compromise, there is considerable evidence that psychological and occupational factors can also play a role [42]. Interestingly, evidence supports the idea that psychosocial variables can be more important in the progression to chronic pain and disability than biomechanical variables [43]. Other risk factors identified have also included cigarette smoking, driving, and lifting objects greater than 11.3 kg (25 lbs) while twisting the body [44, 45]. Frymoyer, in a 1992 review of the epidemiology of degenerative disc disease wrote, "Among the factors associated with its occurrence are age, gender, occupation, cigarette smoking, and exposure to vehicular vibration. The contribution of other factors such as height, weight, and genetics is less certain" [46]. A decade later, following a review of the same topic, which incorporated more recent research, Ala-Kokko concluded, "Even though several environmental and constitutional risk factors have been implicated in this disease, their effects are relatively minor, and recent family and twin studies have suggested that sciatica, disc herniation and disc degeneration may be explained to a large degree by genetic factors" [36]. Recent studies have investigated genetic influences of disc degeneration contributing to risk of radiculopathy using twin models that indicate heredity has a dominant role in disc degeneration and subsequent pathology [47, 48].

Evaluation of Radicular Pain

A thorough history and physical exam are the cornerstone in any clinician's armamentarium for the appropriate diagnosis and treatment of the patient. To develop the best differential diagnosis, one must be aware of correlative signs and symptoms. A key component in the initial evaluation of radicular pain is to rule out serious pathology and non-musculoskeletal diseases as a cause of pain and associated symptoms. Some symptoms that warrant further evaluation would include age less than 20 years old, history of trauma, presence of constitutional symptoms (i.e., fever, chills, weight loss, etc.), history of cancer, recent bacteremia, immunosuppression, unrelenting pain, or presence of cauda equina syndrome [49–51]. A comprehensive physical examination is necessary to aid in determining distributions of symptoms and identify all possible generators of pain. In the diagnosis of a radiculopathy, there is significant clinical utility in understanding the structures in the nervous system responsible for observed sensory deficits over a given area of the skin. Unfortunately, there has been a lack of consensus with regard to the precise localization of specific dermatomes. This variability among dermatomal maps arises from a number of difficulties encountered when attempting to create an accurate representation. Similar to a dermatome, the term myotome is used to describe all of the muscles that receive innervation from a single spinal segment or spinal nerve. Significant overlap in myotomes occurs in a similar fashion to dermatomes. Nearly every muscle receives motor nerve fibers from more than one spinal level [52]. Although many muscles have a dominant innervating nerve root, multiple spinal levels likely contribute to the complete innervation. Similar to dermatomes, there is some disagreement and overlap among varying sources with regard to the spinal levels responsible for the innervation of particular muscles. Despite the challenges present in dermatomal and myotomal mapping, they are very useful in the evaluation and diagnosis of radiculopathy.

Neurologic exam of a patient presenting with radiculopathy secondary to herniated nucleus pulposus will often show a sensory deficit, motor deficit, or combination of both. Sensory modalities including temperature, pinprick, proprioception, and vibration will be reduced in a dermatomal distribution. Deep tendon reflexes are often diminished or absent in the setting of radiculopathy as this causes a lesion of either the afferent or efferent limb of the monosynaptic arc responsible for these reflexes. When examining deep tendon reflexes, signs of upper motor neuron lesions should give the examiner pause. Upper motor neuron lesions will cause hyperreflexia. The Babinski and Hoffman signs may be present in patients with upper motor neuron dysfunction. The Babinski sign is elicited by stroking the lateral aspect of the sole of the foot with a blunt object. A positive test is indicated by dorsiflexion of the great toe. Hoffman sign is tested by briskly flicking the dorsal or palmar aspect of the distal phalanx of the middle finger. A positive result is recorded when the index finger and thumb show reflex flexion [53].

Physical Evaluation of Cervical Radiculopathy

The Spurling test has been described as "almost pathognomonic of a cervical intraspinal lesion" [54]. A study by Shah and Rajshekhar in 2004 evaluated the test on 50 surgical patients with positive herniated nucleus pulposus on magnetic resonance imaging (MRI). The results of the study revealed that the Spurling test was 92% sensitive and 95% specific, with a positive predictive value of 96.4% and a negative predictive value of 90.9%, concluding that the Spurling test is the gold standard for evaluating cervical radiculopathy [55].

The Lhermitte sign, also known as the barber chair phenomenon, is named after Jacques Jean Lhermitte, who described findings in 1920 when evaluating patients with spinal cord concussion and later in other neurologic diagnoses [56, 57]. There are still variations of how the Lhermitte sign is described; however, current description is an electric shock-like sensation that occurs on flexion of the neck that radiates down the spine, often into the legs, arms, and sometimes the trunk [58]. The findings have been described in various pathologic states caused by trauma to the cervical portion of the spinal cord, multiple sclerosis, cervical cord tumor, cervical spondylosis, or even vitamin B12 deficiency. There is limited literature evaluating the effectiveness of the Lhermitte sign in determining cervical radiculopathy. A review by Malanga and colleagues concluded that there is insufficient evidence of the inter-rater reliability, sensitivity, and specificity of the Lhermitte sign specifically. However, the active flexion and extension test described by Sandmark and Nissell resembles the Lhermitte sign and was found to have a high specificity (90%) and low sensitivity (27%) with a negative predictive value of 75% and positive predictive value of 55% [59].

Physical Evaluation of Lumbar Radiculopathy

The straight leg raise (SLR) test, also known as Lasegue sign, is a commonly used provocative test of radicular symptoms for lumbar pathology [60]. The SLR has been described in the literature since the late nineteenth century by numerous investigators, and subsequent eponyms have described the slight variations in testing. Through historical references and descriptions, the consensus of a positive finding using the classic SLR test is the elicitation of radicular pain down the posterior thigh below the knee with the patient supine and the leg, with knee extended, being raised between 30° and 70° [61]. Pain below 30 or beyond 70 is unlikely to be from nerve root irritation and more likely to be secondary to musculoskeletal tension. Overall, a positive SLR was present in 70–98% of patients with a lumbar disc pathology confirmed operatively [62]. The sensitivity of the test ranges from 72% to 97%, whereas specificity is between 11% and 66%. A systemic review and meta-analysis by Deville and colleagues compiled data from numerous studies evaluating the SLR test with surgery as reference standard. The results of the pooled data of these studies revealed the pooled sensitivity for the SLR test was 91% (95% CI 0.82–0.94) and the pooled specificity 26% (95% CI 0.16–0.38) [63].

There have been numerous studies to assess the validity and reliability of the crossed straight leg raise (CSLR). CSLR was compared with SLR to predict the presence of disc herniation on physical examination and found to be strongly reliable. In one study, CSLR was positive in 97% of patients as compared with 64% with SLR alone. When evaluating the presence of herniations at surgery, the study by Kosteljanetz and colleagues revealed that 19 of 20 positive patients had correlative findings [64]. Andersson and Deyo demonstrated that the CSLR had a higher specificity (85–100%) and a lower sensitivity (23–42%) as compared with the SLR when reviewing various studies as well as a high positive predictive value of 79% and negative predictive value of 44% [65]. These findings were confirmed by Deville and colleagues in a meta-analysis, which also revealed a low sensitivity (29%) and high specificity (88%) [63]. A more recent Cochrane review provided a similar conclusion, with CSLR showing high specificity (pooled estimate 0.90, 95% CI 0.85–0.94) with consistently low sensitivity (pooled estimate 0.28, 95% CI 0.22–0.35) [66]. A positive CSLR has been shown to predict poor prognosis of conservative management as well as those who would have positive outcomes with surgical intervention. Until recently there has been very limited evidence-based research on other lumbar provocative tests; however, with these new contributions, there is a better understanding of the utility of these tests.

Electrodiagnostic Evaluation

Electrodiagnostic studies such as electromyography (EMG) and nerve conduction studies (NCS) are common tools employed together in the evaluation of nerve compression or injury. Radiculopathy is suggested when abnormalities are noted in at least two muscles innervated by the same root, but different peripheral nerves, provided that muscles innervated by adjacent roots are normal [67]. While these tests can be a useful adjunct to the history and physical exam, there are several notable limitations to the various needle electrode exams (NEE), which should be taken into account. These tests can be painful to the patient as well as expensive. The electrodiagnosis of radiculopathy also relies on a myotomal pattern of abnormality; therefore variation in anatomic pattern of nerve roots must be accounted for in the interpretation [68]. EMG targets exclusively motor neurons, and nerve conduction studies are typically normal in radiculopathy; however, the more important reason to perform nerve conduction studies is to exclude other conditions that may mimic radiculopathy, especially entrapment neuropathy and plexopathy. Because most radiculopathies are predominantly sensory in nature, EMG lacks sensitivity in their evaluation.

Sensory nerve action potentials (SNAP) can be useful in the diagnosis of sensory radiculopathy; however, abnormalities on these studies are not part of the diagnostic criteria [69]. SNAPs can also be useful to rule out other potential causes such as peripheral polyneuropathy or entrapment mononeuropathy [70]. It is also difficult to localize a radiculopathy to a single nerve root. This effect is more pronounced when evaluating the brachial plexus in cases of cervical radiculopathy, with the most difficult levels to differentiate being C6 and C7 [71]. If lesions are acute or purely demyelinating in nature, the EMG study may be normal because the effect of fibrillating potentials and signs of axonal loss can take weeks to develop after nerve injury. Based on EMG alone, an abnormality of the nerve root cannot be distinguished from an abnormality of the motor neurons supplying that root. While clear and unequivocal clinical differences exist to allow the distinction, this is an important concept to keep in mind when evaluating results of these exams.

Evaluation of the usefulness of electrodiagnostics has been particularly challenging in the literature. Partially due to the limitations mentioned above, no "gold standard" exists by which to compare these methods. Patient selection in most studies that were reviewed was based on clinical symptoms, signs, or radiological findings. None of these indicators, in isolation or when combined, come close to a gold standard for the diagnosis of radiculopathy. The American Association of Neuromuscular and Electrodiagnostic Medicine published a large literature review in which they evaluated 75 studies to evaluate the utility of electrodiagnostic studies in the diagnosis of radiculopathy. The studies evaluated used various reference standards, which is a great limitation; however, sensitivity for EMG in cervical radiculopathy ranged from 30% to 95% with an abnormality rate of 50–71% in patients with clinical signs or radiological findings. Despite low sensitivity, needle EMG evaluation of 404 clinically normal myotomes revealed abnormality in only 1.5% [72]. Although the EMG study is very sensitive to the presence and approximate localization of a radiculopathy, equivocal or false-negative studies are not uncommon in true radiculopathy.

Imaging Evaluation

Clinicians should consider performing diagnostic imaging and testing for patients with low back pain when severe or progressive neurologic deficits are present [31]. Routine advanced imaging, with computed tomography (CT) or magnetic resonance imaging (MRI), has been discouraged due to several factors including the following: it has not been shown to improve patient outcomes if pain is present for less than 6 weeks with no red flag symptoms, and it identifies many radiographic abnormalities that are poorly correlated with symptoms, which could lead to additional or unnecessary procedures, and, in the case of CT, exposes patients to possibly unnecessary ionizing radiation [73–76]. On a similar note, studies have recognized a high prevalence of abnormalities seen on imaging in asymptomatic patients [77–82].

In patients for whom 4–6 weeks of conservative management has been unsuccessful and continued physical exam signs of nerve irritation exist, imaging should be pursued if they are possible candidates for surgery or other intervention or diagnostic uncertainty remains. MRI has become the initial imaging modality of choice, displacing myelography and CT in recent years. However, CT can be performed if a contraindication to MRI exists in the patient. Additionally, in patients who cannot undergo MRI, x-ray myelography with postmyelography CT of the spine is recommended to assess the patency of the spinal canal and thecal sac and of the neural foramen. The sensitivity of MRI in detecting lumbar nerve root compromise was very low at 0.25 (95% CI), while the specificity, which is the probability of getting a negative MRI test result on a patient with negative findings for nerve root compromise by physical examination, was relatively high at 0.92 (95% CI) [83, 84]. When comparing post-myelographic computed tomography (CTM) to MRI, Song et al. showed utility in diagnosis of foraminal stenosis and bony lesion; however, there was limitation in intra- and inter-observer findings in disc abnormality and nerve root compression [85].

Natural History

The advent of CT and MRI has significantly impacted the ability to diagnose and monitor disc herniations in patients with radiculopathy. These imaging studies have also made it possible to follow the natural course of disc herniations and compare the morphologic changes with symptomatic improvement [86, 87]. Key was the first to document the spontaneous regression of a herniated disc in the lumbar spine by myelography in 1945; however, this phenomenon was not confirmed until the use of follow-up CT scans in the lumbar and cervical spine in 1985 [88]. Saal and colleagues published a subsequent study in 1990 of 12 patients with documented lumbar herniations on CT. These patients were rescanned at an average of 25 months, and the following findings were documented: 46% of subjects had 75–100% resorption, 36% had 50–75% decrease in herniation size, and 11% had 0–50% regression. They found that the greatest degree of resorption was most frequently seen in the patients who had the largest herniations. However, they did not find a significant correlation between clinical and morphologic improvement [89].

Maigne and Deligne established a similar relationship between greater spontaneous resolutions in larger herniations in the cervical spine [90]. Bush and colleagues performed repeat CT scans on 106 patients 1 year after being diagnosed with lumbosacral radiculopathy [91]. Disc herniations that decreased or fully resolved were seen in 76% of patients. However, only 26% of disc bulges decreased or resolved. Masui and colleagues found that disc herniation size decreased by 95% in 21 patients who had follow-up MRI imaging 7–10 years after being diagnosed with disc herniation and radiculopathy [92]. Cribb and colleagues focused on massive lumbar disc extrusions that obscured greater than 66% of the spinal canal at the time of diagnosis of radiculopathy. They found that after 25 months, 14 out of 15 herniations had completely resolved [93]. Although Komori and colleagues did not find a correlation between clinical symptom and radiological improvement, this finding has been demonstrated in more recent studies [94]. Dellerud and Nakstad followed 92 patients over 14 months with follow-up CT scans and found a strong association between clinical improvement and reduction in the size of the lumbar herniation. They also found that central herniations and disc bulges were less likely to resolve, and the reduction in size of disc bulges was associated with a lesser degree of symptomatic improvement than with disc herniations [95].

Etiology of Symptoms

After a disc has prolapsed, it may affect nerve roots in many ways. The process of pain generation can be broken into two broad categories: mechanical and chemical [96]. The mechanical process may be caused by direct compression of the nerve root from a disc fragment. This may lead to alteration of the function of the nerve and may manifest as pain, weakness, or paresthesias along the nerve's distribution. Foraminal narrowing is another potential result and has been found to correlate with clinical success of intervention [97]. Herniations typically result in impingement of the adjacent, traversing nerve root. The patient may develop discomfort in a radicular, or dermatomal, distribution due to associated inflammation [98]. Classic posterolateral disc herniations characteristically compress the traversing nerve root and produce symptoms along that dermomyotome. Far lateral herniations, on the other hand, characteristically compress the exiting rather than the traversing nerve root. For example, a typical posterolateral herniated nucleus pulposus of the L4–L5 disc would produce symptoms from the fifth lumbar nerve root or L5 dermatome. Symptoms along this nerve root could also be generated from a far lateral herniation of the L5–S1 intervertebral disc [53]. Unlike the lumbar spine, where the traversing nerve root is most commonly irritated, in the cervical spine, disc herniations and spondylosis most often affect the exiting nerve root, so a C6–C7 disc herniation will usually cause C7 symptoms [99, 100]. The cervical spinal nerves exit the spinal cord oriented obliquely toward their respective neural foramen. The most commonly affected levels are C7 (45–60%), C6 (20–25%), and C5 and C8 (10%), possibly due to the normal anatomic finding of the C7/T1 foramina being the most narrow [101].

The chemical effects that generate pain are believed to stem from local inflammation propagated by the inflammatory cascade in response to components of the nucleus pulposus [102]. Several inflammatory markers have been found in herniated discs including IL-1α, TNF-α, TGF-β, and many others [103–109]. Increased levels of these inflammatory cytokines have been correlated with higher levels of pain in patients. After embryonic development is complete, the nucleus pulposus receives no exposure to the immune system due to the lack of blood vessels in direct contact with the NP itself [110]. Herniated disc material, particularly when sequestered, may release substances, which are capable of inducing an autoimmune response [96]. A growing body of evidence has implicated bioactive molecules within the disc as important in sensitizing nerve roots and participating in the pathogenesis of radiculopathy [111]. Along with inflammation and pain, this response has been shown to generate the production of matrix metalloproteinases, which play a crucial role in disc resorption [112].

Prognosis

The prognosis of radicular pain from a herniated nucleus pulposus is very favorable. Studies that look at back and leg pain specifically from a herniated disc have found resolution of symptoms in 6–12 weeks in up to 80% of patients and up to 90% showing improvement in symptoms without significant long-term disability [94, 113, 114]. Disc protrusion in the cervical region has had a much more complex history in terms of outcome with conservative management. Referral center-based studies have shown that cervical radiculopathy can cause persistent pain and incapacity in two-thirds of patients treated conservatively. In a group of 255 patients treated nonsurgically, only 29% obtained complete relief. Gore et al. followed 205 patients with nonoperatively treated neck and referred pain for an average period of 15 years in the late 1980s. At the end of the study period, only one-third had moderate to severe pain that interfered with their lifestyle [115]. Rothman and Rashbaum observed a similar group of patients for 5 years; 23% remained partially or totally disabled. A more recent study of 563 patients who presented to the Mayo Clinic from 1976 to 1990 also showed that 90% of patients had mild or no symptoms after 4–5 years of follow-up [116]. However, one-fifth of patients did not improve and ultimately underwent surgical treatment. Only one study specifically monitored for recurrent symptoms and found that recurrences occurred in 12.5% of patients during a follow-up period of 1–2 years [117]. The challenge with interpretation of earlier studies is the ever-evolving definition and understanding of the pathologic process associated with the herniated nucleus pulposus and evaluations in which to make an accurate diagnosis. As our understanding and evaluation have improved, so too has our ability to prognosticate in reference to pain caused by this specific pathology. Based on recent review, radiculopathy appears to be self-limiting in the majority of cases with conservative measures only.

Treatment

Medications in several classes have been shown to have moderate, primarily short-term benefits for patients with low back pain [118–122]. While many studies have been performed investigating these medications for efficacy in low back pain, very few have been performed to specifically address radiculopathy. The medication classes will be addressed in more detail; however, acetaminophen, NSAIDs, and skeletal muscle relaxants are popular first-line agents for clinicians [123]. Antiepileptics, such as gabapentin, tricyclic antidepressants, and judicious use of opioid pain medications have also been shown to have a significant but short-term benefit with back pain with or without radiculopathy [124]. Other treatment modalities in an initial conservative approach include physical therapy and low-impact resistance training with or without traction. Remaining active has also been shown to be more effective than resting in bed for patients with acute or subacute low back pain [125, 126]. In addition to medications and physiotherapy, prior to pursuing surgery, many clinicians will recommend less invasive options such as epidural steroid injections. A stepwise approach, in this fashion, has been shown to be therapeutic and cost-effective in those patients suffering from radiculopathy [127, 128]. While epidural corticosteroid injections are associated with early improvements, recent reviews and meta-analyses have shown benefits to be short-lived and have little effect on the natural history of the disease process [129–131]. Because of the inflammatory aspect of the herniated disc, directed anti-inflammatory therapy has been attempted. Transforaminal injection of steroid has shown success in decreasing the symptoms of disc herniation [132, 133]. Efforts to use infliximab, a TNF-blocker, however, have not shown strongly positive results despite success in decreasing inflammation in vitro [134]. Biological therapies including stem cell therapy, nerve growth factor inhibitors, and platelet-rich plasma have been evaluated in other chronic pain conditions and have yielded mixed results.

There is strong evidence to support the use of lumbar transforaminal epidural steroid injection (TFESI) in patients with acute-to-subacute unilateral radicular pain caused by herniated nucleus pulposus or spinal stenosis [135]. Leung et al. showed the technique of TFESI helps give time for better quality of pain relief, but it does not affect the ultimate need of surgery, especially for patients who require spinal fusion for spinal instability, either anticipated preoperatively or after surgical decompression. The patients who received a transforaminal epidural steroid injection for the treatment of symptomatic lumbar disc herniation had significantly better short-term pain improvement and required fewer long-term surgical interventions than patients who were treated with an interlaminar epidural steroid injection [136].

Few nonsurgical treatments have been studied for cervical radiculopathy. Most systematic- and evidence-based reviews have concluded that transforaminal ESI provides more benefit than interlaminar injections, but its use in the neck is limited because of the risk of catastrophic complications such as spinal cord infarction, particularly with depo-steroids [50]. Another randomized study in 169 patients with radicular pain found the combination of ESI and conservative treatment consisting of physical therapy and the adjuvants nortriptyline or gabapentin (or both) provided superior relief compared with either treatment alone (mean reduction in pain score of 3.1 in the combination group versus 1.9 in the others at 1 month; $P = 0.035$) [137]. Several high-quality reviews on the topic of progression to conservative management have led to incomplete or mixed results. Most studies on surgical techniques comparing them to conservative management show a high risk of bias. The benefit of surgery over a more conservative approach is not clear based on current evidence [138, 139].

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