Update on the Management of Sacral Metastases

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Abstract

» Sacral metastases have increased over the past decades as chemotherapy improves and more patients survive common cancers.

» Sacral metastases can present with cauda equina syndrome, radiculopathy, and instability.

» Sacral metastases are often treated with radiation therapy, a surgical procedure, or sacroplasty.

» Patient-reported outcomes are of increasing importance when evaluating patients for the management of sacral metastasis.

In the United States, there were nearly 1.6 million cases of cancer in 2016. In the last several decades, 5-year survival rates have increased from 49.1% in 1980 to 57.7% in 1990, 66% in 2000, and 68.9% in 2008[1]. Metastatic sacral disease is rare, representing 1% to 7% of metastatic spine disease[2]. Although rectal carcinoma can metastasize and directly invade the sacrum, most sacral metastatic tumors are the result of hematogenously spread tumor cells[3]. The spread of metastasis often occurs via the Batson venous plexus, especially in the thoracic spine[4]. In recent years, bone metastases have been attributed to the increased number of chemotherapy drugs used in metastatic colorectal cancer[5]. Additionally, because of the effectiveness of systemic therapy, patients are living longer, and more symptomatic spinal metastases are being identified[6]. Sacral metastases are often diagnosed late when they have already extended beyond the osseous margins around the sacral nerves and other surrounding organs[7]. Patients commonly present with pain due to sacral nerve root compression and pathological fractures. Also, sacral nerve root compression can lead to bowel or bladder incontinence[8]. Decreased ambulation associated with radicular symptoms and/or pathological fractures can increase the risk of thromboembolism that is already increased because of the history of malignancy[9].

Anatomy of the Sacrum

The sacrum is composed of a concave surface (facing the pelvis) and convex outer surface, which articulates superiorly with L5 via the L5-S1 facet, inferiorly with the coccyx, and bilaterally with the iliac bones via the sacroiliac joint. The sacrum projects posteriorly and forms the lumbosacral angle. Because of this projection, the articulation at this angle is subject to shearing forces. Sacral nerve roots help to control the sphincters of the rectum, bladder, and sexual organs, as well as the motor and sensory contributions to the lower extremities[10].

Clinical Presentation

Metastatic tumors are the most common malignancy of the sacrum and can signify advanced disease. These are often characterized by radicular pain due to nerve root compression or even tumor infiltration[7,11]. Pain may radiate into the buttocks, posterior aspect of the leg, and perineal region[12].

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Clinical findings include changes in sensation, radiculopathy, motor deficits, bladder and bowel incontinence, and sexual dysfunction[13]. Cauda equina syndrome can be the initial presentation of sacral metastases. The clinical presentation can include severe back pain, urinary retention, constipation, and, at later stages of presentation, bowel and bladder incontinence. Bowel and bladder incontinence is a surgical emergency and prompt decompression should be performed[14].

Imaging

Radiographs are often the first imaging modality performed. However, these may remain inadequate because of the difficulty in evaluating the sacrum on radiographs[11]. Additionally, radiographic evaluation has proven unreliable even in patients with confirmed sacral pathology. Instead, clinicians should focus their attention on the loss of sacral arcuate lines, which more strongly correlates with the presence of metastatic disease[15]. In the case of sacral insufficiency fractures, these are often not displaced and can be challenging to be visualized in radiographs[16]. The gold standard for evaluating a metastatic lesion to the sacrum is magnetic resonance imaging (MRI) with and without contrast[17]. Computed tomography (CT) helps to evaluate the degree of lytic or blastic involvement by the lesion.

Diagnosis

A tissue diagnosis is always fundamentally critical to establish prior to treatment and must distinguish among infection, sarcoma, and other metastatic histologies. Histological examination will differentiate metastases from uncommon infectious conditions[17,18]. However, culture specimens should also be sent along with the biopsy specimen to rule out any concurrent infections. Biopsies can be performed as open incisional procedures, percutaneously or with CT guidance. CT-guided biopsy is the most frequently used biopsy modality and carries a minimal risk[18]. If enough tissue is not obtained, then an open biopsy can be performed. However, in cases of localized extension of tumor into the sacrum such as in the setting of colon cancer or endometrial cancer, a biopsy may not be needed. Also, in the setting of acute neurological deterioration or cauda equina syndrome, surgical intervention should not be delayed and intraoperative biopsy would suffice.

Management

Conventional radiation therapy remains the first-line intervention for sacral metastasis, and doses for conventional radiation therapy include 30 to 40 Gy over multiple fractions[19]. Stereotactic radiosurgery for the spine and sacrum is being increasingly used in the United States[20]. Recurrent sacral lesions following conventional radiation therapy can also be addressed with stereotactic radiosurgery[21]. Gerszten et al. demonstrated in 103 cases of sacral metastasis that spinal stereotactic radiosurgery is effective in decreasing pain and with fewer complications[22]. Additionally, precise control and treatment volume increase success and decrease the risk of neural element injury. Radiosurgery is not indicated in cases of neurological deficit caused by osseous compression to neural structures. Also, it may not be indicated as the only treatment modality when spinal instability is present. Lastly, when treating larger lesions, radiosurgery may not deliver enough radiation[22,23].

Indications for a surgical procedure include neurological deficits, failed radiation therapy, and spinal instability[24]. Surgical intervention relies heavily on the individual pathology of each patient. Several scoring systems are available to help to guide the type of surgical intervention and to determine if a patient's prognosis precludes surgical intervention. The modified Tokuhashi score is composed of 6 sections, including general condition of the patient (performance status), number of extraspinal bone metastases, number of metastases in the vertebral body, metastases to major organs, primary cancer site, and extent of neurological deficits[25]. A score of 0 to 8 points predicts <6 months to live, a score of 9 to 11 points predicts ≥ 6 months to live, and a score of 12 to 15 points predicts a life expectancy of ≥ 1 year.

A palliative surgical procedure or nonsurgical options may be considered for patients with a low score. The Tomita score is another validated scoring system for prognosis in spine tumors. It has 3 components that evaluate the type of tumor, the presence of visceral metastases, and the presence of bone metastases. Scores of 2 to 10 points can be generated, with a higher score indicating worse prognosis and a lower score indicating consideration for excisional surgical procedures[26]. Tumors can be divided into 3 categories based on the Tomita scoring system: slow, moderate, and fast-growth tumors[27]. There is a minimal role for an excisional surgical procedure in the setting of metastatic sacral lesions; however, a palliative surgical procedure can be considered, especially if neurological deficits such as cauda equina syndrome are present. Spinal stability serves as a critical decision criterion when evaluating patients for a sacral surgical procedure. The Spinal Instability Neoplastic Score (SINS) is a validated instrument that provides an objective means of grading spinal stability. A score of 0 to 6 points is a stable spine, a score of 7 to 12 points suggests impending instability, and a score of 13 to 18 points is an unstable spine[28]. The SINS can help to guide treatment for symptomatic upper sacral lesions.

With some minor exceptions, a surgical procedure for sacral metastases is performed via laminectomy with or without instrumentation and/or fusion. A decompression surgical procedure generally involves laminectomy for the evacuation of a tumor causing nerve root compression or cauda equina syndrome, and instrumentation (lumbopelvic fixation) and fusion are employed for impending instability with concurrent nerve root compression.

For the majority of sacral metastases, conventional radiation therapy and stereotactic radiosurgery are adequate treatment modalities. Surgical intervention should be reserved for when neurological deficits are present and/or spinal instability is present. There is also no role for radiation treatment in the setting of cauda equina syndrome associated with sacral metastases, and this should be considered a surgical emergency and prompt decompression should be performed.

In one of the largest series on sacral metastases, Du et al. found that a surgical procedure for sacral metastases was an effective palliative technique to improve bowel function and quality of life[27]. Patients who underwent a surgical procedure without preoperative radiation therapy had a significantly decreased risk ($p = 0.003$) of postoperative complications compared with patients who underwent a surgical procedure after preoperative radiation therapy[27]. Du et al. also reported that better local control was associated with tumors with rapid growth and the use of aortic balloon occlusions[27]. Feiz-Erfan et al. had previously demonstrated similar success on a much smaller cohort of 25 patients. In that study, 24 of 25 patients underwent a surgical procedure for pain relief, with instrumentation and fusion used in 12 of the 25 patients[24]. The median overall survival time was 11 months, reinforcing the perception that a surgical procedure is mainly a palliative intervention. In the senior author's practice, sacral metastases with no evidence of instability but symptomatic nerve root compression are managed via laminectomy alone (Fig. 1). In the setting of nerve root compression and impending instability as measured on the SINS, lumbopelvic instrumentation (lumbar pedicle screws and iliac screws) along with a laminectomy is performed (Fig. 2). For concurrent unilateral involvement of the ilium along with the sacral metastases and instability, the senior author would perform unilateral lumbopelvic instrumentation in the unaffected side (Fig. 3).

Selective Arterial Embolization

Selective arterial embolization can be used for pain control in the setting of metastatic spine and sacral disease[29]. A reduction in tumor size can occur, with associated improvement in pain; however, in 1 series, post-embolization complications were common (56.7%)[29]. Preoperative embolization is also useful when treating vascular lesions (renal cell, hepatocellular, thyroid cancers)[30] and can decrease intraoperative blood loss. An intraoperative means of decreasing blood loss during a sacral metastatic surgical procedure is the use of abdominal aortic balloon occlusion. In a series of 215 patients with sacral lesions, 57 (26.5%) underwent surgical debulking of sacral metastatic lesions[31]. The 30 metastatic patients without aortic balloon occlusion had 4.12 L of blood loss, and the 27 metastatic patients with aortic balloon occlusion had 2.78 L of blood loss[31]. In the entire cohort of patients, there was significantly decreased blood loss with aortic balloon occlusion (4,337 compared with 2,963 mL; $p < 0.001$). Complications included femoral artery embolism and puncture-site hematomas.

Sacroplasty

Sacroplasty, a minimally invasive procedure, can be useful in sacral metastases without instability or epidural disease[32]. Polymethylmethacrylate (PMMA) is injected into the involved region of the sacrum. Indications for sacroplasty include unrelenting pain in the setting of previously irradiated sacral metastatic lesions. Sacroplasty is contraindicated in the presence of epidural disease. Sacroplasty provides pain relief and stability in the setting of diseased sacral segments[33]. Interventional radiologists and interventional neuroradiologists often perform sacroplasty.

Hirsch et al. suggested that the development of percutaneous sacroplasty lagged behind vertebroplasty

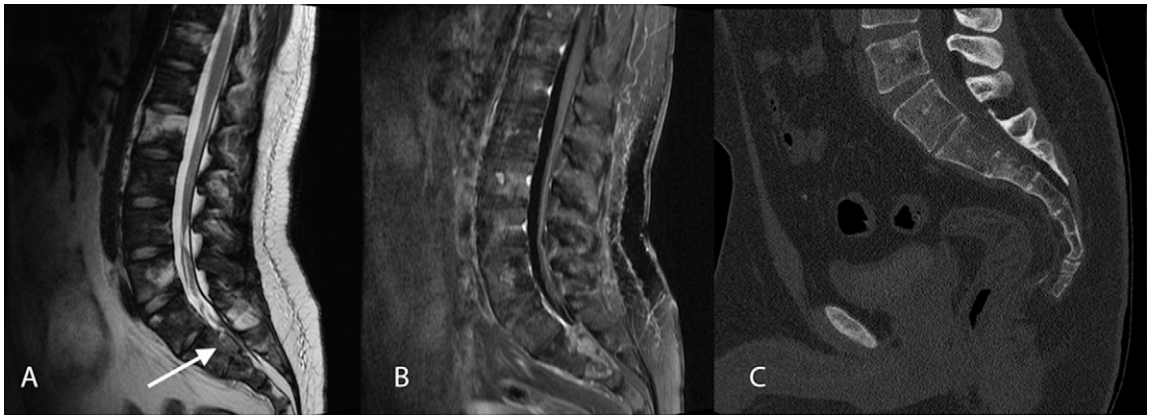

Fig. 1

Figs. 1-A, 1-B, and 1-C A 23-year-old man who presented with cauda equina syndrome associated with metastatic melanoma to the sacrum. **Fig. 1-A** Sagittal T2-weighted MRI of the sacrum demonstrating epidural compression causing severe stenosis (arrow). **Fig. 1-B** Sagittal MRI, with contrast, of the sacrum demonstrating sacral canal enhancement associated with the metastatic compression. **Fig. 1-C** Sagittal CT of the sacrum demonstrating no fracture or lytic lesion. The patient was managed with sacral laminectomy without instrumentation.

Fig. 2

Figs. 2-A through 2-F A 78-year-old man who presented with severe pain and radicular symptoms associated with a lytic lesion of S1 from colon cancer. The patient had a SINS of 9 points, or impending instability. Sagittal T2-weighted MRI of the sacrum (**Fig. 2-A**) and sagittal MRI of the sacrum with contrast (**Fig. 2-B**) demonstrate involvement of S1 and S2. Sagittal CT (**Fig. 2-C**) and axial CT (**Fig. 2-D**) of the sacrum demonstrate a lytic lesion of S1 with associated S1 fracture. The patient was managed with L4-to-pelvis lumbopelvic fixation and sacral laminectomy followed by radiation therapy. An anteroposterior radiograph (**Fig. 2-E**) and lateral radiograph (**Fig. 2-F**) of the lumbar spine demonstrate the L4-pelvis instrumentation. The patient was still alive at 15 months following the procedure and continued to have minimal pain.

because of the likelihood of misdiagnosis as well as the inherent difficulties of sacral anatomy[34]. Several other reports have experienced difficulty in defining good landmarks for needle placement, including difficulty visualizing the ventral cortical margin of the sacrum[35,36]. Safe sacroplasty can be performed with meticulous preoperative planning and use of MRI or CT for delivery of the PMMA[37]. Although radiation therapy is an important component of decreasing pain and local disease burden, up to two-thirds of patients with radiation therapy do not experience complete pain relief[38] and radiation therapy does not alleviate underlying mechanical pain caused by associated pathological fractures[39]. With the exception of 1 multicenter report on 204 cases of sacral insufficiency fractures[9], 24 due to sacral metastasis, the literature comprises case reports and single-center studies. Madaelil et al. demonstrated that sacroplasty can be successfully paired with radiofrequency ablation for pain relief and local tumor control[40].

In a large cohort undergoing sacroplasty for symptomatic lesions and sacral insufficiency fractures, Kortman et al. demonstrated a mean reduction in visual analog scale (VAS) pain from 9.0 to 2.6 in a series of 39 patients (of a total 243 cases), with complete resolution of pain in 18%, pain reduction in 72%, and no pain relief in 10% of patients[9]. These data are largely representative of the subsequent studies at other single-center cohorts and in case reports. In the cohort examined by Moussazadeh et al., 84% of patients experienced severe pain before treatment (scores of 7 to 10 on a 10-point scale) and 80% experienced pain reduction at a median follow-up of 6.5 months, with 56% of patients

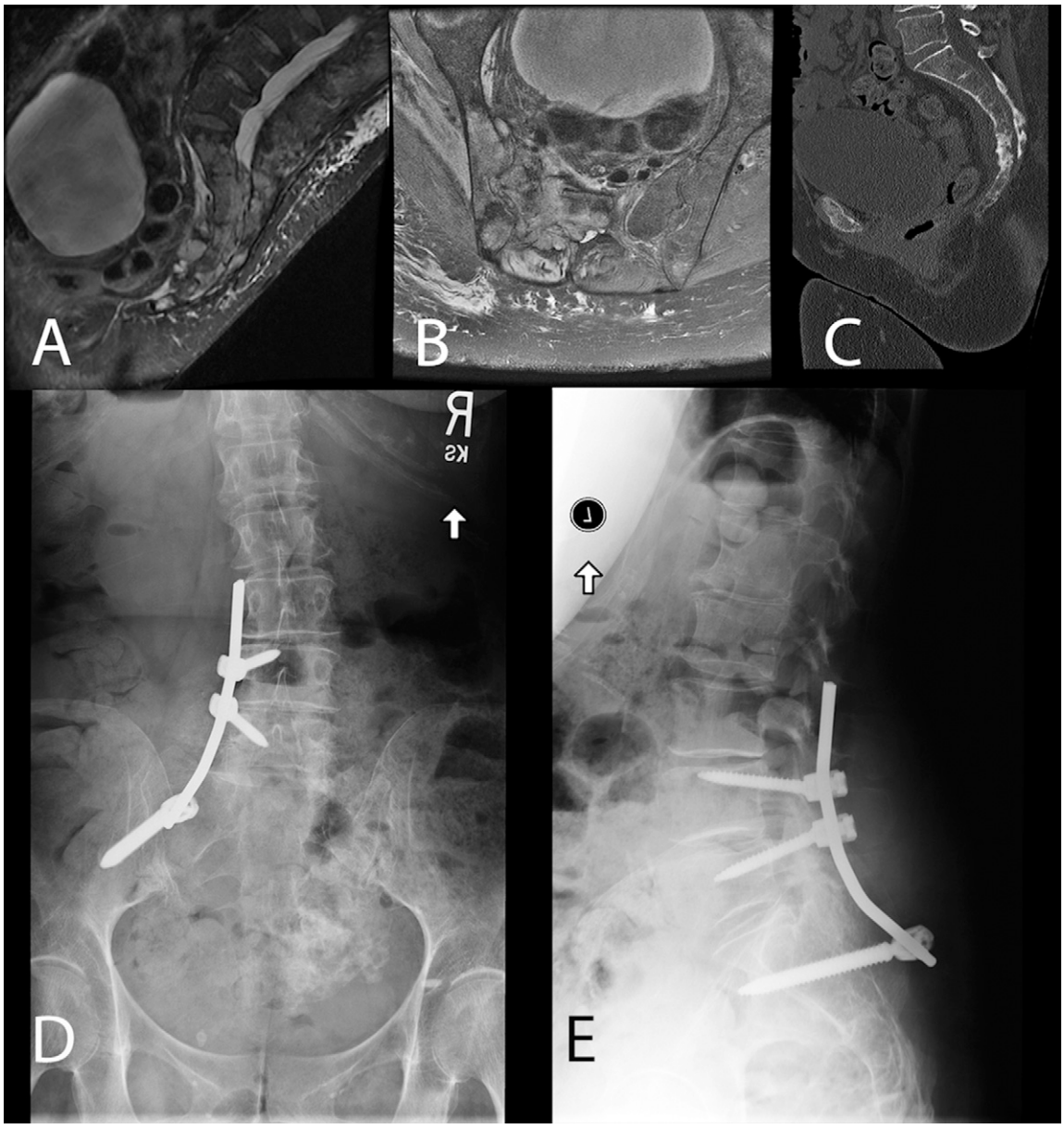

Fig. 3

Figs. 3-A through 3-E A 63-year-old woman with pain and radicular symptoms associated with metastatic endometrial cancer affecting the right ilium and sacrum. Radiation therapy was administered to the region, but disease progression ensued. Because of the patient's S3-S4 fracture and mechanical pain with ambulation associated with the metastatic lesion of the right ilium and sacroiliac joint, we performed left lumbopelvic instrumentation to provide stability and pain control. **Fig. 3-A** Sagittal T2 short tau inversion recovery (STIR) MRI of the sacrum demonstrating multilevel sacral canal stenosis. **Fig. 3-B** Axial STIR MRI of the sacrum demonstrating the predominant involvement of the right sacrum and ilium along with canal compromise. **Fig. 3-C** Sagittal CT demonstrating the fracture of the sacrum at the S3-S4 level. The patient was managed with left-sided L4-to-pelvis instrumentation and multilevel sacral laminectomy. An anteroposterior radiograph (**Fig. 3-D**) and lateral radiograph (**Fig. 3-E**) demonstrate the L4-pelvis instrumentation.

having mild pain (scores of 1 to 4 points on a 10-point scale) at the time of the latest follow-up. Additionally, of the 17 patients needing ambulatory aid, 6 required less aid and 3 returned to ambulation[41]. Similar improvements in the pain VAS, from a median of 8.0 preoperatively to 4.0 postoperatively, have also been reported by Gupta et al. but without improvements in scores on the functional mobility scale. Instead, patients with osteoporotic insufficiency or traumatic fractures experienced greater improvement in the pain VAS than patients with cancer-related fractures[16]. Improvements in the pain VAS may be the most important criterion as they allow for some further therapeutic measures to be tolerated by patients[42]. Although the results are promising, it is important to remember that sacroplasty is effective only in a select group of patients having sacral pain and reinforces the fact that sacral

metastasis requires a multidisciplinary approach.

Complications associated with sacroplasty include hemorrhage, infection, cerebrospinal fluid leakage, and nerve root or lumbosacral plexus injury[41,43]. Misplacement of the injection needle can lead to direct sacral nerve damage or imprecise cement deposition. These cases can lead to bowel and bladder incontinence and motor weakness (foot drop, plantar flexion weakness)[37]. Cement leakage may also lead to radiculopathy, which can be treated by surgical decompression of the encased nerve root via sacral laminectomy to remove the PMMA[43]. It has been suggested that balloon insertion can prevent leakage by compaction of the peripheral tissues leading to closure of possible fissures[42].

Radiofrequency Ablation

Radiofrequency ablation uses thermal energy to cause tumor necrosis and to destroy pain-generating pain fibers[44]. Radiofrequency ablation is used to manage symptomatic metastatic spine disease in the absence of epidural metastatic disease. Spinal instability is also a relative contraindication for radiofrequency ablation. In a series of 11 of radiofrequency ablation procedures to treat 16 sacral metastases, Madaelil et al. reported no complications and a decrease in pain score from 8 to 3 ($p = 0.004$). They also did cement augmentation in 7 of the 11 procedures[40]. Goetz et al. reported on 43 patients with osseous metastases undergoing radiofrequency ablation, 12 (28%) of whom underwent radiofrequency ablation treatment of sacral metastases[45]. A reduction in pain scores compared with baseline was noted, although 1 of the patients undergoing radiofrequency ablation in the sacrum developed bowel and bladder incontinence following the procedure. Although, to our knowledge, there have been no large series or randomized trials on the efficacy of radiofrequency ablation for sacral metastases, it is an option for painful sacral metastases that have not responded to radiation treatment and do not have neural element involvement.

Surgical Complications

Surgical intervention in the sacrum represents a complex problem, which, dependent on the selected surgical approach, can lead to either minor or major complications. Complications include poor wound-healing, wound infections, neurological damage, cerebrospinal fluid leakage, deep vein thrombosis, loosening of instrumentation, blood vessel damage, wound seroma, and urinary tract ;infections[24,27]. A surgical procedure is not usually indicated for S1/S2 lesions without epidural extension because of the risk of associated surgical complications such as surgical-site infection. The exception would be the presence of instability[46]. En bloc resection with reconstruction is also associated with high rates of complications[47] and should only be reserved for an isolated metastatic lesion in a patient with a prognosis of longer than a few years of life expectancy. Additionally, patients who undergo preoperative radiation therapy have a significantly increased risk of postoperative complications compared with patients who underwent a sacral surgical procedure prior to radiation therapy ($p < 0.003$)[24]. Some strategies to decrease wound complications and infections include collaborating with plastic surgeons on the closure of the wound, administration of intrawound vancomycin powder, and, if performing lumbopelvic instrumentation, considering placing minimally invasive screws with concurrent open decompression[48-50].

Patient-Reported Outcomes

There is growing recognition that evaluation of the success of surgical interventions should ideally incorporate the patient's self-assessment of functional outcomes[48]. In general, the literature on clinical outcomes of metastatic tumors has been limited to survival, local recurrence, complications, and gross measures of function (ambulatory status, Frankel score) and lacks patient-reported self-assessment. A systematic review of the literature found that few studies on metastatic spine disease used patient self-assessment instruments to assess health status[51]. Established outcome instruments for oncology and spinal disorders are not designed for patients with metastatic spine disease and a disease-specific instrument is necessary to increase specificity and sensitivity to detect change[51]. The Spine Oncology Study Group Outcomes Questionnaire (SOSGOQ) was developed as a quality-of-life instrument specific to patients with metastatic lesions of the spine[52]. The SOSGOQ may provide a better measure of disease burden compared with other patient self-assessment instruments previously identified[52]. Most recent recommendations involve use of the SOSGOQ for measuring quality of life, the Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function for measuring physical function, and the PROMIS Pain Intensity for measuring pain[53]. Alternatively, recommendations have also been made to use questionnaires that best address 7 domains governing patient outcomes: mental health, physical health, pain, gastrointestinal symptoms, urinary incontinence, sexual function, and social health[54]. The study of patient-reported outcomes in metastatic spine and sacral disease is still in an early stage, with the potential for further research and improvement.

Conclusions

Sacral metastasis is approached in a multidisciplinary manner. Sacral metastases, although historically uncommon, have been increasing in frequency. Management can be a combination of conventional radiation therapy, radiosurgery, sacroplasty, radiofrequency ablation, surgical decompression, and stabilization. Complications include poor wound-healing, wound infections, neurological damage, cerebrospinal fluid leakage, deep vein thrombosis, loosening of instrumentation, and blood vessel damage. Having a plastic surgeon assist with wound closure

in the setting of prior radiation can decrease the rate of wound complications. Patient-reported outcomes for sacral metastases are mostly still being defined and studied, including the PROMIS and SOSGOQ questionnaire.

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