

3 Neurological Presentation and Clinical Diagnosis of Spine Tumors

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Abstract

The clinical presentation of spinal tumors consists of a broad array of signs and symptoms, reflecting the diversity of tumor types and locations within the spine. A comprehensive clinical history and physical examination is critical to facilitating an early diagnosis. Neck and back pain are common presenting symptoms in nearly all patients with spine tumors. Several red flags have been described that increase suspicion of a malignant cause compared to a degenerative cause. Compression of dorsal and ventral nerve roots can produce radiculopathy, which includes sharp pain, sensory loss, and/or weakness in a dermatomal or myotomal distribution. Direct compression or infiltration of the spinal cord can produce symptoms of myelopathy, including muscle weakness and bowel and bladder deficits. Several grading and scoring systems have been proposed to classify spine tumors, establish the prognosis, and determine the optimal treatment regimen. Clinical suspicion of a spine tumor should be followed by imaging studies, including plain radiography, computed tomography, or magnetic resonance imaging, which constitute the gold standard for workup.

Keywords: spine, tumors, oncology, diagnosis, neurological examination

the incidence of spine tumors, with an estimated $\geq 70\%$ people experiencing at least one episode of back pain in their lifetime.⁸ Particularly in the elderly population, neck and back pain frequently arises from degenerative conditions and spondylosis.⁹ Indeed, the prevalence of malignancy in patients with back pain is estimated at only less than 1%, so that the consideration of malignancy is not usually at the forefront of clinical assessment in patients presenting with neck or back pain.^{10,11} Neck and back pain in the pediatric population is less likely attributable to a degenerative condition.

Patients often describe the pain stemming from a tumor as constant and unremitting, increasing in intensity over time, and worse at night or early in the morning.^{12,13} Patients may therefore report a history of disrupted sleep due to pain, which may reflect lower levels of endogenous steroids in the body at night compared to daytime.¹⁴ The pain usually localizes to the region of the tumor and generally improves with anti-inflammatory medications.¹⁵ Patients can also develop mechanical pain from spinal instability caused by destruction of the bony spine from the tumor. Mechanical back pain worsens with standing, ambulation, and weight bearing; improves with recumbency; and typically does not improve with anti-inflammatory medication.¹⁵ Surgical stabilization of the spine is required to alleviate pain and prevent worsening instability.

3.1 Introduction

Spinal tumors represent a heterogeneous group of pathologies including both benign and malignant neoplasms within the intramedullary, intradural extramedullary, and extradural compartments. Consequently, their clinical presentation varies in scope, reflecting the range of osseous and neurovascular structures affected by a given pathology.¹ The spectrum of presentation can pose a challenge to diagnosis, and spinal tumors can be initially mistaken for non-neoplastic processes, such as degenerative disorders of the spine, vascular lesions, inflammatory lesions, and cysts.^{2,3} The insidious course of most spine tumors can result in a significant delay until diagnosis.⁴

A comprehensive clinical history, a standardized neurological examination, and modern neuroimaging tools, along with a robust foundation of neuroanatomy and neurophysiology, are necessary to facilitate an accurate diagnosis. This chapter provides an overview of subjective and objective patient parameters, along with scoring calculators that aid in decision-making, to improve the early detection of spinal malignancy, prevent irreversible neurological damage, and curtail the spread of metastatic spinal diseases.

3.2 Neck or Back Pain

Nearly all patients with spinal tumors present with neck or back pain as the initial or presenting symptom.^{5,6,7} However, the incidence of neck and back pain is substantially higher than

3.2.1 Red Flags of Back Pain

Given that most causes of back pain are not neoplastic in origin, several “red flags” have been proposed to describe an essential set of clinical symptoms and signs that should prompt consideration of a neoplastic etiology.¹⁶ Attempts have been made to develop screening tools to help identify high-risk patients while avoiding unnecessary and expensive ancillary tests in low-risk patients.¹⁷ Several clinical practice guidelines have been proposed to evaluate these red flags; however, there is a lack of consensus on the optimal set of criteria.^{16,18} ▶ Table 3.1 details a comprehensive list of 21 red flag signs and symptoms and their pooled likelihood ratios identified from a systematic review of six studies of patients with low back pain, although the precise flags differ across clinical practice guidelines.¹⁹ A review of eight clinical practice guidelines published around the world between 2000 and 2008 found consensus that workup should focus on identifying red flags of back pain, including age at onset, unexplained weight loss, and concomitant neurological deficits. Magnetic resonance imaging (MRI) is warranted when red flags are identified.²⁰

The 2007 American College of Physicians clinical practice guideline for the diagnosis and treatment of low back pain sought to provide standardized recommendations for the evaluation of lower back pain and present high-risk features concerning for spinal malignancy. Features identified by the guidelines suspicious for a neoplasm included a prior history of cancer with new onset of lower back pain, multiple risk factors for spinal malignancy, age greater than 50 years, unexplained

Table 3.1 Red flags of back pain and associated likelihood ratios identified by Henschke et al that trigger suspicion of spinal malignancy¹⁷

Red flag	Likelihood ratios
Clinical history	
Age > 50 y	2.2
Duration > 1 mo	2.6
Failure to improve after 1 mo	3.0
History of cancer	23.7
Insidious onset	1.0
No relief with bed rest	1.7
Recent back injury	0.2
Severe pain	1.7
Thoracic pain	1.2
Unexplained weight loss	3.0
Physical examination	
Fever > 100 °F	1.8
Muscle spasm	0.5
Neurological symptoms	7.5
Neuromotor deficit	0.4
Spine tenderness	0.4
Laboratory evaluation	
Anemia	3.9
ESR ≥ 20	2.3
ESR ≥ 50	18
ESR ≥ 100	55.6
Hematocrit < 30%	18.2
WBC ≥ 12,000	4.1
Abbreviations: ESR, erythrocyte sedimentation rate; WBC, white blood cell.	

weight loss, and failure of symptoms to improve after 1 month. These risk factors prompt further workup, including plain radiography and MRI. In contrast, patients without suspicion for a serious condition can be initially treated with conservative and pharmacological interventions.²¹

A 2013 systematic review assessed the diagnostic accuracy and reliability of red flags identified from 14 studies against the risk factors identified by the American College of Physicians in their clinical practice guidelines.¹⁶ The authors found that most red flags identified by the guidelines had posttest probabilities of less than 3% for the likelihood of spinal malignancy, while the red flag “history of cancer” had the highest posttest probability at 7% in primary care settings. Red flags from other studies were similarly uninformative, with the exception of the presence of concomitant neurological symptoms.¹⁶ Laboratory tests can be used as further workup in patients with lower back pain, and elevated inflammatory markers and low hematocrits have been identified as significantly increasing the likelihood of cancer.

In addition to the red flags associated with back pain, malignant tumors of the spine can be associated with systemic findings, particularly when they arise from metastatic disease. Systemic symptoms and signs of malignancy include fatigue, unintentional weight loss, dermatologic changes, night sweats, muscle atrophy, persistent low-grade fever, lymphadenopathy, bowel changes, and confusion, although these are not unique to malignant spinal tumors.^{22,23} The presence of these symptoms

in addition to back pain should prompt further workup for a malignant cause.^{5,24,25} Our algorithm for the workup of patients presenting with neck or back pain in the setting of spinal tumors is presented in ► Fig. 3.1.

3.3 Radiculopathy

Radiculopathy can result from compression or invasion of the spinal nerve roots by a neoplastic process and is defined by pain, sensory loss, and/or weakness in a dermatomal or myotomal distribution. Therefore, radiculopathy in the cervical or lumbar spine results in pain or numbness along the upper or lower extremities, respectively, while radiculopathy in the thoracic spine is associated with bandlike pain around the chest or abdomen.¹⁵ The pain is often described as a burning, sharp, or electric sensation.²⁶

The dorsal nerve roots emerge from the posterior aspect of the spinal cord and transmit sensory information. Dorsal root compression therefore results in sensory deficits including loss of fine touch, proprioception, and vibration. Irritation of the afferent root and subsequent inappropriate firing of dorsal root axons can produce sharp pain and paresthesias over a dermatomal distribution.²⁷ The pain of radiculopathy is worsened by activities that stretch the compressed nerve root. Valsalva maneuvers, such as coughing and straining, can worsen or reproduce the radicular pain, although reproducibility may be poor.²⁸ Pinprick sensation, which ultimately converges into the spinothalamic tracts, has less dermatomal variability and overlap compared to the sensation of light touch, and is therefore the preferred modality for evaluation and localization of the affected dorsal nerve root(s).^{27,29,30}

Ventral root compression can manifest as weakness, with subsequent muscle atrophy and diminished tone in the extremities. However, weakness does not typically arise from monoradiculopathies as muscles often receive innervation from multiple adjacent roots.²⁷ Chronic radiculopathy can result in spontaneous muscle fiber contractions, known as fasciculations, in a myotomal distribution.²⁷ The ventral root axons also have a small number of sensory afferents, such that ventral radiculopathy can produce diffuse aching pain in the muscles innervated by those nerve roots.^{31,32} However, the sensory modalities of touch, proprioception, and vibration would be preserved, distinguishing this pain from a dorsal radiculopathy.

3.4 Myelopathy

Myelopathy results from damage to the spinal cord caused by tumor compression or invasion. In addition to the aforementioned symptoms of pain and numbness, myelopathy can produce muscle weakness and bowel and bladder deficits. Neurological deficits and myelopathy are a common presenting symptom of spinal tumors, generally arising from invasion of spinal tumors into the spinal canal or neural foramina, producing compression of the spinal cord or nerve roots.³³ Symptoms reflect involvement of spinal cord tracts and nerve pathways (► Fig. 3.2). Pathological fractures can also produce compression of the neural elements. Although neurological deficits rarely occur as a first symptom, they are present in an estimated 35 to 75% of patients at the time of diagnosis.^{6,34,35}

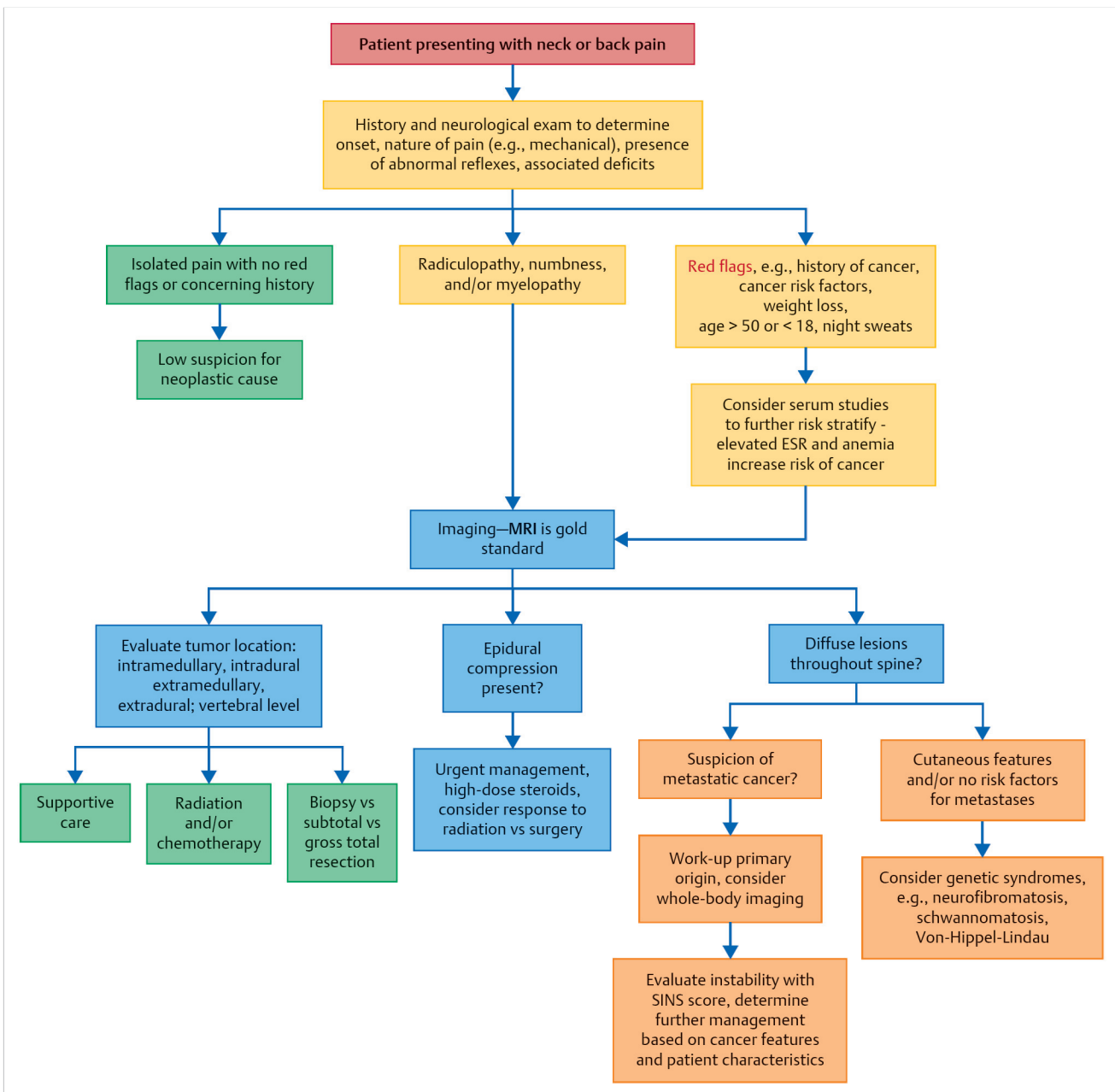


Fig. 3.1 Workup of patients presenting with neck or back pain. The presence of numbness, neurological deficits, or red flags should prompt further workup with magnetic resonance imaging (MRI). The radiographic features and location of the lesion then guide further management. Note: Created in BioRender.com.

Early symptoms of myelopathy generally include weakness and difficulty with ambulation, which progresses to bladder and bowel dysfunction and worsening of ambulatory capacity.¹⁵ The severity of neurological deficits depends on the tumor location, number of spinal cord levels involved, and extent of tumor invasion. Thoracic and conus intramedullary tumors have been shown to produce more substantial neurological deficits at the initial presentation, such as muscle weakness and difficulty with ambulation, compared to tumors of the cervical spinal cord.³³ The differential effects may reflect the larger size of the cervical spine, which would require larger tumors to produce

the same degree of motor deficits seen in more caudal segments of the spinal cord.³⁶

3.4.1 Motor and Sensory Deficits

Muscle weakness in the extremities is a common symptom of myelopathy arising from spinal tumors. Compression of the motor tracts from a tumor is analogous to a spinal cord injury, and early diagnosis is crucial to allow for early intervention and prevent worsening dysfunction. The motor neurons originate within the motor area of the cerebral cortex and transmit their

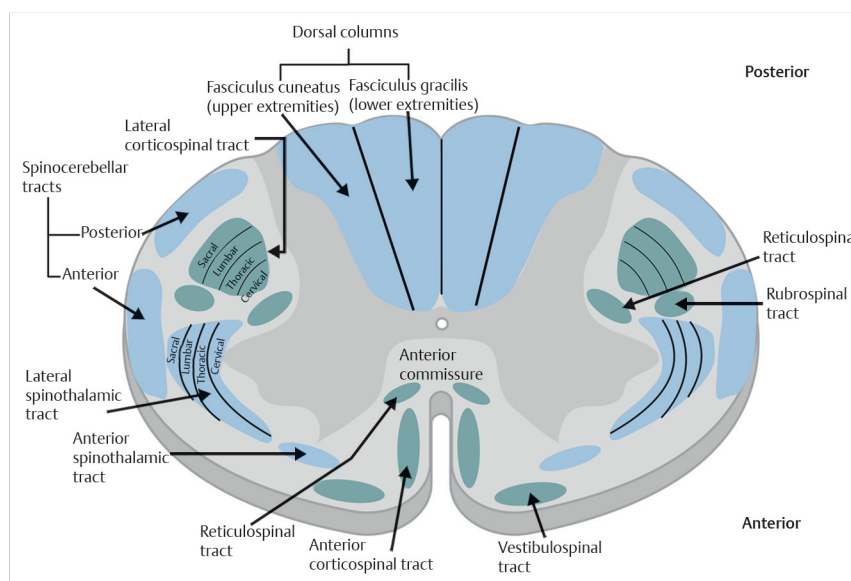


Fig. 3.2 Overview of major spinal cord tracts including descending pathways in *blue* and ascending pathways in *green*. Spinal cord compression or lesions can produce motor and sensory deficits by interfering with the physiological function of these tracts. The dorsal columns transmit vibration and proprioception, the spinothalamic tracts transmit pain, temperature, and crude touch, and the spinocerebellar tract relays proprioceptive information to the cerebellum. The corticospinal tract is the major motor pathway and transmits motor information from the motor cortex to the muscles. The reticulospinal tract arises from the reticular formation and facilitates reflex responses and influence muscle tone. The rubrospinal and vestibulospinal tracts are extrapyramidal tracts involved in motor control.
Note: Created in BioRender.com.

axons to the spinal cord via the pyramidal tracts, decussating in the inferior medulla before entering the spinal cord as the lateral funiculus. Within the spinal cord, they are labeled the corticospinal tracts. These first-order neurons then synapse on lower motor neurons and premotor interneurons.³⁷

Impairment of the corticospinal tracts produces signs consistent with an upper motor neuron (UMN) lesion, including spastic weakness manifesting as a “clasp-knife” phenomenon, described as a sudden increase in tone and resistance to movement upon brisk stretching of muscles followed by a rapid decrease in resistance at the end range of motion. Classically, the spasticity of a UMN lesion is associated with hypertonicity, clonus, hyperreflexia, and a positive Babinski sign.³⁷ In contrast, impairment of the ventral nerve roots from radiculopathy results in lower motor neuron deficits, characterized by flaccid paralysis, decreased tone, hyporeflexia, muscle atrophy, and fasciculations.³⁸ The pattern of motor weakness, tone, and deep tendon reflexes are essential clues to distinguishing between these two types of spinal injuries.

The spasticity associated with UMN injury differs from the rigidity of basal ganglia disease, such as Parkinson's disease, which produces a “lead pipe” rigidity in which the resistance to a range of motion is not rate or force dependent and is constant throughout the range of motion.³⁹ Neurogenic claudication can also manifest as a symptom of spinal tumors, consisting of pain and a sensation of heaviness in the extremities that affects ambulatory capacity.²⁷ The pain is relieved by sitting or lumbar flexion and is often an early symptom of spastic weakness from a UMN lesion.⁴⁰ Neurogenic claudication should be distinguished from intermittent claudication of vascular origin, which can be assessed by determining the strength of the pulse in the lower extremities on clinical examination.^{27,41,42}

The dorsal columns and lateral and anterior spinothalamic tracts are responsible for sensory modalities. Deficits in the posterior columns produce paresthesia, numbness, or a sensation of tightness in the ipsilateral limb, along with loss of

proprioception and vibration, which can even manifest as an ataxic gait.^{43,44} Disruption of the spinothalamic tracts produces pain described as an aching or burning sensation in the contralateral extremity or loss of pain and temperature sensation.²⁷

3.4.2 Bowel and Bladder Function

Tumor compression or infiltration of the cord can also produce autonomic dysfunction, particularly bowel and bladder deficits, including incontinence or retention. These deficits can significantly deteriorate patients' quality of life and tend to present later in the disease course.⁴⁵ Rates of bowel and bladder deficits can be high in patients with spine tumors, with various studies reporting urinary incontinence in nearly 17% of patients with cauda equina tumors and 20% of patients with intramedullary tumors, while bowel dysfunction is present in around 8% of patients with intramedullary tumors.^{33,46} Moreover, the rate of bowel and bladder dysfunction has been reported to be higher when tumors are present in caudal regions of the spinal cord compared to more cranial regions, such as the cervical spine.³³

The sympathetic and parasympathetic nervous systems regulate bladder function under control of the micturition center in the pons. Sympathetic efferents originating from the L1–L3 levels relax detrusor smooth muscles to produce urinary retention, while parasympathetic efferents from the S2–S4 levels promote contraction of detrusor muscles to produce urinary voiding.²⁷ Lumbar splanchnic and sacral pelvic nerves provide innervation to the colon and rectum.⁴⁷ Impairment of descending cortical tracts above S1 can produce overactivity of the detrusor muscles and urinary sphincter, causing involuntary emptying and urinary incontinence. Moreover, conus medullaris syndrome and cauda equina syndrome, which can arise from compression of these regions by tumors, can affect bowel and bladder function bladder.⁴⁸ Assessment of bowel and bladder function should include testing of the anal wink and bulbocavernosus reflexes, with initiation of bowel and bladder management programs for patients with deficits.⁴⁹

3.5 Grading and Scoring Systems

Several scoring systems have been designed to assist in workup and management of patients with spine tumors, particularly for extradural and metastatic tumors. Prognostic scoring systems for spine metastases include the Tokuhashi score, Tomita score, Baur score, Linden score, Katagiri score, and Rades score, which incorporate the primary site of the tumor and presence of visceral metastases.⁵⁰ These systems can predict life expectancy and be used to assess the benefits of operative intervention, although variability between the estimated and actual survival period can occur.

The Tokuhashi score was published in 1989 and revised in 2005 to feature greater differentiation of the primary tumor site, increasing the number of total points from 12 to 15 (► Table 3.2). Tokuhashi et al reported that the revised score was 63% accurate in predicting prognosis among 128 patients with metastatic spinal tumors.⁵¹ The score includes points for patients' general condition, number of extraspinal bone metastases, numbers of vertebral metastases, metastases to visceral organs, primary site of cancer, and Frankel score, which classifies the extent of motor and sensory deficits. The Tomita score for spinal metastases is simpler, reflecting three primary factors with several subcategories: primary tumor grade (slow, moderate, or rapid growth), presence of visceral metastases to the lungs, liver, kidneys, or brain, and presence of bone metastases. The total score informs the surgical strategy, with lower scores preferring wide excisions for long-term local control, while higher scores preferring palliative surgery or supportive care.⁵²

The spinal instability neoplastic score (SINS) was introduced in 2010 by the Spine Oncology Study Group to help determine the presence of instability in patients with spinal tumors (► Table 3.3). Instability can arise from pathological fractures or destruction of vertebral bodies by neoplastic processes.⁵³ Instability is associated with poor outcomes and requires prompt treatment; however, disagreements concerning the evaluation of oncologic instability can complicate the diagnosis. The SINS score was designed to introduce consensus in the workup of oncologic instability and assigns patients up to 18 points on the basis of six elements, including location of the tumor within the spine, type of pain, nature of the bony lesion (lytic, blastic, or mixed), spinal alignment, degree of collapse of the vertebral body, and involvement of the posterolateral spinal elements.⁵³ Assessment of SINS reliability has shown a high degree of interobserver and intraobserver agreement.⁵⁴

In addition to scoring systems, in which various risk factors or signs/symptoms are summed to produce a prognostic score, grading systems can be used to assess patients' preoperative functional status. The modified McCormick scale is commonly used for assessment of patients with intradural tumors, with grades ranging from I to V depending on the extent of motor and sensory deficits and degree of functional independence (► Table 3.4).⁵⁵ The scale is similar to the American Spinal Injury Association Impairment Scale, which also measures motor and sensory function on a 5-point grading scale.

3.6 Radiographic Evaluation

Workup of a patient with back pain and/or myelopathy often begins with plain anteroposterior and lateral X-ray films, which

Table 3.2 The revised Tokuhashi score published in 2005 consists of six parameters and correlates with survival in patients with metastases to the spine

Parameter	Score
Karnofsky's performance status	
Poor (<50%)	0
Moderate (50–70%)	1
Good (>70%)	2
Frankel grade of spinal cord injury	
Grades A–B (complete injury)	0
Grades C–D (incomplete injury)	1
Grade E (no injury)	2
Primary site of origin	
Bladder, esophagus, lung, osteosarcoma, pancreas, stomach	0
Gallbladder, liver, unidentified	1
Other	2
Kidney, uterus	3
Rectum	4
Breast, carcinoid tumor, prostate, thyroid	5
Number of extraspinal bone metastases	
≥ 3	0
1–2	1
0	2
Number of vertebral body metastases	
≥ 3	0
2	1
1	2
Metastases to major organs	
Unresectable	0
Resectable	1
No metastases	2
Total score	
Poor prognosis, conservative treatment	0–8
Palliative surgery, or excisional for patients with single lesions without metastases to major internal organs	9–11
Best prognosis, excisional surgery	≥ 12

Note: A score of 0 to 8 is associated with a poor prognosis and favors conservative treatment, scores of 9 to 11 favor palliative surgery and occasionally excisional surgery (in the case of single lesions without metastases to major internal organs), and scores of 12 to 15 favor excisional surgery.

Source: Based on Tokuhashi Y, Uei H, Oshima M, Ajiro Y. Scoring system for prediction of metastatic spine tumor prognosis. *World J Orthop* 2014;5(3):262–271.

can show pathological fractures, instability, scoliosis, sclerosis, and loss of pedicle height stemming from malignancies and tumor infiltration. Vertebral body destruction often reflects a primary tumor, as metastatic tumors typically infiltrate the bone marrow rather than the cortical bone.⁵⁶ However, X-ray films have low sensitivity and specificity and are consequently inadequate for screening and depicting the tumor contours.⁵⁷ Significant destruction of the bony cortex is required for detection on X-rays.⁵⁸ Further workup and treatment planning requires computed

Table 3.3 Components of the spinal instability neoplastic score for assessment of instability in the setting of spinal neoplastic disease

Parameter	Score
Location	
Junctional (O–C2, C7–T2, T11–L1, L5–S1)	3
Mobile (C3–C6, L2–L4)	2
Semirigid (T3–T10)	1
Rigid (S2–S5)	0
Posterolateral involvement	
Bilateral	3
Unilateral	1
Neither	0
Spinal alignment	
Subluxation/translation	4
De novo deformity	2
Normal alignment	0
Bone lesion	
Lytic	2
Mixed	1
Blastic	0
Vertebral body collapse	
> 50%	3
< 50%	2
No collapse, > 50% body involved	1
None of above	0
Pain	
Mechanical	3
Present but not mechanical	1
No pain	0
Total score	
Stable	≤ 6
Indeterminate	7–12
Unstable	≥ 13

tomography (CT) to visualize the bony anatomy in high resolution and MRI to assess the soft tissue, presence of epidural compression, and bone marrow infiltration.⁵⁹ CT scans are particularly helpful for extradural tumors, where they can help evaluate lesion morphology and growth rate. CT scans can also differentiate osteolytic and osteoblastic lesions.¹⁵ Moreover, CT scans are necessary for planning surgeries involving spine hardware.

MRI, the gold standard for imaging spine tumors, is especially vital for evaluating intradural tumors and neural structures.^{59,60} Heterogeneous enhancement patterns on MRI can represent vertebral collapse, while involvement of the pedicles suggests a malignant cause, rather than a benign osteoporotic cause. Heterogeneous signal intensity and diffuse involvement of the vertebral bodies is suggestive of metastases.⁵⁷ Contrast enhancement on T1-weighted MRI further helps confirm the diagnosis of a primary spine tumor and can be seen in both primary and metastatic lesions in the extradural and intradural space.⁶¹ Differential patterns of enhancement on T1- and T2-weighted MRI, such as isointense, hypointense, or hyperintense, can be used to narrow the differential diagnosis of spinal

Table 3.4 Components of the modified McCormick scale frequently used to assess neurological function in patients with intradural tumors

Grade	Definition
I	No deficits
II	Mild motor or sensory deficit with functional independence
III	Moderate deficit limiting function, independent with an external aid
IV	Severe motor or sensory deficit limiting function, dependent functional status
V	Paraplegia or quadriplegia

tumors. However, caution must be applied, as some tumors can display heterogeneous enhancement patterns, such as intramedullary subependymomas, or lack enhancement altogether.⁶² Identification of a vertebral lesion on radiographic imaging should be followed by a pan-spine MRI to determine if the finding represents an isolated primary tumor or a metastatic lesion.^{56,63}

The morphological features of intradural tumors and location within the thecal sac provide useful information. For example, intramedullary ependymomas typically appear as well-circumscribed lesions within the central canal and often present with syringomyelia and cystic changes, astrocytomas classically arise eccentrically in the cord and present diffuse margins, and hemangioblastomas localize to the pial surface.⁶³ Dynamic contrast-enhanced MRI can be used to characterize tumor vascularity and determine the value of preoperative embolization.⁶⁴ Patients with contraindications to MRI, such as MR-incompatible instrumentation or claustrophobia, can undergo CT myelography, whose higher spatial resolution compared to MRI scans allows for improved visualization of the thecal sac.⁶⁵

Patients with a known history of cancer presenting with sudden neurological deficits, such as difficulty ambulating, should undergo emergent MRI.⁶⁶ Metastases can invade the epidural space and compress the cord, producing acute back pain, radicular pain, and neurological deficits. Rapid evaluation and diagnosis are critical to improving outcomes after treatment, which includes corticosteroids, surgery, and radiotherapy.⁶⁷

Interpretation of radiographic images should also consider the patient's age and neurological presentation to refine the differential diagnosis of potential lesions. Adjunctive radiographic modalities, such as bone scintigraphy and positron emission tomography, are less commonly used for workup but can be considered when the diagnosis is unclear. Bone scintigraphy can depict lesions of the bony spine while screening the entire skeleton but suffer from poor specificity and difficulty differentiating benign and malignant tumors.^{56,59,68,18} F-fluorodeoxyglucose positron emission tomography/CT scans offer greater accuracy and can noninvasively illustrate tumor metabolic activity, which may correlate with tumor growth and survival.^{69,70} Percutaneous CT-guided needle biopsies can be performed for diagnosis of vertebral lesions of unknown primary origin, including metastatic tumors, which can help formulate a treatment plan.⁷¹ Accuracy of percutaneous biopsies is best below the cervical spine.^{56,59} In contrast, intradural tumors often require surgical resection for definitive diagnosis by pathology.

3.7 Electrophysiology

Electrophysiological studies can aid workup in patients presenting with radiculopathies. Compression of nerve roots from tumor mass can result in numbness, weakness, and radiating pain along a myotomal or dermatomal distribution.⁷² Nerve conduction studies can assess sensory nerve action potentials and motor evoked potentials, while needle electromyography can detect abnormal spontaneous activity and fibrillations that suggest radiculopathy.⁷³ Nonetheless, electromyogram (EMG) is not routinely obtained for spine tumors, with the clinical history, physical examination, and imaging modalities generally sufficient.

3.8 Laboratory Markers

Abnormalities in a complete blood cell count, such as anemia, neutropenia, thrombocytopenia, pancytopenia, or leukocytosis, increase the likelihood of malignancy, and may be discovered incidentally during routine laboratory screens or as part of the workup for other diagnoses. Metastatic spine tumors can be further evaluated with tests unique to the tumor's primary origin, such as prostate-specific antigen for prostate tumors and protein electrophoresis for multiple myeloma.¹⁵ Comprehensive metabolic panels can be used to stratify patients preoperatively and predict surgical morbidity. Hypoalbuminemia has been associated with increased risk of sepsis, need for transfusions, prolonged length of stay, and nonhome discharge in patients undergoing surgery for spine tumors.⁷⁴ Lower preoperative hematocrit and mean corpuscular hemoglobin concentrations have also been shown to increase the risk of intraoperative transfusion.⁷⁵ The neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio have also been shown to differ between benign and malignant tumors and can assist in diagnosis.⁷⁶ Several web-based calculators are freely available to predict surgical risks using preoperative laboratory values in patients with spine tumors.^{75,77,78}

There is also increasing interest in the development of liquid biopsies, which sample cell-free DNA in the cerebrospinal fluid, for the evaluation of spinal tumors.⁷⁹ These tests would allow for a preoperative pathological diagnosis that also can evaluate the unique genomic and mutational landscape of the tumor, allowing for the possibility of targeted therapeutic approaches. They would also allow continued evaluation of patients over time, replacing expensive imaging and enabling more frequent follow-up to determine treatment response.⁸⁰ However, most investigations into liquid biopsies for central nervous system neoplasms have focused on brain tumors, and the spine remains an underexplored but active area of interest.^{81,82}

3.9 Conclusion

Tumors of the spine and spinal cord can produce an array of signs and symptoms, including neck and back pain, radiculopathy, muscle weakness, ataxia, and bowel and bladder dysfunction. Evaluation of patients presenting with isolated back pain should consider red flags in order to avoid missing a potential neoplastic cause. A thorough history and physical examination can help localize the lesion and narrow the differential

diagnosis. Suspicion of a tumor should prompt imaging, particularly MRI and CT, which can determine the tumor's neuraxial location and position within the spinal compartments. Early diagnosis of malignancy is essential for preserving neurological function and improving overall survival. Initiating an early oncologic workup offers greater opportunity for treatment prior to the onset of irreversible deficits and potential oncological emergencies, such as spinal cord compression and cauda equina syndrome.

References

- [1] Kumar N, Tan WLB, Wei W, Vellayappan BA. An overview of the tumors affecting the spine-inside to out. *Neurooncol Pract*. 2020; 7 Suppl 1:i10–i17
- [2] Fanous AA, Olszewski NP, Lipinski LJ, Qiu J, Fabiano AJ. Idiopathic transverse myelitis mimicking an intramedullary spinal cord tumor. *Case Rep Pathol*. 2016; 2016:8706062
- [3] Wein S, Gaillard F. Intradural spinal tumours and their mimics: a review of radiographic features. *Postgrad Med J*. 2013; 89(1054):457–469
- [4] Kim DH, Chang UK, Kim SH, Bilsky MH. Neurologic presentation of spinal tumors. In: Kim DH, Chang UK, Kim SH, Bilsky MH, eds. *Tumors of the Spine*. Philadelphia, PA: W.B. Saunders; 2008:115
- [5] Riley LH, III, Frassica DA, Kostuik JP, Frassica FJ. Metastatic disease to the spine: diagnosis and treatment. *Instr Course Lect*. 2000; 49:471–477
- [6] Helweg-Larsen S, Sørensen PS. Symptoms and signs in metastatic spinal cord compression: a study of progression from first symptom until diagnosis in 153 patients. *Eur J Cancer*. 1994; 30A(3):396–398
- [7] Levack P, Graham J, Collie D, et al. Scottish Cord Compression Study Group. Don't wait for a sensory level: listen to the symptoms: a prospective audit of the delays in diagnosis of malignant cord compression. *Clin Oncol (R Coll Radiol)*. 2002; 14(6):472–480
- [8] Koes BW, van Tulder MW, Thomas S. Diagnosis and treatment of low back pain. *BMJ*. 2006; 332(7555):1430–1434
- [9] Bellut D, Mutter UM, Sutter M, Eggspuehler A, Mannion AF, Porchet F. Back pain in patients with degenerative spine disease and intradural spinal tumor: what to treat? when to treat? *Eur Spine J*. 2014; 23(4):821–829
- [10] Henschke N, Maher CG, Refshauge KM, et al. Prevalence of and screening for serious spinal pathology in patients presenting to primary care settings with acute low back pain. *Arthritis Rheum*. 2009; 60(10):3072–3080
- [11] Deyo RA, Rainville J, Kent DL. What can the history and physical examination tell us about low back pain? *JAMA*. 1992; 268(6):760–765
- [12] Elliott K, Foley KM. Neurologic pain syndromes in patients with cancer. *Neurol Clin*. 1989; 7(2):333–360
- [13] Welch WC, Jacobs GB. Surgery for metastatic spinal disease. *J Neurooncol*. 1995; 23(2):163–170
- [14] Bilsky MH, Lis E, Raizer J, Lee H, Boland P. The diagnosis and treatment of metastatic spinal tumor. *Oncologist*. 1999; 4(6):459–469
- [15] Fridley JS, Syed S, Niu T, Leary OP, Gokaslan ZL. Presentation of spinal cord and column tumors. *Neurooncol Pract*. 2020; 7 Suppl 1:i18–i24
- [16] Downie A, Williams CM, Henschke N, et al. Red flags to screen for malignancy and fracture in patients with low back pain: systematic review. *BMJ*. 2013; 347:f7095
- [17] Henschke N, Maher CG, Ostelo RWJG, de Vet HCW, Macaskill P, Irwig L. Red flags to screen for malignancy in patients with low-back pain. *Cochrane Database Syst Rev*. 2013; 2013(2):CD008686
- [18] Verhagen AP, Downie A, Popal N, Maher C, Koes BW. Red flags presented in current low back pain guidelines: a review. *Eur Spine J*. 2016; 25(9):2788–2802
- [19] Henschke N, Maher CG, Refshauge KM. Screening for malignancy in low back pain patients: a systematic review. *Eur Spine J*. 2007; 16(10):1673–1679
- [20] Koes BW, van Tulder M, Lin CWC, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J*. 2010; 19(12):2075–2094
- [21] Chou R, Qaseem A, Snow V, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians, American College of Physicians, American Pain Society Low Back Pain Guidelines Panel. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007; 147(7):478–491

- [22] Murphy B, Epstein J. Chronic systemic symptoms in cancer patients. *Translational Systems Medicine and Oral Disease*. 2020:353–369
- [23] Desai J, Gold M, Fullerton S, Cebon J. Systemic manifestations of cancer and paraneoplastic syndromes. In: *Current Cancer Therapeutics*. London: Current Medicine Group; 2001:427–441
- [24] Joines JD, McNutt RA, Carey TS, Deyo RA, Rouhani R. Finding cancer in primary care outpatients with low back pain: a comparison of diagnostic strategies. *J Gen Intern Med*. 2001; 16(1):14–23
- [25] Chou R, Qaseem A, Owens DK, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Diagnostic imaging for low back pain: advice for high-value health care from the American College of Physicians. *Ann Intern Med*. 2011; 154(3):181–189
- [26] Berry JA, Elia C, Saini HS, Miulli DE. A review of lumbar radiculopathy, diagnosis, and treatment. *Cureus*. 2019; 11(10):e5934
- [27] Mason WP. Neurologic manifestations of tumors of the spine, spinal cord, and peripheral nerves. In: Dickman CA, Fehlings MG, Gokaslan ZL, eds. *Spinal Cord and Spinal Column Tumors: Principles and Practice*. New York, NY: Georg Thieme Verlag KG; 2006
- [28] Caridi JM, Pumberger M, Hughes AP. Cervical radiculopathy: a review. *HSS J*. 2011; 7(3):265–272
- [29] Wolff MW, Levine LA. Cervical radiculopathies: conservative approaches to management. *Phys Med Rehabil Clin N Am*. 2002; 13(3):589–608, vii
- [30] Poletti CE. C2 and C3 pain dermatomes in man. *Cephalalgia*. 1991; 11(3): 155–159
- [31] Maynard CW, Leonard RB, Coulter JD, Coggeshall RE. Central connections of ventral root afferents as demonstrated by the HRP method. *J Comp Neurol*. 1977; 172(4):601–608
- [32] Kunam VK, Velayudhan V, Chaudhry ZA, Bobinski M, Smoker WRK, Reede DL. Incomplete cord syndromes: clinical and imaging review. *Radiographics*. 2018; 38(4):1201–1222
- [33] Hersh AM, Patel J, Pennington Z, et al. Perioperative outcomes and survival after surgery for intramedullary spinal cord tumors: a single-institution series of 302 patients. *J Neurosurg Spine*. 2022:1–11
- [34] Bach F, Larsen BH, Rohde K, et al. Metastatic spinal cord compression. Occurrence, symptoms, clinical presentations and prognosis in 398 patients with spinal cord compression. *Acta Neurochir (Wien)*. 1990; 107 (1–2):37–43
- [35] Gilbert RW, Kim J-H, Posner JB. Epidural spinal cord compression from metastatic tumor: diagnosis and treatment. *Ann Neurol*. 1978; 3(1):40–51
- [36] Klekamp J. Spinal ependymomas. Part 1: intramedullary ependymomas. *Neurosurg Focus*. 2015; 39(2):E6
- [37] Emos MC, Agarwal S. Neuroanatomy, Upper Motor Neuron Lesion. StatPearls. Published online August 22, 2022. Accessed November 19, 2022 at: <https://www.ncbi.nlm.nih.gov/books/NBK537305/>
- [38] Javed K, Daly DT. Neuroanatomy, Lower Motor Neuron Lesion. StatPearls. Published online August 22, 2022. Accessed November 19, 2022 at: <https://www.ncbi.nlm.nih.gov/books/NBK539814/>
- [39] Guttman M, Kish SJ, Furukawa Y. Current concepts in the diagnosis and management of Parkinson's disease. *CMAJ*. 2003; 168(3):293–301
- [40] Stacpoole S, McGuigan C, Phadke SL, Stevens J, Choi D, Kapoor R. Spinal claudication due to myxopapillary ependymoma. *BMJ Case Rep*. 2009; 2009: bcr09.2008.0969
- [41] Schliack H. Segmental innervation and the clinical aspects of spinal nerve root syndromes. In: Vinken PJ, Bruyn GW, eds. *Handbook of Clinical Neurology*. Amsterdam: North-Holland; 1969:157–177
- [42] Hawkes CH, Roberts GM. Neurogenic and vascular claudication. *J Neurol Sci*. 1978; 38(3):337–345
- [43] Behan P. Neurological differential diagnosis. *J Neurol Neurosurg Psychiatry*. 1978; 41(6):579
- [44] Karp SJ, Ho RTK. Gait ataxia as a presenting symptom of malignant epidural spinal cord compression. *Postgrad Med J*. 1986; 62(730):745–747
- [45] Tobin MK, Geraghty JR, Engelhard HH, Linninger AA, Mehta AL. Intramedullary spinal cord tumors: a review of current and future treatment strategies. *Neurosurg Focus*. 2015; 39(2):E14
- [46] Yang KS, Ho CS, Tai PA, Kung WM. Intraspinal schwannoma and neurogenic bladder. *Ann R Coll Surg Engl*. 2018; 100(4):e69–e72
- [47] Brierley SM, Hibberd TJ, Spencer NJ. Spinal afferent innervation of the colon and rectum. *Front Cell Neurosci*. 2018; 12:467
- [48] Brouwers E, van de Meent H, Curt A, Starremans B, Hosman A, Bartels R. Definitions of traumatic conus medullaris and cauda equina syndrome: a systematic literature review. *Spinal Cord*. 2017; 55(10): 886–890
- [49] Knowlton SE, Andrews C, Bindler C, Ruppert LM. Managing bowel and bladder impairments in sacral chordoma patients: a case-based approach. *Spinal Cord Ser Cases*. 2017; 3(1):17094
- [50] Tokuhashi Y, Uei H, Oshima M, Ajiro Y. Scoring system for prediction of metastatic spine tumor prognosis. *World J Orthop*. 2014; 5(3):262–271
- [51] Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine*. 2005; 30(19):2186–2191
- [52] Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine*. 2001; 26(3):298–306
- [53] Fisher CG, DiPaola CP, Ryken TC, et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. *Spine*. 2010; 35(22): E1221–E1229
- [54] Fox S, Spiess M, Hnenny L, Fourny DR. Spinal instability neoplastic score (SINS): reliability among spine fellows and resident physicians in orthopedic surgery and neurosurgery. *Global Spine J*. 2017; 7(8):744–748
- [55] Bellut D, Burkhardt JK, Mannion AF, Porchet F. Assessment of outcome in patients undergoing surgery for intradural spinal tumor using the multidimensional patient-rated Core Outcome Measures Index and the modified McCormick Scale. *Neurosurg Focus*. 2015; 39(2):E2
- [56] Mendel E. Tumors of the extradural spine. In: DeMonte F, Gilbert MR, Mahajan A, McCutcheon IE, Buzdar AU, Freedman RS, eds. *Tumors of the Brain and Spine*. Boston, MA: Springer; 2007:273–294
- [57] Pinter NK, Pfiffner TJ, Mechtler LL. Neuroimaging of spine tumors. *Handb Clin Neurol*. 2016; 136:689–706
- [58] Shah LM, Salzman KL. Imaging of spinal metastatic disease. *Int J Surg Oncol*. 2011; 2011:769753
- [59] Kim YS, Han IH, Lee IS, Lee JS, Choi BK. Imaging findings of solitary spinal bony lesions and the differential diagnosis of benign and malignant lesions. *J Korean Neurosurg Soc*. 2012; 52(2):126–132
- [60] Asiltürk M, Abdallah A, Sofuoglu EO. Radiologic-histopathologic correlation of adult spinal tumors: a retrospective study. *Asian J Neurosurg*. 2020; 15 (2):354–362
- [61] Patnaik S, Jyotsnani Y, Uppin SG, Susarla R. Imaging features of primary tumors of the spine: a pictorial essay. *Indian J Radiol Imaging*. 2016; 26(2): 279–289
- [62] Rincon-Torroella J, Rakovec M, Khalafallah AM, et al. Clinical features and surgical outcomes of intracranial and spinal cord subependymomas. *J Neurosurg*. 2022; 137(4):1–12
- [63] Shih RY, Koeller KK. Intramedullary masses of the spinal cord: radiologic-pathologic correlation. *Radiographics*. 2020; 40(4):1125–1145
- [64] Meng XX, Zhang YQ, Liao HQ, et al. Dynamic contrast-enhanced MRI for the assessment of spinal tumor vascularity: correlation with angiography. *Eur Spine J*. 2016; 25(12):3952–3961
- [65] Patel DM, Weinberg BD, Hoch MJ. CT myelography: clinical indications and imaging findings. *Radiographics*. 2020; 40(2):470–484
- [66] Sun H, Nemecek AN. Optimal management of malignant epidural spinal cord compression. *Emerg Med Clin N Am*. 2009; 27(2):195–208
- [67] Cole JS, Patchell RA. Metastatic epidural spinal cord compression. *Lancet Neurol*. 2008; 7(5):459–466
- [68] Mechri M, Riahi H, Sboui I, Bouaziz M, Vanhoenacker F, Ladeb M. Imaging of malignant primitive tumors of the spine. *J Belg Soc Radiol*. 2018; 102(1):56
- [69] Sandu N, Pöpperl G, Toubert ME, et al. Current molecular imaging of spinal tumors in clinical practice. *Mol Med*. 2011; 17(3–4):308–316
- [70] Matsumoto Y, Baba S, Endo M, et al. Metabolic tumor volume by ¹⁸F-FDG PET/CT can predict the clinical outcome of primary malignant spine/spinal tumors. *BioMed Res Int*. 2017; 2017:8132676
- [71] Feroz I, Makhdooni RH, Khursheed N, Shaheen F, Shah P. Utility of computed tomography-guided biopsy in evaluation of metastatic spinal lesions. *Asian J Neurosurg*. 2018; 13(3):577–584
- [72] Tamarkin RG, Isaacson AC. Electrodiagnostic Evaluation of Lumbosacral Radiculopathy. StatPearls. Published online September 26, 2022. Accessed October 31, 2022 at: <https://www.ncbi.nlm.nih.gov/books/NBK563224/>
- [73] Rubin DL. Needle electromyography waveforms during needle electromyography. *Neurol Clin*. 2021; 39(4):919–938
- [74] Hussain AK, Cheung ZB, Vig KS, et al. Hypoalbuminemia as an independent risk factor for perioperative complications following surgical decompression of spinal metastases. *Global Spine J*. 2019; 9(3):321–330
- [75] Pennington Z, Ehresman J, Feghali J, et al. A clinical calculator for predicting intraoperative blood loss and transfusion risk in spine tumor patients. *Spine J*. 2021; 21(2):302–311

- [76] Li Y, Wang B, Zhou S, et al. Do routine blood test results help in the diagnosis of spine tumors? A retrospective study of the significance of pretreatment neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios from 503 spine tumor patients. *Medicine (Baltimore)*. 2019; 98(15):e14902
- [77] Ehresman J, Pennington Z, Feghali J, et al. Predicting nonroutine discharge in patients undergoing surgery for vertebral column tumors. *J Neurosurg Spine*. 2020; 34(3):1–10
- [78] Hersh AM, Patel J, Pennington Z, et al. A novel online calculator to predict nonroutine discharge, length of stay, readmission, and reoperation in patients undergoing surgery for intramedullary spinal cord tumors. *Spine J*. 2022; 22(8):1345–1355
- [79] Connolly ID, Li Y, Pan W, et al. A pilot study on the use of cerebrospinal fluid cell-free DNA in intramedullary spinal ependymoma. *J Neurooncol*. 2017; 135(1):29–36
- [80] Hersh AM, Jallo GI, Shimony N. Surgical approaches to intramedullary spinal cord astrocytomas in the age of genomics. *Front Oncol*. 2022; 12:982089
- [81] Rincon-Torroella J, Khela H, Bettgowda A, Bettgowda C. Biomarkers and focused ultrasound: the future of liquid biopsy for brain tumor patients. *J Neurooncol*. 2022; 156(1):33–48
- [82] Wang J, Bettgowda C. Applications of DNA-based liquid biopsy for central nervous system neoplasms. *J Mol Diagn*. 2017; 19(1):24–34