

Spinal metastasis: narrative reviews of the current evidence and treatment modalities

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Abstract

The treatment for spinal metastasis has evolved significantly during the past decade. An advancement in systemic therapy has led to a prolonged overall survival in cancer patients, thus increasing the incidence of spinal metastasis. In addition, with the improved treatment armamentarium, the prediction of patient survival using traditional prognostic models may have limitations and these require the incorporation of some novel parameters to improve their prognostic accuracy. The development of minimally-invasive spinal procedures and minimal access surgical techniques have facilitated a quicker patient recovery and return to systemic treatment. These modern interventions help to alleviate pain and improve quality of life, even in candidates with a relatively short life expectancy. Radiotherapy may be considered in non-surgical candidates or as adjuvant therapy for improving local tumour control. Stereotactic radiosurgery has facilitated this even in radio-resistant tumours and may even replace surgery in radiosensitive malignancies. This narrative review summarizes the current evidence leading to the paradigm shifts in the modern treatment of spinal metastasis.

Keywords

Spinal metastasis, spinal metastasis surgery, spinal cord compression

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Introduction

Spinal metastases are a challenging oncological problem, affecting up to 70% of cancer patients.^{1,2} Up to 20% of spinal metastases become symptomatic, leading to pain, neurological deficit and disruption of health-related quality of life.³ The common primary malignancies that cause spinal metastases include breast, lung and prostate cancer, accounting for up to two-thirds of all cases.^{4,5} The frequently affected spinal regions are the thoracic, lumbar and cervical.⁶ In recent years, the advancement in cancer pharmacotherapy, including chemotherapy, targeted therapy, hormone-targeting drugs and immunotherapy, has led to substantially improved patient survival in almost all cancer types.⁷⁻¹¹ This amplifies the magnitude of the problems caused by spinal metastases. Furthermore, the novel development of stereotactic radiation surgery and minimally-invasive surgical techniques has allowed for good treatment outcomes in spinal metastases compared with traditional surgery.¹²⁻¹⁵ This review article aims to summarize the current evidence regarding the management of spinal metastases.

Article search methodology

The two authors performed literature searches using electronic databases, including MEDLINE (PubMed®), Embase® (Ovid), Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews (CDSR) on 15 December 2021. The literature search was performed using the following search terms in combination with Boolean “OR” and “AND” phrases: “spinal metastasis”, “spinal metastasis surgery”, “spinal cord compression”, “spinal tumour”, “corticosteroid”, “spinal fracture”, “instability”, “bisphosphonate”, “denosumab”, “skeletal related events”,

“NOMS framework”, “SINS score”, “Tohukashi score”, “Tomita score”, “Bollen score”, “life expectancy prognostication”, “embolization”, “vertebroplasty”, “kyphoplasty”, “minimally invasive surgery”, “minimal access surgery”, “hybrid therapy”, “stereotactic radiosurgery” and “complication”. The resulting articles were screened for relevance to spinal metastasis. Articles published within the past 5 years, landmark articles and articles receiving high citations were included. The reference lists of the included studies were further reviewed for additional articles. Data from the included studies were reviewed independently by the two authors.

Clinical presentation

The presenting signs and symptoms of spinal metastases depend on the tumour location and size. Up to 95% of patients experience pain as their initial symptom.^{16,17} Pain in spinal metastases can be caused by tumour invasion and expansion in the vertebral body causing pressure on the periosteum, spinal instability due to vertebral destruction, fractures or neural compression. In mechanically stable spinal metastases, the patient can develop pain during rest and severe pain that wake them up from sleep. By contrast, mechanical instability causes pain that is worsened by motion and improved with recumbency. Combined with vertebral collapses, this could lead to spinal deformity such as kyphosis. Nerve root compression or invasion by the tumour leads to pain, sensory and/or motor deficit following certain dermatomes. Bilateral radicular symptom, weakness of the limbs, gait abnormality, symmetric paresthesia, and bowel and bladder dysfunction may suggest malignant spinal cord or cauda equina compression, requiring emergency treatment.

Investigations

On radiographs, spinal metastases are osteolytic in 70%, osteoblastic in 8% and mixed osteolytic and osteoblastic in 21%.¹⁸ Primary tumours that commonly cause osteolytic lesions include lung, breast, melanoma, thyroid and renal cancers.² Osteoblastic lesions can be caused by medulloblastoma, nasopharyngeal cancer, prostate cancer and urothelial cancer.² Mixed osteolytic and osteoblastic lesions can result from cervix, lung, breast and ovarian cancers.²

Magnetic resonance imaging (MRI) of the whole spine remains the imaging modality of choice for detecting spinal metastases.^{19–21} The recommended views of study include sagittal T1 and T2 weighted images of the whole spine and axial T2 weighted images of the affected spinal region.^{22,23} Hypointense lesions on T1-weighted images suggest spinal metastases.²⁴ On T2-weighted images, hypointense and hyperintense signals represent osteoblastic and osteolytic lesions, respectively.²⁴ Gadolinium contrast enhancement is not strictly required for the detection of spinal metastases but is essential in diagnosing leptomeningeal metastases.²⁴ Furthermore, gadolinium contrast can disrupt spinal metastasis detection on T1-weighted images.²⁴ Thus, non-contrast enhanced T1-weight imaging should be obtained beforehand.²⁴

The recovery of patient's functional status after treatment associates with the duration of symptoms and neurological compression.²⁵ The Dutch national guideline for the clinical management of spinal metastases recommends obtaining immediate MRI in clinical spinal cord compression or bilateral radicular compression.²⁴ In those with radicular compression causing unilateral dermatomal/myotomal deficit, MRI should be done within 48 hours.²⁴ In patients with unilateral radicular pain and

localized pain, MRI should be completed within 1 and 2 weeks, respectively.²⁴

In instances where MRI is contraindicated or not available, computed tomography of the spine with intravenous or intrathecal contrast should be alternatively considered.²⁴ Other imaging modalities such as plain X-ray and bone scintigraphy are not suitable for early diagnosis as metastatic lesions only become apparent with advanced bony destruction or soft tissue involvement. Furthermore, in purely osteolytic lesions, such as multiple myeloma, bone scintigraphy may yield a false-negative result as their tracers are absorbed only by osteoblasts.²⁶

Tissue histology remains the gold standard for diagnosing skeletal metastasis, including in the spine. Other than at vertebral metastatic lesions, biopsy can also be performed from an epidural mass or from masses at other sites that are more easily accessed.^{24,27} In cases of unknown primary malignancy, urgent positron emission tomography-computed tomography of the chest and abdomen are recommended.²⁴ The Dutch national guideline advises that tissue diagnosis should be performed within 24 hours and 72 hours in the setting of clinical and radiological spinal cord compression, respectively.²⁴ After biopsy, treatment, including surgical decompression, stabilization and radiotherapy, can be started immediately, whenever indicated, without waiting for the histological results.

Despite the high incidence of spinal metastasis in cancer patients, the treating physician should also be aware of other possible causes of pain and neurodeficit.²⁴ Differential diagnosis for back or neck pain includes osteoporotic spinal fractures, spinal infections, spondylosis, herniated nucleus pulposus, and referred pain from other sites, including visceral organs. Other pathology leading to neurodeficit in a patient with cancer includes leptomeningeal metastasis, radiation myelopathy,

meningitis, epidural abscess/haematoma, spinal lipomatosis and intramedullary metastasis.

Corticosteroids

In patients with symptomatic spinal cord compression, corticosteroids can be administered to reduce the swelling of the spinal cord. The available evidence suggests that the optimal dosage of intravenous dexamethasone is a 10 mg bolus, followed by 16 mg daily in divided doses.²⁸ After completing definitive treatment, corticosteroid should be weaned off rapidly. Studies indicate that steroid administration leads to an increased number of patients with preserved ambulatory function at 1 year after treatment.^{28,29} Furthermore, steroids should be given within 12 hours of spinal cord compression onset.³⁰ A delayed steroid administration is associated with a six-fold risk of remaining non-ambulatory after treatment.³⁰

In cases of asymptomatic radiological spinal cord compression, omitting corticosteroid does not lead to a negative impact on the patient's ambulatory capacity after radiotherapy.²⁸ After radiation, the patient can experience significant pain due to inflammation along the irradiated regions. These pain flares can also be effectively treated with corticosteroid.²⁴

In the setting of an unknown primary malignancy, corticosteroids should be deferred until after tissue histology/microbiology samples have been obtained. Evidence suggests that the histological diagnosis of haematological malignancy can be obscured by corticosteroid treatment.²⁴ Furthermore, the administration of steroids could lead to detrimental results in cases of spinal infection.

The use of steroids in spinal cord compression is not without complications. Their administration has been reported to be associated with complications such as

pneumonia, infected decubitus ulcer, urosepsis, gastrointestinal bleeding, duodenal ulcer and peritonitis.³⁰⁻³³ However, these adverse effects are reported in historical studies where high dexamethasone dosage of 100 mg intravenous bolus and followed by 96 mg daily were used.³⁰⁻³³ When using low-dose steroids, the rate of gastrointestinal bleeding is reported to be as low as 1.9%.²⁸ This may further be mitigated by the concurrent use of proton pump inhibitors.²⁸ The risk of perioperative wound infection in low-dose steroid usage remains unreported. Overall, the benefits of steroid therapy on patient recovery and pain reduction are promising. Their usage should be weighed against the possible complications based on the presenting risk factors of complications in individual patients.

Bisphosphonates and denosumab

Spinal metastasis patients can be affected by skeletal-related events (SREs), including bone pain, fracture, hypercalcaemia and spinal cord compression.²⁷ Bisphosphonates inhibit bone resorption mediated by osteoclasts which, in turn, leads to a lower risk of SREs in patients with selected primary cancer.²⁷ Zoledronic acid is the most commonly used intravenous bisphosphonate and it is approved for the treatment of bone metastasis in multiple myeloma and solid tumors.³⁴ Its administration effectively reduces serum calcium in patients with hypercalcaemia and delays the occurrence of SREs in patients with spinal metastases.³⁴

For the treatment of metastatic disease, 4 mg zoledronic acid is given intravenously every 3-4 weeks.³⁴ With this rate of frequency, the patient is faced with the risk of adverse events such as renal failure, hypocalcaemia and osteonecrosis of the jaw.³⁴ Thus, an alternative dosing interval of every 3 months has been proposed. Current evidence suggests that a 12-week

dosing interval does not negatively affect SRE prevention.^{35–37} This longer interval has also been shown to improve patient compliance and reduce the occurrence of bisphosphonate-related adverse outcomes.^{35–37}

Denosumab, a human monoclonal antibody that inhibits the receptor activator of nuclear factor kappa-B ligand, provides an alternative to zoledronic acid for SRE prevention.^{38–41} It is administered at a dose of 120 mg subcutaneously every 4 weeks.³⁸ Compared with zoledronic acid, denosumab is superior in delaying the occurrence of first and subsequent SREs in solid tumours and multiple myeloma.^{39,40} Denosumab has shown no superiority in reducing the incidence of spinal cord compression compared with zoledronic acid.⁴¹ Denosumab also demonstrated a lower incidence of renal toxicity and acute phase reactions such as fever.³⁸ However, denosumab treatment is associated with a higher risk of hypocalcaemia and osteonecrosis of the jaw.³⁸ Unlike zoledronic acid, there is currently no evidence to support the length of the dosing interval of denosumab as it does not accumulate in the bone. Thus, a reduction in the dose frequency might negatively impact on the benefits of denosumab.

Treatment considerations

The treatment of spinal metastases is palliative in nature. The aim is to alleviate pain, improve/maintain functional and neurological status and achieve local control of the tumour.^{42,43} Care of a patient with spinal metastasis involves a multidisciplinary team, including the initial treating specialist for the primary cancer, medical oncologist, radiation oncologist, radiologist and spine surgeon. The authors propose a treatment algorithm for spinal metastasis as presented in Figure 1.

The presentation of spinal metastasis varies with tumour size, location and progression.²⁴ Surgical indications usually

include intractable pain, mechanical instability and neurological compromise.²⁴ The urgency of treatment varies according to the severity of the patient's symptoms.²⁵ The Dutch national guideline recommends definitive treatment within 24 hours for symptomatic spinal cord compression, within 72 hours for asymptomatic radiological spinal cord compression and within 14 days for patients presenting with pain only.²⁴

In 2013, the NOMS framework for guiding the comprehensive assessment of spinal metastasis patients was proposed.¹² The framework consists of four pillars including neurological, oncological, mechanical stability and systemic condition parameters.¹² First, the neurological and oncological parameters are evaluated together in combination. The neurological considerations include clinical neurological status and radiographic severity of epidural spinal cord compression (ESCC). The patient is clinically assessed for evidence of radiculopathy or myelopathy. Clinical myelopathy is highly associated with a high grade ESCC on MRI. The severity of ESCC is classified according to a 6-point grading scale according to the Spine Oncology Study Group.²³ Grades 0, 1a, 1b and 1c represent low-grade ESCC where the thecal sac may be impinged, but no visible spinal cord compression is seen.¹² Grades 2 and 3 represent high-grade ESCC, showing radiographical evidence of spinal cord compression.¹² For oncological considerations, the primary malignancy is classified according to the anticipated response to available therapies, especially to conventional external beam radiotherapy (cEBRT).¹² Tumours with high-to-moderate radiosensitivity include haematological malignancies such as multiple myeloma, lymphoma and plasmacytoma, and solid tumours including prostate, breast, ovarian and neuroendocrine carcinomas.^{44,45} The majority of other solid tumours, including colon, non-

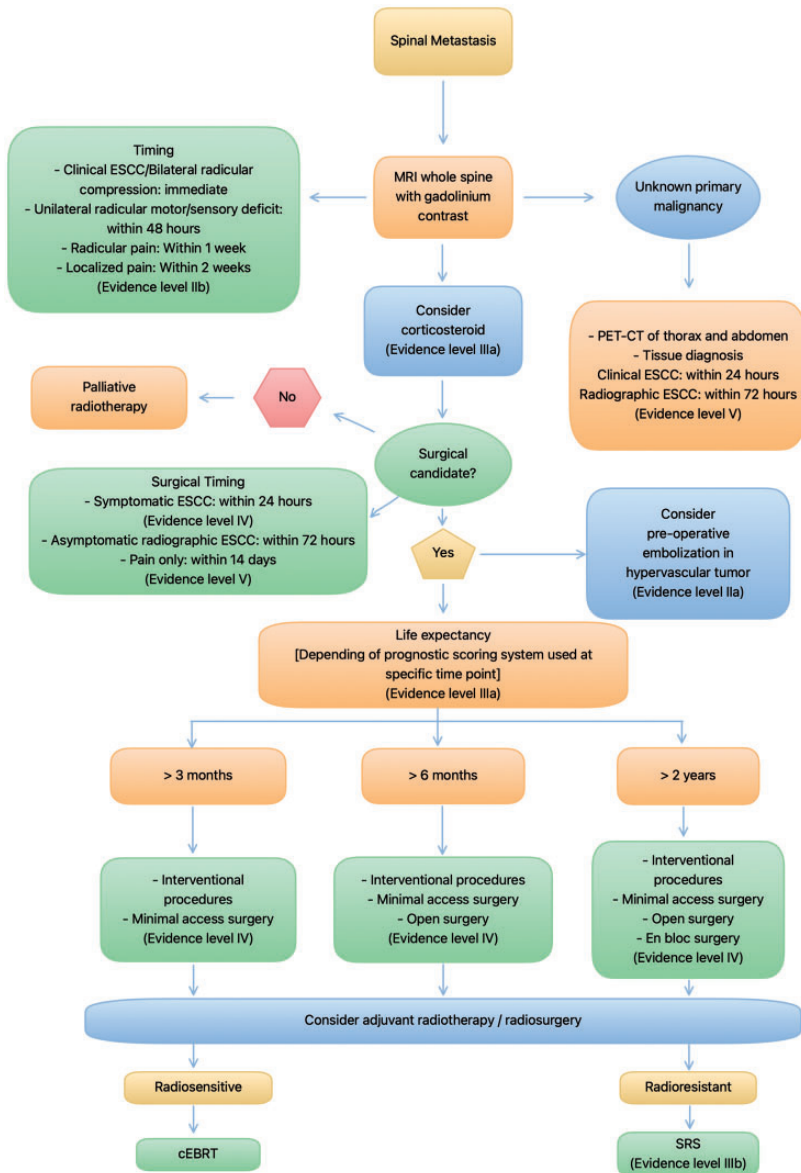


Figure 1. Treatment algorithm for spinal metastasis. ESCC, epidural spinal cord compression; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; cEBRT, conventional external beam radiotherapy; SRS, stereotactic radiosurgery. The colour version of this figure is available at: <http://imr.sagepub.com>.

small cell lung carcinoma, thyroid, renal cell carcinoma, melanoma, hepatocellular carcinoma, and sarcoma, are radioresistant to cEBRT.^{44,45}

The patient without evidence of myelopathy or high-grade ESCC can be treated, without surgery, by cEBRT in radiosensitive cancer and by spinal stereotactic

radiosurgery (SRS) in radioresistant tumours.¹² In those presenting with high-grade ESCC and/or myelopathy in radio-sensitive cancer, cEBRT can be administered as definitive treatment as rapid tumour response is anticipated. However, in the real-world setting, this patient group may be offered upfront decompressive spinal surgery in order to optimize their neurological outcome. In radioresistant tumours presenting with high-grade ESCC and/or myelopathy, spinal stabilization and decompression followed by spinal SRS are recommended.¹²

Mechanical stability of the metastatic spinal segment is evaluated according to the Spinal Instability Neoplastic Score (SINS), a score proven to have substantial to excellent interobserver reliability.^{46–48} Six parameters are evaluated in determining the stability of the metastatic spinal column: location, pain, alignment, type of bone lesion, radiographical spinal alignment, vertebral body collapse and posterolateral involvement of spinal elements.⁴⁹ SINS scores of 0–6, 7–12 and 13–18 indicate stable, indeterminate stability and unstable spine, respectively.⁴⁹ Indeterminate and unstable spines signify the need for consultation to a spine surgeon. Mechanical instability independently provides a surgical indication irrespective of ESCC severity and the presence of myelopathy. The necessity and plan of surgical treatment are decided based on the spine surgeon's experience and available facilities.

Lastly, the patient's condition is evaluated systemically to determine if the patient could withstand the formulated plan of treatment.¹² In this process, the patient's comorbidities, life expectancy and disease burden are weighed for the risk and benefit of the treatment. With a palliative nature, spinal metastasis surgery aims to alleviate pain, provide stability, improve/maintain neurological function and facilitate an early return to systemic treatment.

Survival prediction

The estimation of the patient's life expectancy by the treating physician can be inaccurate, especially in terminally ill patients.^{50–52} Thus, several predictive models of patient survival have been developed to prevent undertreatment or overtreatment.

Revised Tokuhashi, Tomita and modified Bauer scores are among the prognostic models widely used to predict remaining life expectancy.^{51,53,54} However, these scores were developed in the 1990s, prior to the recent advancements in pharmacotherapy that has significantly improved the outcomes of cancer treatment. These novel developments, including immunotherapy, targeted therapy, hormonal therapy and anti-vascular endothelial growth factor, have resulted in prolonged cancer progression-free survival and overall survival in virtually all types of malignancy.^{7–11} A French nationwide retrospective study of 739 patients surgically treated between 2014–2017 demonstrated poor sensitivity and specificity of the traditional survival predictive scores.⁵⁵ In this study, the accuracy of the revised Tokuhashi and Tomita scores were 42.8% and 25.6% in predicting survival of cancer patients in the modern era, respectively.⁵⁵

Thus, the development of novel prognostic models has shifted toward incorporating individualized risk parameters for patients rather than using traditional risk score tables that predict survival from a generalized cluster of risk factors. The Skeletal Oncology Research Group (SORG) nomogram is a model composed of age, primary tumour type, Eastern Cooperative Oncology Group (ECOG) performance scale, presence of brain/visceral metastasis, number of spinal metastases, laboratory markers (white blood cell count and haemoglobin) and previous systemic treatment.⁵⁶ The risk magnitude of each factor is

weighted from the value individually measured in the specific evaluated patient. The SORG nomogram has demonstrated great accuracy in estimating survival at 3 months and 12 months for patients with operable spinal metastasis.⁵⁶ Its accuracy in predicting 3-, 6- and 12-month survival was 90%, 71% and 78%, respectively.⁵⁶ It is also amongst the limited scores showing good discriminative ability, consistently displaying an area under curve above 0.70 in receiver operating characteristic analysis for various time frames.^{55,57}

Novel survival prognostic models should strongly consider incorporating biological parameters such as targetable genetic mutations as treatment specifically targeting these mutations has been shown to significantly improve progression-free and overall survival in selected malignancies.⁵⁵ The example of actionable mutations includes epidermal growth factor receptor/anaplastic lymphoma kinase in nonsmall-cell lung cancer, B-Raf in melanoma and hormonal status in breast cancer.⁵⁸⁻⁶¹

Despite the development of various survival prediction models, the treating physician should not strictly adhere to rigid predictions. Surgical management should be considered when indicated if postoperative systemic treatment is available.

Indications for surgery

In the era of spinal stereotactic surgery, spinal surgery is indicated in radioresistant tumours presenting with high-grade ESCC and/or myelopathy.¹² Mechanical instability also serves as an independent indication for surgical stabilization.⁴⁸

Surgery in spinal metastasis is known to be associated with a high complication rate up to 37%.⁶² Thus, the risks and benefits of surgery should be cautiously weighed against the patient's expected survival and systemic condition. In patients with an expected survival of less than 3 months,

surgery is generally not recommended.²⁴ Furthermore, the presence of more than three contiguous level spinal metastases precludes the surgeon from achieving stable spinal stabilization.²⁴ Thus, surgery should be avoided. In patients with life expectancy of more than 3 months, interventional procedures or minimal access surgery may be performed.²⁴ Open spinal surgery requires a longer time to recover and is recommended in patients that are expected to live longer than 6 months.²⁴ En bloc spondylectomy is a highly complex procedure and is only recommended in patients with an expected survival of at least 2 years.⁶³

Non-surgical management: radiotherapy and stereotactic radiosurgery

Radiotherapy is the cornerstone of cancer treatment. The delivery of radiation destroys tumour cells by causing disruption of double-stranded DNA and damage to the tumour vasculature.⁶⁴ However, organs adjacent to the target treatment area may also be collaterally affected, especially in cEBRT, leading to adverse effects such as oesophagitis, stomatitis and dermatitis.⁶⁵ Thus, SRS was developed, allowing image-guided delivery of a high radiation dose to a defined small target area with a sharp drop off gradient around the border of target radiation area. SRS delivers a relatively high radiation dose per fraction (>10 Gy) compared with cEBRT.⁶⁶ Such a high dosage leads to microvascular dysfunction and apoptosis, causing tumour hypoperfusion. Additionally, SRS helps generate a host immune response against the tumour cells, ultimately leading to tumour destruction with minimal damage to the adjacent tissues.⁶⁶

In non-surgical candidates that present with neurodeficit, a single fraction of 8 Gy cEBRT is advised in those with a short life

expectancy.^{67,68} At least 30 Gy of cEBRT in divided fractions is recommended in patients that are expected to survive more than 6 months. In patients with spinal pain without spinal cord compression, a single fraction of 8 Gy cEBRT is recommended.^{69,70} Evidence suggests that a higher radiation dose does not provide a more effective pain reduction nor a longer duration of tumour response.⁶⁸

In patients with solitary metastasis or oligometastasis, a more aggressive plan of treatment, such as a combination of decompressive surgery and radiotherapy, is advised.²⁴ This may help prolong progression-free survival and possibly lead to curative outcome in selected cases.²⁴ In this setting, adjuvant radiotherapy is given at an ablative dose of 30–39 Gy in 10–13 divided fractions.²⁴ More advanced radiation techniques such as SRS may also be considered.⁷¹

In radioresistant tumours, SRS is recommended over cEBRT, irrespective of the severity of ESCC.¹² In radioresistant patients with low-grade ESCC, SRS can replace en bloc spondylectomy as a definitive therapy.¹² This can be applied even in radioresistant tumours, showing a local control rate up to 88%.⁷²

Due to the high radiation dosage, SRS is delivered in only 1–3 fractions compared with 10–20 fractions in cEBRT. This also leads to a better patient compliance to radiation treatment.⁷³ However, SRS also leads to a higher risk of vertebral compression fracture (VCF), reported in up to 36% of irradiated vertebral segments.⁷⁴ Evidence suggests that limiting the radiation dose below 16–18 Gy per fraction could help mitigate the risk of SRS-induced VCFs.⁷⁴

In surgical candidates with a history of preoperative radiation, the rate of wound complications is reported as 6%.⁷⁵ However, preoperative radiation, regardless of radiation dosage, was not shown to be an independent risk factor for wound problems.⁷⁵

The evidence supporting the delay in adjuvant radiation after spinal metastasis surgery remains debatable. A previous study suggested that adjuvant SRS can be administered within 24 hours of surgical stabilization without the occurrence of wound complications at 90 days after surgery.⁷⁶ For cEBRT, a delay of at least 5–21 days after surgery is recommended before initiating radiotherapy in order to mitigate wound complications.^{77,78} A delay of greater than 4 weeks has shown no benefit regarding wound problems.⁷⁹ Conversely, a 1-month delay increases local radiographic progression of spinal metastasis, leading to poorer quality of life, local control and overall survival.⁸⁰

Preoperative embolization

Spinal metastasis surgery is complicated by extensive bleeding during surgery, especially in hypervascular primary tumours such as thyroid and renal cell cancers. Massive intraoperative haemorrhage may cause surgical challenges by impairing surgical visualization, prolonging operative time and increasing the blood transfusion rate. A systematic review and meta-analysis has shown that preoperative embolization in hypervascular tumours leads to less intraoperative blood loss, a lower transfusion rate and a shorter operative time.⁸¹ However, in non-hypervascular and mixed tumours, no significant differences were observed regarding transfusion requirement, intraoperative blood loss and operative time.⁸¹ The complication rate and patient's overall survival were shown to be similar in the embolized and non-embolized groups.⁸¹

Surgical management

Interventional procedures

Vertebroplasty and kyphoplasty involve a polymethyl methacrylate (PMMA) bone

cement injection into the vertebral body under image guidance. Cement augmentations provide spinal stability and thermal necrosis of the tumour leading to a substantial reduction in pain.^{82–84} These procedures are indicated in patients with intractable pain without frank mechanical instability nor spinal cord compression.⁸² In cases where pain is caused by nerve root compression, vertebroplasty and kyphoplasty are not recommended as they do not lead to a reduction in tumour size. Studies have shown that these procedures reduce pain by 56–100% and lead to a complete response in 31% of patients.^{85–88} However, vertebroplasty and kyphoplasty are complicated by perioperative cement leakage. The incidence is reported in up to 75% of cases, with most being asymptomatic.⁸⁹ Symptomatic cement leakage may cause catastrophic neural compromise, requiring emergency evacuation.⁹⁰ The risk factors of cement leakage include greater cortical destruction, larger cement quantity and the use of low viscosity PMMA.⁹⁰

Radiofrequency ablation (RFA) is a percutaneous procedure where high frequency radio waves are delivered into the metastatic vertebral body, where they induce a high temperature at the target site leading to tumour cell necrosis. RFA is often combined with vertebroplasty or kyphoplasty, showing effectiveness in reducing pain and disability up to 3 months.⁹¹

Decompression-alone surgery

Spinal decompression is the workhorse treatment for patients presenting with neurodeficit. However, decompression without stabilization is rarely indicated in the setting of spinal metastasis.^{24,73} Spinal invasion by tumours often involves the posterolateral elements of the vertebral column. Laminectomy alone poses a high risk of creating iatrogenic instability, possibly leading to postoperative morbidities.

Minimal access surgery

To minimize blood loss and hasten recovery after surgery, minimal access surgical techniques have been developed over recent years. Spinal stabilization can be achieved with image-guided percutaneous instrumentation or the mini-open Wiltse approach, allowing for less soft tissue trauma.^{92,93} Furthermore, spinal decompression can be done with minimal exposure via the mini-open midline approach, the use of tubular or expandable retractors and endoscopy.^{13–15,92,93}

Minimal access surgery has been shown to be associated with less perioperative complications, intraoperative blood loss, blood transfusion rate, duration of postoperative bed rest and length of hospital stay compared with open surgery.^{13–15} Comparable changes in postoperative pain, neurological outcome, ECOG performance score, odds of survival and the rate of reoperation have been demonstrated in both open and minimal access surgery.^{13–15}

Prompt recovery from minimally-invasive surgery allow cancer patients to quickly return to their oncological treatment. In open surgery, studies suggest a delay of 14 days to 1 month after surgery before initiating adjuvant systemic treatment such as chemotherapy, radiotherapy and targeted therapies in order to minimize the rate of wound complications.^{15,24} In patients that had undergone minimal access surgery, cEBRT may be started 1 week postoperatively and SRS may be initially immediately after the surgery.^{73,94,95}

Hybrid therapy

In the era of SRS, a hybrid therapy, combining separation surgery and postoperative SRS may be performed in radioresistant tumours. The posterior element of the metastatic spinal segment is removed unilaterally or bilaterally. The posterior

longitudinal ligament is then resected. A plane is created between the tumour at the posterior vertebral body and the thecal sac, with a minimum space of 3 mm, allowing for the safe delivery of postoperative SRS.⁹⁶ This technique can be achieved via both minimal access and open spinal surgery. Evidence suggests that hybrid therapy yields an excellent outcome in local tumour control, with a recurrence rate of 4.3 to 22%.⁹⁶ The overall 1-year survival after surgery is reported to be up to 78.4%.⁹⁶ The rate of complications and reoperations are reported as 5.4–14% and 5%, respectively.⁹⁶

En bloc spinal surgery

En bloc spinal surgery has reduced in popularity due to high perioperative morbidity and surgical complexity and has been replaced by hybrid therapy. Limited surgical indications remain in patients with an expected survival over 2 years, controlled primary tumour without extraspinal metastases, adequate cardiopulmonary reserve to tolerate surgery, acceptable preoperative performance status (ECOG 0–2) and in patients treated in centres without SRS in metastasis with known resistance to cEBRT.⁶³ The ideal candidate for en bloc surgery is a patient with a solitary metastasis that can be completely resected. It is the surgery of choice especially in single metastatic lesions from renal cell carcinoma and thyroid cancer.⁶³ The current guidelines for the management of isolated skeletal metastasis, including the spine, suggest complete metastatectomy when this is feasible in these two primary cancers, due to their poor response to radiation and systemic treatments relative to metastases from other tumour types.^{27,63}

En bloc surgery may also be considered in spinal oligometastasis (≤ 3 contiguous vertebrae involvement) that cannot be effectively treated with other systemic or local modalities.⁶³ Overall, en bloc surgery

can be performed via piecemeal total excision in the cervical spine and total en bloc spondylectomy in the thoracic or lumbar spine. The result of en bloc spinal surgery is reported to be excellent, with a local recurrence rate ranging from 1.1% to 15.3%.⁶³ In cases where complete tumour resection is achieved, superior local control and postoperative survival are expected when compared with cytoreductive surgery, including debulking of the tumour at the anterior vertebral column and decompression of the posterior elements.⁶³ However, the rate of major perioperative complications is up to 39.7% and the rate of perioperative mortality ranges from 1.3% to 9.7%.⁶³ Thus, it is recommended that en bloc spinal surgery should only be performed in high volume and experienced centres.

Complications

Due to the frailty of cancer patients, spinal metastasis surgery is reported to have a high complication rate, ranging from 5.3% to 51%.⁹⁷ A previous study suggests that 30-day complications after spinal metastasis surgery leads to a worsened patient survival.⁹⁷ The occurrence of 30-day complications can be predicted by using the Charlson co-morbidity index (CCI) score where the patient's age, comorbidities and primary cancer are considered.⁹⁷ A CCI score ≥ 2 is a robust predictor of perioperative 30-day complications.⁹⁷ Treating physicians must be alert to the need for aggressive monitoring, intensive care, and prevention of possible adverse outcomes in surgical candidates with a high risk of complications.

Hardware failure is another major postoperative concern in patients treated with spinal stabilization. Bone quality of the metastatic vertebrae may be hindered by tumour invasion, systemic cancer treatment and poor nutritional status.⁹⁸ While the

benefit of spinal fusion is robust in preventing hardware failure in degenerative spine surgery, its necessity is still debatable in the setting of spinal metastasis.⁹⁷⁻⁹⁹ In metastatic patients, evidence suggests a low fusion rate at 1 year, with only 16.1% achieving complete fusion, after the surgery.⁹⁸ The rate of spinal fusion over a longer time period may be difficult to evaluate due to the high mortality rate. The rate of hardware failure requiring reoperation is reported to be 4.2% at 1 year and 12.5% at 2 years.⁹⁷⁻⁹⁹ The risk factors for hardware failure include a construction greater than six levels, increasing age and chest wall resection.⁹⁸ A strategy for the prevention of hardware failure has been proposed by using fenestrated pedicle screw and PMMA augmentation in the vertebral body.¹⁰⁰⁻¹⁰² This augmentation is shown to decrease the risk of screw pull out in both open and minimal access spinal surgery.¹⁰⁰⁻¹⁰²

Conclusion

Spinal metastasis and spinal cord compression greatly affect the patient's quality of life and survival. Major advancements in systemic cancer treatment have led to longer patient survival and better treatment outcomes. The development of SRS and minimally-invasive surgical techniques have allowed for excellent local tumour control and a quicker return to systemic treatment. Treating physicians should be aware of the new survival prognostic models and treatment armamentarium in order to optimize the results of spinal metastasis treatment.

Author contributions

P.J. and P.C. determined the objective of this review, established the research questions, performed the literature search, reviewed the literature and selected the relevant articles. P.J. drafted the manuscript. P.C. reviewed the manuscript and critically revised the manuscript.

Both authors contributed to the article and approved the submitted version.

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