



Instability and impending instability in patients with vertebral metastatic disease

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Abstract

Metastatic disease commonly involves the spine with an increasing incidence due to a worldwide rise of cancer incidence and a longer survival of patients with osseous metastases. Metastases compromise the mechanical integrity of the vertebra and make it susceptible to fracture. Patients with pathological vertebral fracture often become symptomatic, with mechanical pain generally due to intervertebral instability, and may develop spinal cord compression and neurological deficits. Advances in imaging, radiotherapy, as well as in spinal surgery techniques, have allowed the evolution from conventional palliative external beam radiotherapy to modern stereotactic radiosurgery and from traditional open surgery to less-invasive, and sometimes prophylactic stabilization surgical treatments. It is therefore clear that fracture risk prediction, and maintenance or restoration of intervertebral stability, are important objectives in the management of these patients. Correlation between imaging findings and clinical manifestations is crucial, and a common knowledge base for treatment team members rather than a compartmentalized view is very important. This article reviews the literature on the imaging and clinical diagnosis of intervertebral instability and impending instability in the setting of spine metastatic disease, including the spinal instability neoplastic score, which is a reliable tool for diagnosing unstable or potentially unstable metastatic spinal lesions, and on the different elements considered for treatment.

Keywords Spine · Spine, instability · Spine, metastases · Spine, stabilization · Spine imaging

Introduction

Metastases are the most frequent cause of bone tumors and the spine represents the most frequent site of skeletal metastases [1, 2]. Pain is the presenting complaint in the majority of cases. Three different pain syndromes are associated with spinal tumors: biologic or “tumor-related” pain, mechanical pain that is a consistent feature of oncologic instability [3], and radiculopathy. Biologic pain is nocturnal or early morning pain and resolves over the course of the day. It arises from a reaction

to inflammatory mediators released by the tumor, and its flare-up is due to the nocturnal decrease of steroid secretion by the adrenal glands. Biologic pain can be caused by the tumor confined to the vertebral body [3], without elements of instability. This type of pain is often very responsive to steroids and radiotherapy. Mechanical pain is instead a movement-related pain, relieved by recumbence, which may be caused by destruction or collapse of the vertebral body, with frank intervertebral instability [3, 4]. Non-operative treatments do not improve mechanical instability pain; therefore, these patients generally require some form of invasive or minimally invasive stabilization. Biologic and mechanical pain may progress to radiculopathy, which refers to nerve root symptoms due to epidural disease that extends into the neural foramen, and may also predict epidural spinal cord compression (ESCC), eventually causing myelopathy. Treatment decisions for spinal metastases depend on several factors such as general clinical conditions (i.e., age, comorbidities, life expectancy), presence and degree of radiculopathy or myelopathy, radiosensitivity of the tumor, extent of disease, and medical comorbidities, as well as on two important anatomical factors: the degree of radiological ESCC and the presence of intervertebral instability [5–7]. The Spine Oncology Study

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Group has designed and validated an ESCC six-point grading system based on axial T2-weighted magnetic resonance (MR) images at the site of most severe compression (Fig. 1) [8]. This grading system has been shown to be the most reliable for both inter- and intra-rater reliability, and an informative instrument that accounts for recent advances in the treatment of spinal metastases (Table 1) [8]. Spinal instability has not received the same degree of scrutiny in the literature as ESCC, but depicting signs of instability, and maintaining or restoring spinal stability is an important objective in the management of patients with osseous spinal tumors. Rising awareness of this issue has recently led to the introduction in clinical practice of the spinal instability neoplastic score (SINS) [9], which is a reliable tool to diagnose unstable or potentially unstable metastatic spinal lesions, based on imaging elements and clinical notion of presence or absence of pain. This article reviews the literature on the imaging and clinical diagnosis of intervertebral instability and impending instability in the setting of spine metastatic disease, and on the different elements considered for treatment decisions.

Definition of intervertebral instability

Despite many efforts to define intervertebral instability, no generally accepted definition is yet available, especially in

Table 1 ESCC six-point grading system

Grade	Defining characteristics
Grade 0	Osseous disease only
Grade 1a	Epidural impingement, without thecal sac deformation
Grade 1b	Deformation of the thecal sac, without spinal cord contact
Grade 1c	Deformation of the thecal sac with spinal cord contact, but without cord compression
Grade 2	Spinal cord compression with preservation of some cerebrospinal fluid around the cord
Grade 3	Spinal cord compression with complete effacement of cerebrospinal fluid around the cord

patients with metastatic disease. The concept of instability means in fact different things to different specialists (clinicians, radiologists, bioengineers) [10]. A reasonable biomechanical definition is the one proposed by Pope and Panjabi [11] and Frymoyer and Selby [12]. These authors defined instability as an abnormal response to applied loads characterized kinematically by abnormal movement in the motion segment, consisting of two vertebrae and the interconnecting soft tissue, beyond normal constraints [10, 12]. By advocating a clinical approach, this abnormal movement results in damage or irritation to the spinal cord or nerve roots with development

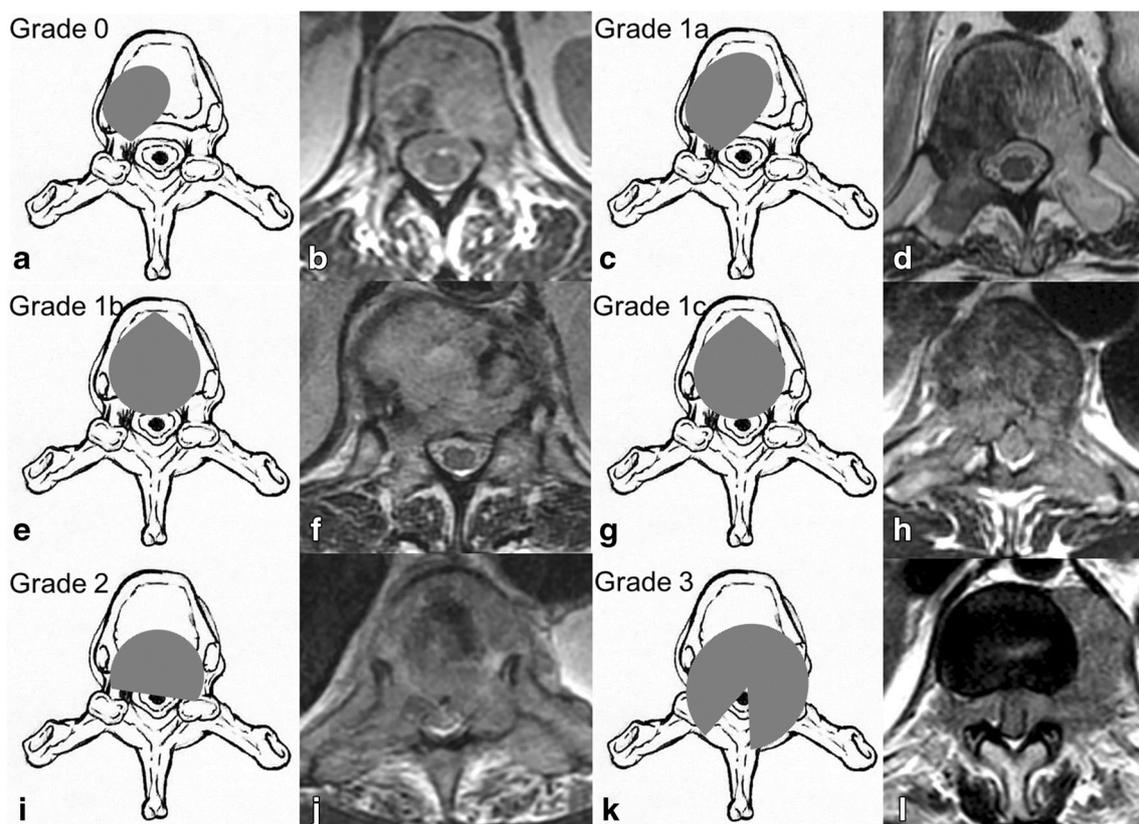


Fig. 1 a, c, e, g, i, k Schematic representations and (b, d, f, h, j, l) axial T2-weighted MR images representing the ESCC six-point grading system proposed by the Spine Oncology Study Group. a, b Grade 0. c, d Grade 1a. e, f Grade 1b. g, h Grade 1c. i, j Grade 2. k, l Grade 3

of incapacitating deformity or pain due to structural changes [9, 13]. The assessment of spinal instability is dependent not only on clinical but also on radiological criteria. In 1983, Denis [14] proposed the “three-columns” concept, which is widely accepted as the mechanical model to judge a thoracolumbar fracture as unstable based on involvement of the middle column. Although Kostuik and Weinstein [15] attempted to assess stability in the setting of spinal metastases applying the “three-columns” theory of Denis, this model, which was originally developed for use in trauma, is not directly applicable in the setting of spine neoplastic disease. In fact, the pattern of bone and soft tissue disruption in neoplastic lesions is extremely different from that observed in high-energy traumatic injuries [13]. In neoplastic spinal involvement, ligaments and disks are rarely affected, the mechanism of injury is not as important, the potential for healing and bony quality (tissue-level material properties and architecture) are often poor in cancer patients [13]. Furthermore, Denis’ model is not useful in predicting risk of pathologic fracture, since impending instability, with the potential for subsequent collapse, is a concept that specifically applies to neoplastic disease. In summary, instability in the metastatic fractured or at risk of collapse vertebrae is poorly defined [16], and there is a lack of guidelines available to aid in defining the presence and degree of spinal instability. Nevertheless, spinal instability is a key decision point in the treatment of spinal metastases.

Pathological fractures

To precisely define features and extent of neoplastic spine lesions, complementary use of CT and MR imaging are recommended, to differentiate pre-lytic, lytic, and sclerotic components, soft tissue extra-osseous components, bony or soft tissue encroachment of the central canal, and the possible mass effect on the neural elements in the central canal and foramina (Fig. 2).

Metastases can disrupt the mechanical integrity of the vertebral bone, rendering vertebrae susceptible to fracture under normal physiologic stress, potentially resulting in neurologic compromise.

Two major pathological fracture patterns can be discerned: (1) typical compression (wedge) fracture, and (2) burst fracture. With a wedge fracture, the anterior aspect (column) of the vertebra collapses and becomes wedge shaped; the posterior wall of the vertebral body is intact [17]. In the more severe burst fractures, there is failure of both the anterior and middle columns, often associated with spinal canal compromise caused by retropulsion of osseous fragments of the posterior wall or of epidural soft tissue mass (Fig. 2) [18]. The fracture pattern is determined by the position of the point of force application in relation to the instantaneous axis of rotation (IAR). Each motion segment has an IAR, which is a point

around which the motion segment rotates; it is not constant depending upon spinal alignment and forces acting on the spine [19]. Compressive forces applied ventral to the IAR often result in forced flexion, compression of the vertebral elements ventral to the IAR and thus, in wedge compression fractures (Fig. 3). The thoracic spine is particularly prone to this type of injury because of its normal kyphosis. Pure axial loading in line with the IAR leads to a burst fracture pattern. The point of force application is generally in line with the IAR in the lower cervical and lumbar spine because of their intrinsic lordosis [19]. Burst fractures are generally induced by pressurization of the tumor tissue, weakening the vertebral body under physiological loading. Pressurization can induce high radial tension in the cortical shell and, under sufficient load, can cause failure of the vertebral body with retropulsion of bony fragments and/or tumor into the spinal canal [16].

Impending instability

Individuating risk factors of intervertebral instability due to pathological fracture is important in directing prophylactic treatment and improving outcome and survival. The vertebral body is the most common location of metastases [20]; partial or total destruction of the vertebral body results in a decrease of its load-bearing capacity. A cadaver study by Dimar et al. [21] showed that the best parameter for predicting pathologic fracture in the thoracic spine is the product of the remaining intact vertebral cross-sectional area and the bone mineral density. The vertebral body becomes prone to pathologic fracture when a critical threshold is reached (from 51 to 96% of cross-sectional area depending on bone mineral density).

In another cadaveric study, Windhagen et al. [22] used axial rigidity analysis of thoracic vertebrae to determine the relationship between load-bearing capacity and measurements from quantitative CT data, including defect size and bone density. Axial rigidity analysis is a method that considers the elemental material composition of the vertebra and the geometry of the structure [23]. In their study, Windhagen et al. [22], showed a high positive correlation between axial rigidity (strength in the longitudinal plane) and absolute failure load, but no correlation between defect size and failure load was found.

The location of the metastasis within the vertebral body is also important in predicting risk of pathologic fracture. Krishnaney et al. [4] considered the vertebral body to be a cube composed of a series of 27 identically shaped adjacent smaller cubes and emphasized that removing these cubes (similarly to the substitution in lytic lesions) in certain parts of the vertebral body had different effects on overall stability. Destruction of the middle third in the axial plane would result in gross instability, whereas loss of the middle third in the sagittal plane would not be associated with important

Fig. 2 A 67-year-old man with lung cancer and multiple vertebral metastases. **a** Sagittal multiplanar reformatted CT image clearly demonstrates the bony lesions and the T4 vertebral body collapse in particular (*arrow*). **b** Sagittal T1-weighted, **c** corresponding contrast-enhanced fat-suppressed, and **d** axial T2-weighted MR images show soft tissue extra-osseous components, with retropulsed tumor (*arrow* in **b**, and **c**), and an ESCC grade 2 (*arrows* in **d**)



instability. Also, metastasis location within the coronal plane has a different effect on stability, with a ventrally located lesion affecting stability more than lesions in the middle or dorsal portions of the vertebral body.

In their retrospective study, Taneichi et al. [24] determined the risk factors for thoracic and lumbar pathologic vertebral body collapse, estimating the probability of collapse under various conditions of metastatic spine disease, and suggested

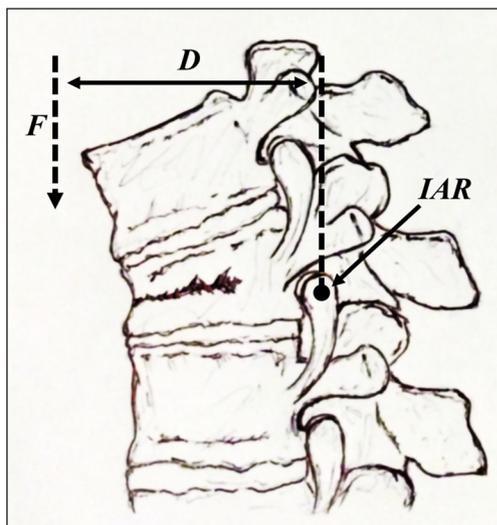


Fig. 3 Diagram showing a wedge compression fracture due to an applied force vector (F) ventral to the instantaneous axis of rotation (IAR). D = The length of the moment arm, which can be assumed as the perpendicular distance between the IAR and the point of force application

the criteria for impending vertebral body collapse. The risk factors for vertebral body collapse in the thoracic region (T1–T10) were tumor size and costovertebral joint destruction, whereas in the thoracolumbar and lumbar spine (T10–L5), tumor size and posterior elements destruction were the main factors (Table 2) (Figs. 4 and 5). Other authors tried to develop a better understanding of factors affecting burst fracture risk using finite element analysis [25–29]. The parametric analysis by Whyne et al. [25] suggested that the principal factors affecting the initiation of burst fracture are tumor size, magnitude of spinal loading, and bone density. Tschirhart et al. [26] used a poroelastic parametric finite element modeling to quantify the effects of tumor location and shape on vertebral body stability and burst fracture risk. The authors found that metastases with dorsal location and a medial to lateral dimension caused the greatest increase in vertebral posterior wall retropulsion. In the study by Tschirhart et al. [27], the effect of load type on a metastatic thoracic spinal motion segment was evaluated. Axial loading resulted the predominant load type leading to the increased potential of burst fracture initiation, while rotational loading led to only a moderate increase in risk. To determine the effects of vertebral level, geometry, and metastatic compromise to the cortical shell on the risk of burst fracture in the thoracic spine, Tschirhart et al. [28] used parametric finite element modeling and demonstrated that upper thoracic vertebrae are at increased risk of burst fracture, while increased kyphotic angles and the ribcage decrease the risk of burst fracture.

Table 2 Criteria of impending pathological vertebral body collapse suggested by Taneichi et al.

Thoracic spine (T1-T10)	Thoracolumbar and lumbar spine (T10-L5)
50–60% involvement of the vertebral body with no destruction of other structures	35–40% involvement of the vertebral body with no destruction of other structures
25–30% involvement of the vertebral body with costovertebral joint destruction	20–25% involvement of the vertebral body with posterior elements destruction

In summary, the risk factors for intervertebral instability include increased axial rigidity [22], location of metastasis within the anterior third of the vertebral body on sagittal plane or middle third on axial plane [5], tumor size [24, 25], decreased bone density [21, 25], dorsal location of the metastasis within the vertebral body [26], and increased force of spinal loading [25, 27]. Other risk factors that specifically contribute to instability of the thoracic and lumbar spine are destruction of the costovertebral joint [24], and upper thoracic locations [28] in the thoracic spine, and posterior elements destruction in the thoracolumbar and lumbar spine (T10-L5) [24]. However, these variables have been studied in isolation or independently, whereas their effect is interactive and/or cumulative, and definitive conclusions cannot be reached due to lack of evidence [16].

Spinal instability neoplastic score

A validated and reliable classification system could lead to standardized therapeutic approach for treatment of metastatic intervertebral instability. However, no accepted evidence-

based guidelines for the classification of metastatic intervertebral instability were accepted before 2010. In that year, the integration of the best evidence provided by two systematic reviews [16, 29] with expert consensus from the Spine Oncology Study Group was used to develop the Spine Instability Neoplastic Score (SINS) [9]. In this comprehensive and easy-to-use classification system, tumor-related intervertebral instability is assessed by adding together five imaging and one clinical component score: lesion spinal level, presence and type of pain, lesion bone quality, spinal alignment, extent of vertebral body collapse, and posterolateral involvement of the spinal elements (Table 3). The total SINS score (range, 0-18 points) is converted into one of the following three clinical categories: 0-6 points suggesting stability (Fig. 6); 7-12 points suggesting impending instability (Fig. 7); and 13-18 points warning for instability (Fig. 8). In addition, the SINS score can also be analyzed as a binary indicator of surgical referral status: ‘stable’ (0-6 points) or ‘current or possible instability’ (7-18 points). A surgical consultation is recommended for patients with SINS scores equal or greater than 7. The SINS system, however, does not account for a “global spinal score”. In case of multiple

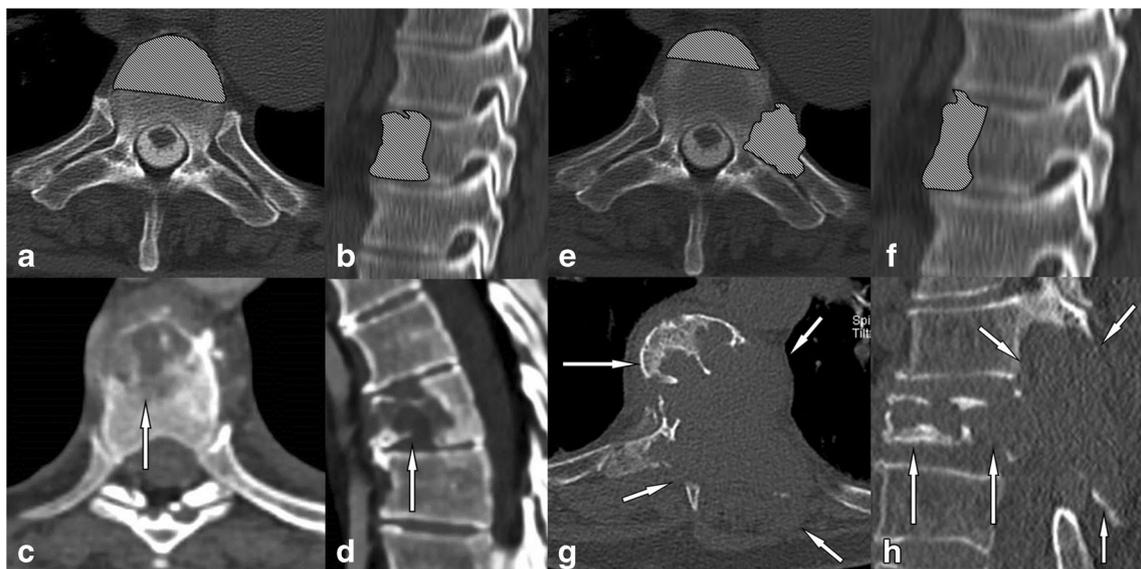


Fig. 4 Risk factors for vertebral body collapse in the thoracic spine (T1-T10) suggested by Taneichi et al. **a, b** Schematic representations, **c** axial, and **d** sagittal multiplanar reformatted CT images representing 50–60% involvement of the vertebral body with no destruction of other structures (arrow in **c**, and **d**). **e, f** Schematic representations showing 25–30%

involvement of vertebral body, and costovertebral joint destruction. **g** Axial, and **h** sagittal multiplanar reformatted CT images representing involvement of vertebral body (> 80% in this patient) (arrows in **g**, and **h**), and diffuse involvement of the vertebral arch with costovertebral joint destruction (small arrows in **g**, and **h**)

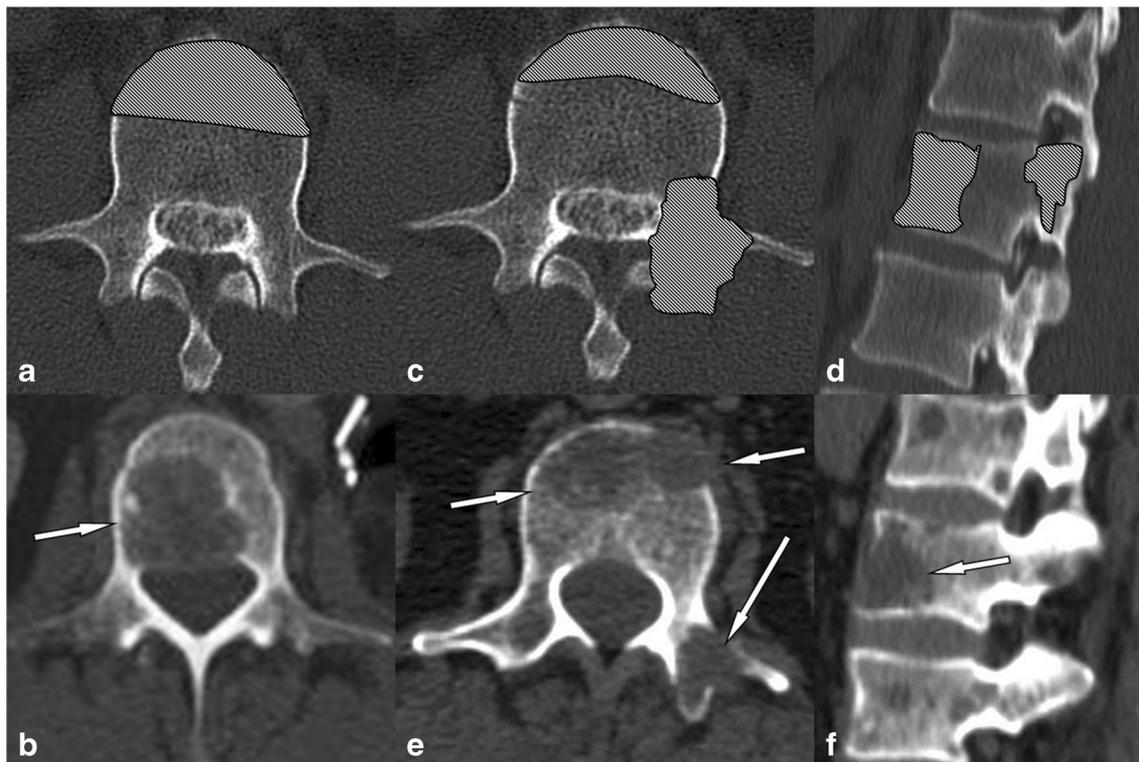


Fig. 5 Risk factors for vertebral body collapse in the thoracolumbar and lumbar spine (T10-L5) suggested by Taneichi et al. **a** Schematic representation, and **b** axial CT image representing 35–40% involvement of the vertebral body with no destruction of other structures (*arrow* in **b**). **c**, **d**

Schematic representations, **e** axial, and **f** sagittal multiplanar reformatted CT images showing approximately 25% involvement of vertebral body (*arrows* in **e**, and **f**) and posterior elements destruction (*long arrow* in **e**)

metastatic lesions, stability scores are not summed. Each lesion should be evaluated, but scores be assigned separately

[9]. The reliability and validity of SINS were tested in different, independent studies [30–36]. Total SINS scores had

Table 3 SINS criteria from Spine Oncology Study Group

	SINS criteria	Score
Location	Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)	3
	Mobile spine (C3-C6, L2-L4)	2
	Semirigid (T3-T10)	1
	Rigid (S2-S5)	0
Pain	Mechanical	3
	Occasional not mechanical	1
	Pain-free lesion	0
Bone lesion	Lytic	2
	Mixed (lytic/blastic)	1
	Blastic	0
RX spinal alignment	Subluxation/translation present	4
	De novo deformity (kyphosis/scoliosis)	2
	Normal alignment	0
Vertebral body collapse	> 50% collapse	3
	< 50% collapse	2
	No collapse with 50% body involved	1
	None of the above	0
Posterolateral involvement	Bilateral	3
	Unilateral	1

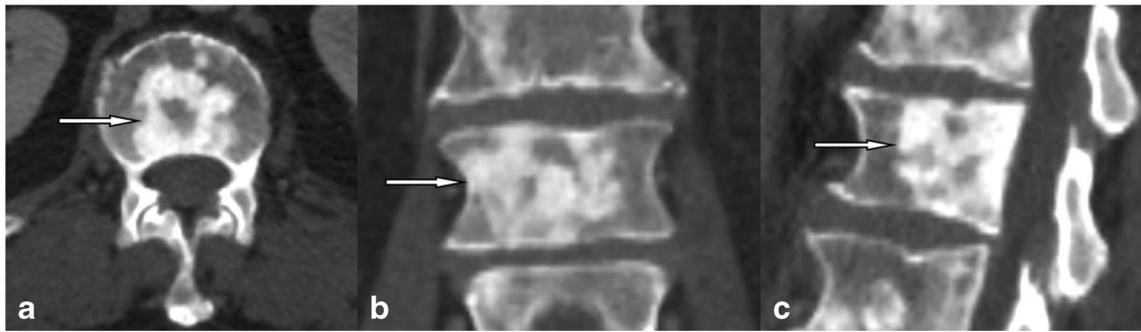


Fig. 6 A 67-year-old man with prostate adenocarcinoma. **a** Axial, **b** coronal, and **c** sagittal multiplanar reformatted CT images show blastic lesion of L1 vertebral body (arrow in **a**, **b**, and **c**). SINS scoring for this patient would proceed as follows: spine location - junctional = 3; pain - lack of pain = 0; bone lesion - blastic = 0; spinal alignment - normal = 0;

vertebral body collapse - no collapse with > 50% body involved = 1; posterolateral involvement of spinal elements - absence of involvement = 0. The final tally of component scores yields 4 out of a possible 18. This score indicates that the patient is in a stable condition

excellent inter- and intra-observer reliability in determining stability, impending instability, and instability [30]. The sensitivity and specificity of SINS for potentially unstable or unstable lesions were 95.7 and 79.5%, respectively [30].

No unstable spine was classified as stable by any SINS rater or vice versa; all errors (false negative rate of 4.3%), resulted from distinguishing stable and potentially unstable conditions [30]. SINS may be considered a valid tool to aid

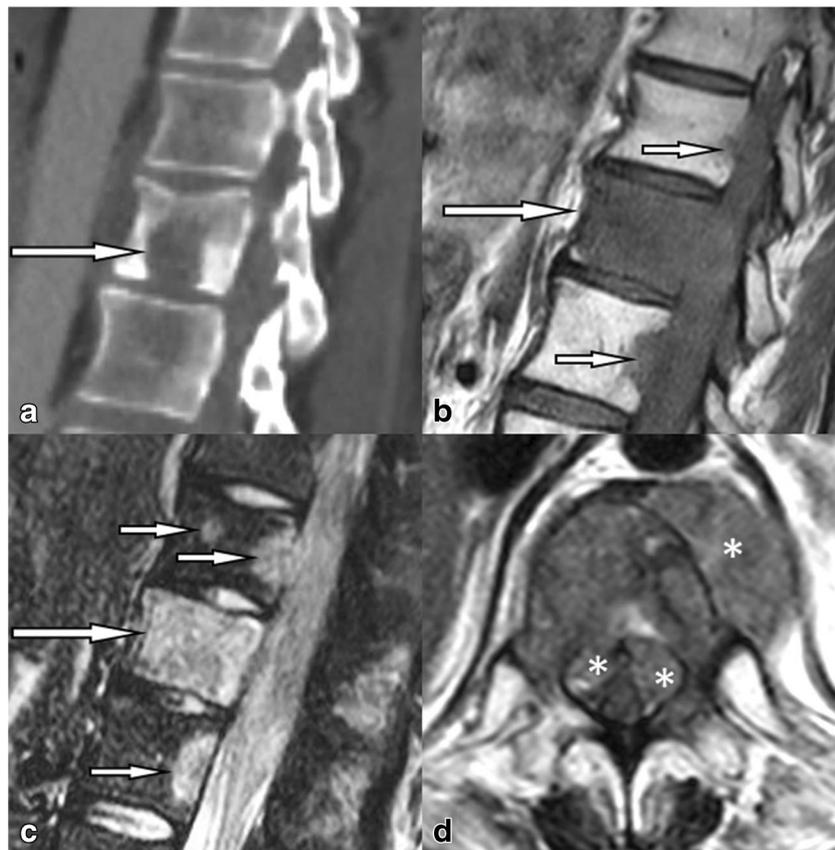


Fig. 7 A 48-year-old woman with uterine leiomyosarcoma. **a** Sagittal multiplanar reformatted CT image, **b** sagittal T1-weighted, **c** corresponding, and **d** axial T2-weighted MR images show lytic lesion of T12 vertebral body with diffuse bone marrow edema (arrow in **a**, **b**, and **c**), epidural space involvement with spinal cord compression, and a neoplastic mass along the left aspect of the T12 vertebral body (* in **d**). Note also the other three focal lesions in the T4, and T6 vertebral bodies (small

arrows in **b**, and **c**). SINS scoring for this patient would proceed as follows: spine location - junctional = 3; pain - occasional pain but not mechanical = 1; bone lesion - lytic = 2; spinal alignment - normal alignment = 0; vertebral body collapse - no collapse with > 50% body involved = 1; posterolateral involvement of spinal elements - bilateral = 3. The final tally of component scores yields 10 out of a possible 18. This score indicates that the patient is in an indeterminate unstable condition

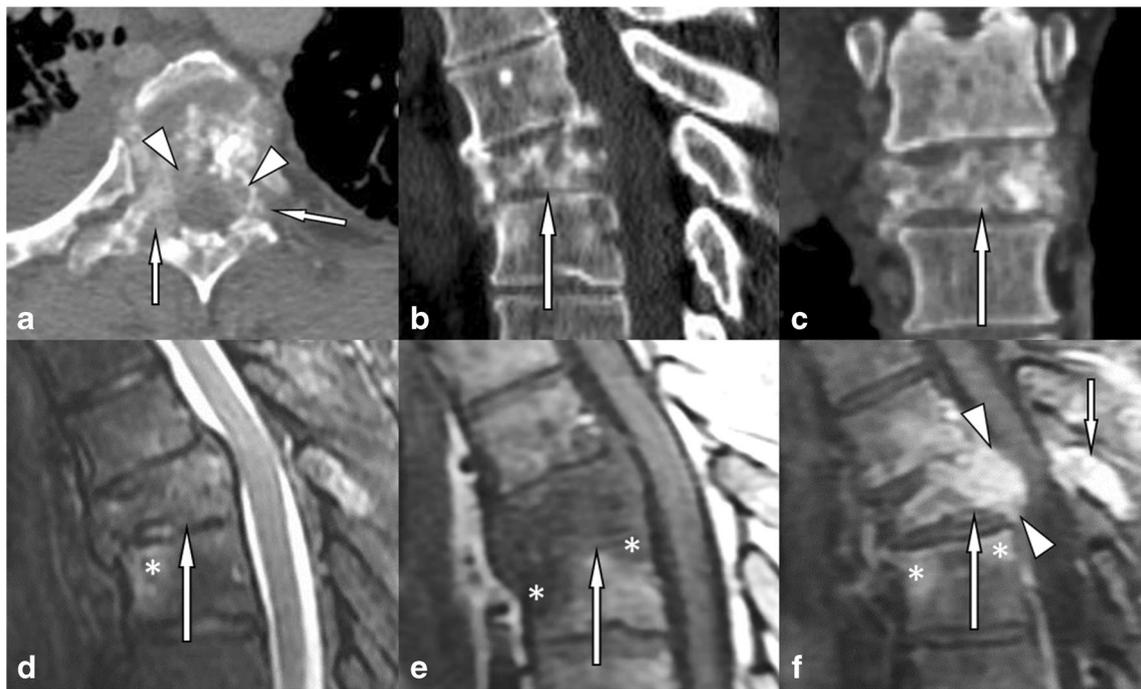


Fig. 8 A 62-year-old man with renal cell carcinoma. **a** Axial, **b** sagittal, and **c** coronal multiplanar reformatted CT images. **d** Sagittal T1-weighted, **e** corresponding T2-weighted, and **f** contrast enhanced fat-suppressed MR images. T5 vertebral body collapse greater than 50% of vertebral height (arrows in **b**, **c**, **d**, **e**, and **f**) with bilateral involvement of posterior vertebral arch (small arrows in **a**, and **f**), as well as epidural space involvement with spinal cord compression (arrowheads in **a**, and **f**) are clearly defined. Note also other two focal lesions in the T6 vertebral body

(* in **d**, **e**, and **f**). SINS scoring for this patient would proceed as follows: spine location - semirigide (T5) = 1; pain - presence of mechanical pain = 3; bone lesion - mixed = 1; spinal alignment - de novo deformity (kyphosis) = 2; vertebral body collapse - > 50% collapse = 3; posterolateral involvement of spinal elements - bilateral = 3. The final tally of component scores yields 13 out of a possible 18. This score indicates that the patient is in an unstable condition

communication between oncologists, radiologists, and spine surgeons allowing more organized and prompt treatment plans for instability, thereby preventing potential neurological catastrophe [30–36]. Obviously, further determination of SINS reliability is required as well as its prospective application in different patient populations to assess the validity of this tool in therapeutic decision-making. Almost all the studies [30–36] that have assessed the reliability and validity of SINS did not define the age of subject groups, and no study has specifically addressed the applicability of SINS in children and adolescents. This is very understandable since metastatic disease to the spine in younger patients is very uncommon; however, understanding the validity of SINS in these patients could be important for improving outcomes and chances of cure. It also should be noted that additional factors that contribute to spinal instability and not accounted for by SINS system should be considered when assessing global spinal stability in the setting of neoplastic disease. Previous laminectomies or other surgical procedures and previous radiation therapy may influence spinal loading and impending instability as well as poor bone quality, patient body weight, and activity level. Multilevel (contiguous and non-contiguous) spinal disease may also influence the fracture risk, but its role is not fully understood [9].

Treatment options

A wide spectrum of improved systemic, radiation, minimally invasive, and surgical options are available to maintain or restore intervertebral stability, reduce pain, and safeguard functional status in patients with metastatic spine disease. The proper indication for one of these therapeutic measures, or a combination thereof, and their respective timing may allow to achieve long-term local control with reduced morbidity for these patients [37]. Such complex treatment decisions are likely to benefit from a multidisciplinary approach including oncologist, radiotherapist, spine surgeon, diagnostic and interventional radiologist, and pain specialist.

Cement augmentation procedures

Cement-augmentation minimally invasive procedures, such as vertebroplasty and kyphoplasty, are increasingly being recognized as safe and effective methods for providing mechanical stability of the anterior column, control local pain, and prevent disability in carefully selected patients with malignant spinal involvement [38–49].

In vertebroplasty, a catheter is inserted and polymethylmethacrylate is injected under continuous

fluoroscopic visualization into the collapsed vertebral body. The kyphoplasty procedure differs from vertebroplasty in that an inflatable balloon catheter is inserted within the vertebral body prior to polymethylmethacrylate injection, in attempting to restore vertebral body height and reduce kyphotic deformity [40]. More recently, intrasomatic metallic permanent expandable implants, such as vertebral body stents [50] and SpineJacks [51], have been introduced to obtain vertebral body fracture reduction prior to cement injection (Fig. 9). Injection of polymethylmethacrylate into the involved vertebral body allows for immediate stabilization of the fracture and this might be the mechanism of pain relief. The efficacy of these procedures in pain relief has been consistently documented [43–47] as producing an analgesic effect in 73 to 92% of patients [44–46] for osteolytic spinal lesions [44, 46] as well as for pure blastic or mixed spinal metastases [46–49]. Pain relief is usually obtained rapidly, within 24 to 48 h following the procedure, allowing patients to improve their quality of life and resume their daily activities. Although the release of cytotoxic polymers related to hyperthermia at the time of cement polymerization may cause tissue necrosis, the cell lysis effect is not constant, limited to a depth of few millimeters, and extremely variable depending on the cements used [39, 52, 53]. Thus, cement augmentation procedures are not anticancer treatments, and should be considered complementary to standard oncological treatments, such as chemotherapy and/or radiotherapy, which can be administered prior, during, or after the cement augmentation procedure. This combined modality approach resulted well tolerated with excellent results of pain control in patients with symptomatic pathological compression fractures [54]. In order to combine a carcinolytic effect with an analgesic effect, several authors [55–57] performed vertebroplasty or kyphoplasty following targeted bipolar radiofrequency ablation. In the last two decades, its

effectiveness in reducing pain and improving function in patients with symptomatic metastatic spinal disease has been documented [55, 56]. Combined radiofrequency ablation and cement augmentation have theoretical benefits, however, comparative trials have not been performed to establish superiority of combined therapy [57]. Thus, further studies are required before the true management value of this combined treatment can be determined.

Cement leakage into the perivertebral veins, soft tissues, and intervertebral disks is the most common complication, often due to vertebral cortical defect, but remains most of the time asymptomatic [58]; more rare and potentially more hazardous complications consist in polymethylmethacrylate embolism to the pulmonary arteries and leakage into the epidural space. Indications to cement augmentation procedures are painful or non-painful fractured or at risk of collapse vertebral lesions, with the intent of pain palliation and stabilization. Contraindications for cement vertebral augmentation are severe uncorrectable coagulopathy and local or systemic infection [59]. Destruction of the vertebral body posterior wall and the presence of epidural soft tissue involvement by the tumor represent more challenging technical conditions, but are no longer absolute contraindications. Some authors reported good results for percutaneous vertebroplasty in patients with osteolysis of the posterior wall of the vertebral body [43, 60, 61] and epidural soft tissue mass [61, 62], with low complication rate. Other authors [41, 42] advocate prophylactic vertebral stabilization with polymethylmethacrylate for properly selected patients at risk of impending collapse to prevent fractures and their associated morbidities. By referring to SINS score system, cement vertebral augmentation has been validated as an appropriate procedure in the stable and potentially unstable groups [41].

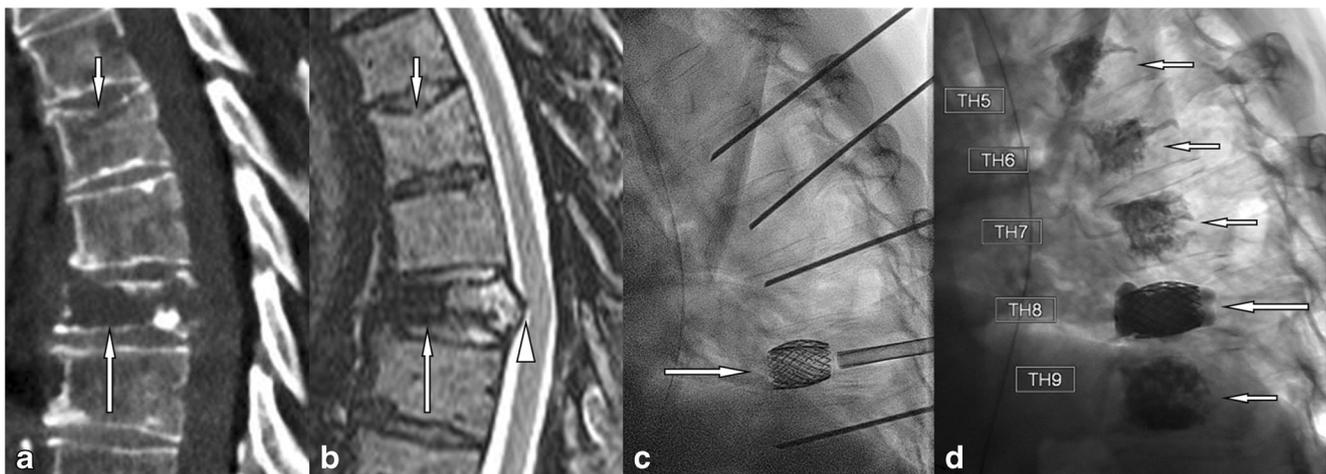


Fig. 9 A 58-year-old patient with lung cancer. **a** Sagittal multiplanar reformatted CT, **b** corresponding T2-weighted MR, and **c**, **d** intraoperative radiographic images show body collapse of T8 vertebral body (arrow in **a**, and **b**) with mild spinal cord compression (arrowhead in **b**),

and some height loss of T6 vertebral body (small arrow in **a**, and **b**). The patient underwent percutaneous intrasomatic stent delivery (arrow in **c**) prior to cement injection (arrow in **d**) at T8 level, and prophylactic vertebroplasty at the adjacent levels (small arrows in **d**)

Stereotactic body radiotherapy

Conventional external beam radiotherapy has been widely used for palliation of painful spinal metastases. However, its benefit is not uniform, with only 0–20% of patients experiencing complete pain relief [63–65], often only temporary pain relief [66], and radioresistance of some tumor histotype. Furthermore, due to improving therapies, advanced radiation technology, and increasing life expectancy of patients with metastatic spinal disease, demand for treatment options that offer long-term tumor control and, when possible, tumor sterilization, has increased. The advent of spinal stereotactic body radiotherapy (SBRT), also known as spinal stereotactic radiosurgery, offers the opportunity to deliver high biologically effective doses to spinal metastases with very tight margins, therefore more safely, even in the presence of epidural involvement, and minimize the issue of radioresistance. The modality implies the delivery of locally ablative tumor doses, which range from 16 to 24 Gy to 30–40 Gy, in only 1–5 fractions [67, 68]. Despite the fact that the radiation dose is highly conformed to the target, with a rapid radiation dose fall-off outside the target, minimizing the dose to surrounding normal tissues, the risk of radiation myelopathy remains a rare but serious late complication [69]. Several authors [70–74] reported significant pain relief, with complete relief in 51 to 54% of patients within 7 days and 1 year from the start of spinal SBRT, along with satisfactory progression-free survival and no late spinal cord toxicities. At the same time, other authors [75–78] demonstrated an increased incidence of post-SBRT vertebral body compression fractures of up to 39%, compared with less than 5% with conventional external beam radiotherapy. Radiation-induced osteonecrosis is the potential mechanism underlying SBRT-induced vertebral compression fractures as demonstrated by Al-Omair et al. [79] on the basis of biopsy results, with most of them (65%) occurring within the first 4 months after SBRT [80]. Radiation itself may be considered an independent factor with respect to the risk of vertebral compression fracture, and caution should be observed when treating with ≥ 20 Gy/fraction [80]. This finding may motivate prophylactic vertebral body stabilization measures in selected patients.

To define the proper use of SBRT, the American Society of Therapeutic Radiation Oncology [81] developed, in 2011, evidence-based guidelines which suggest SBRT for oligometastatic and some postoperative patients, for previously radiated spinal metastases, and preferably, for patients in a spinal SBRT clinical trial, all expected to live for at least 3 months. The primary exclusion criteria included mechanical intervertebral instability and a high-grade ESCC (grade 2 to 3). In summary, spinal SBRT may be considered a highly efficacious and safe therapeutic option in the treatment of mechanically stable spinal metastases in properly selected patients.

Surgery

Non-surgical therapeutic options are unable to provide stability to an unstable spine and relieve metastatic spinal cord compression resulting from extradural soft tissue metastasis and/or pathological fracture with vertebral body collapse. When spinal cord damage is due to soft tissue metastasis rather than bony compression, radiotherapy and surgery have both been shown to be effective, but when there is structural failure of the spine, usually associated with severe mechanical pain, impaired ambulatory ability, and neurologic dysfunction, surgical decompression with stabilization is the primary treatment of choice for metastatic disease of the spine [82]. The approach for decompression surgery is determined by the location of metastatic disease within the vertebra, most often involving primarily the vertebral body. Irrespective of the chosen surgical approach, indications for surgery include radioresistant tumors, clinically significant neural compression secondary to retropulsed vertebral body fragment or to spinal deformity, spinal instability, intractable mechanical pain unresponsive to non-operative treatment options, and radiation failure [83]. Although the primary aims of surgery are relief of motor impairment by circumferential decompression of the neural elements, and relief of pain by stabilization of the spine, identification of patients with short survival is needed to avoid time-consuming and invasive treatment such as open surgical techniques with instrumentation and long-term radiotherapy. Life expectancy for patients with metastatic spinal disease may be limited to a few months and open surgery for spinal metastases is generally not indicated if the patient is expected to survive less than 3 months [84]. Determining this estimate is difficult although various scoring systems, such as the modified Tokuhashi [85] and Tomita [86] scores, have been created. The main prognostic parameters for survival are the histology of the primary tumor and its sensitivity to adjuvant chemotherapy and/or radiotherapy [87]. Prompt open surgery leads to marked improvement in neurological function and performance status [88], however, as the anatomy of the spine makes a radical tumor resection impossible in almost all cases, patients with a favorable overall prognosis should undergo postoperative adjuvant radiotherapy to achieve durable local tumor control [89]. Furthermore, open surgery requires a long postoperative recovery period that can interrupt the patient's oncological management, and has associated significant morbidity and mortality. Local and systemic surgical complications rates have ranged from 20 to 48% [90, 91] and include thromboembolic disease, pneumonia, postoperative hematoma, failed fixation requiring revision, and wound dehiscence or infection that is the most common complication [92].

Innovations in spine surgery technology have resulted in a large variety of new less-invasive surgical techniques aimed at reducing the morbidity of invasive open surgery and

facilitating the return to early systemic and radiation therapy [93]. These minimally invasive spinal procedures, using image-guided percutaneous pedicle screws, have fewer adverse events than do open surgery ones, and offer a treatment option for patients who do not have indications for an invasive open circumferential decompression and instrumentation, but have epidural disease and mechanical pain [94]. In selected patients, the required stability of the anterior and posterior spinal elements may be provided by minimally invasive surgery with posterior instrumentation and vertebral body cement augmentation with the additional benefit of minimizing delays to adjuvant SBRT without an increase in the risk of wound complications [94].

Conclusions

The concepts of spinal instability and impending instability resulting from neoplastic destruction of spinal elements are poorly defined as evidenced by a wide variety of criteria and scoring systems published in the literature. The SINS is a reliable tool for diagnosing potentially unstable or unstable metastatic spinal lesions and ensuring proper communication within a multidisciplinary team. Spinal instability is an indication for surgical treatment; however, a large variety of choices may be offered to the patient since innovations in spine surgery technology have resulted in: (j) new surgical techniques also including cement augmentation procedures and emerging minimally invasive interventions, and (jj) a large variety of surgical internal fixation devices for stabilization. Surgery alone is not sufficient for durable tumor control and adjuvant radiation treatment is always required. In this context, SBRT has demonstrated improved local tumor control and overall survival, in properly selected patients, compared to conventional external beam radiation therapy. Therefore, it seems clear that management of neoplastic intervertebral instability requires a multidisciplinary approach to promote interdisciplinary group discussion, thereby providing comprehensive care for spinal metastatic patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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