Spinal Cord Compression in Patients With Advanced Metastatic Cancer

"All I Care About Is Walking and Living My Life"

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As 1 of the 12 700 US cancer patients who, each year, develops metastatic spinal cord compression, Ms H wishes to walk and live her life. Sadly, this wish may be difficult to fulfill. Before diagnosis, 83% to 95% of patients experience back pain, which often is referred, obscuring the site(s) of the compression(s). Prediction of ambulation depends on a patient's ambulatory status before therapy and time between developing motor defects and starting therapy. Ambulatory patients with no visceral metastases and more than 15 days between developing motor symptoms and receiving therapy have the best rate of survival. To preserve ambulation and optimize survival, magnetic resonance imaging should be performed for cancer patients with new back pain despite normal neurological findings. At diagnosis, counseling, pain management, and corticosteroids are begun. Most patients are offered radiation therapy. Surgery followed by radiation is considered for selected patients with a single high-grade epidural lesion caused by a radioresistant tumor who also have an estimated survival of more than 3 months. Team discussions with the patient and support network help determine therapy options and include patient goals; assessment of risks, benefits, and burdens of each treatment; and discussion of the odds of preserving prognosis of ambulation and of the effect of therapy on the patient's overall prognosis. Rehabilitation improves impaired function and its associated depression. Clinicians can help patients cope with transitions in self-image, independence, family and community roles, and living arrangements and can help patients with limited prognoses identify their end-of-life goals and preferences about resusitation and entering hospice.

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THE PATIENT'S STORY

Ms H is a 56-year-old interventional radiology technician living alone in a 2-story house. In 1986, she developed breast cancer, initially treated by left mastectomy followed by chemotherapy and chest wall radiotherapy. In 1990, she developed bony metastases. Bisphosphonates were initiated and a left rib resection done; after a salpingo-oophorectomy, she had regression of a left hip metastasis. In 2000, a T7 vertebral metastasis was treated with 44 Gy to the T6 to T8 vertebral area. In 2004, a recurrent lesion required T7 vertebral corpectomy with structural rib autograft and a T4 to T10 instrumented fusion. Capecitabine was begun and continued through November 2006, when she developed thoracic pain and progressive difficulty walking. The T7 vertebral tumor now involved the T6 to T7 ventral epidural space with significant cord impingement. The posterior spinal fixation had loosened, and she had progressive deformity of her spine. Ms H's original surgeon, Dr L, recommended surgery by Dr O followed by stereotactic radiosurgery (1500 centigray in 5 fractions over 5 days) at a university hospital 400 miles from her home. Ms H agreed.

On admission, she had difficulty with her gait and with urinary retention and had episodes of overflow urinary incontinence. Her midthoracic pain was incapacitating despite a transdermal fentanyl patch and oral rescue opioids. She was largely confined to bed but ambulated to the bathroom holding onto walls and using a walker.

On physical examination, Ms H was distraught. She had a left mastectomy scar and postradiation chest wall changes. She walked with an ataxic gait and had increased tone in the lower limbs bilaterally. Her motor examination was remarkable for 4 of 5 strength in the left extensor hallucis longus, tibialis anterior, and bilaterally in her iliopsoas muscles. Sensation was decreased in the left first toe web, and there

See also Patient Page.

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was loss of proprioception bilaterally. Knee and ankle jerks were hyperactive and symmetrical; there were 3 beats of clonus bilaterally, with a positive Babinski sign on the left foot.

Following administration of preoperative medications, including 4 mg of dexamethasone orally twice a day; 20 mg of famotidine orally once a day; 50 µg/h of fentanyl through a transdermal patch that was changed every 3 days; and 4 mg of hydromorphone orally every 4 hours as needed for pain, she underwent revision posterior surgery with laminectomies of the T6 through T8 vertebrae and excision of tumor from the dorsal aspect of the spine followed by instrumented spinal fusion from the T3 to L2 vertebrae. Five days later, she underwent corpectomies of the T6 to T8 vertebrae with resection of epidural tumor and anterior column reconstruction from the T5 to T9 vertebrae using a cage, rods, and structural rib. Eight days after the anterior surgery, Ms H was transferred to a rehabilitation facility where she stayed for 3 weeks. Five months later, she required only nonopioid medications, had good strength and proprioception, and was walking more than 2 miles daily.

PERSPECTIVES

Ms H and Dr O were interviewed by a Perspectives editor in March 2007.

MS H: *I was lying around . . . not doing a lot, so I started to atrophy. . . . I didn't go to work. . . . My social activities were cut to nothing, and I'm a very active person. I didn't go to basketball games, and I missed a football game. I just couldn't go.*

DR O: *[She] had been a very active woman. Unfortunately, with her tumor's progressive involvement of the spine, and her progressive deformity, she became disabled to the point where she was not really able to ambulate around the house. . . . She was only 55 years old and she was really losing her independence. This is always an issue, even for older patients, but for someone this age, this is a very difficult thing.*

About 500 000 patients die of cancer annually. Ms H is among the 12 700 cancer patients in the United States who, each year, develop spinal cord compression, putting them at risk for pain, paraparesis or paralysis, incontinence, and institutionalization.[1] Breast, prostate, and lung cancer each account for 15% to 20% of cases; non-Hodgkin lymphoma, myeloma, and renal cell carcinoma each account for 5% to 10% of cases. The remainder are primarily from colorectal cancer, cancer of unknown primary, and sarcoma.[2,3]

Assessment of Spinal Cord Compression

MS H: *At first it was just pain. After they diagnosed it, it gradually got worse. I started getting numbness in my feet and by the time I [flew] up to my surgery, they were practically carrying me through security. I could hardly even walk.*

DR O: *When she came to see me, she had progressive pain as well as difficulty walking [and] difficulty sitting. . . . [In]a patient presenting with a new onset of [back] pain, especially a patient with a history of tumor, we always have to have tumor very high on our differential diagnosis.*

Back pain is the most common symptom of spinal cord compression, noted by 83% to 95% of patients prior to its diagnosis.[3,4] Pain, which can be local, referred, radicular, or all 3 is caused by the expanding tumor in the bone, bone collapse, or nerve damage. Referred pain is common: cervical compressions often cause midscapular pain, thoracic compressions can cause hip or lumbosacral pain,[5] and lumbosacral compressions can cause thoracic pain.[6] Sixty percent of the metastases are thoracic, 30% lumbosacral, and 10% cervical.[3] Commonly, breast and lung cancers cause thoracic lesions, while colon and pelvic carcinomas affect the lumbosacral spine.[7] In 20% of patients, cancer presents as a spinal cord compression.[5,8]

Patients with cauda equina syndrome experience diminished sensation over the buttocks, posterior-superior thighs, and perineal region, and, in 20% to 80%, decreased anal sphincter tone. Urinary retention and overflow incontinence are pathognomonic of the syndrome (90% sensitivity; 95% specificity).[9] Absence of a postvoid residual virtually excludes it (99.99% negative predictive value).[9]

Common signs of spinal cord compression include radiculopathy, weakness,[10] sensory changes (eg, paresthesias, loss of sensation), sphincter incontinence, and autonomic dysfunction (eg, urinary hesitancy, retention). One useful scale for functional assessment is the Frankel grading system[11] which consists of (A) complete paraplegia, (B) only sensory function, (C) nonambulation, (D) ambulation, and (E) no neurological symptoms or signs. Other scales include the Frankel/American Spinal Injury Association scale,[12] the International Medical Society of Paraplegia scale,[12] and the Tomita scale.[13] The Barthel index, originally designed for geriatric patients, additionally assesses transfer from bed to chair or commode and bowel and bladder function.[14]

It is difficult to determine the current prevalence of these signs of spinal cord compression because most studies were conducted before diagnosis by magnetic resonance imaging (MRI) became available. In 1 study, 60% to 85% of patients at diagnosis had weakness and two-thirds were nonambulatory.[3] In others, more than half presented with sensory changes beginning in the toes[15] or 1 to 5 levels below the lesion.[3] About half needed Foley catheters,[3] but autonomic dysfunction was never the sole presenting symptom.[7,15]

Diagnosis of Spinal Cord Compression

DR O: *Her main risk for mortality was progressive paraplegia. . . . The real risk factors here are infection problems, pulmonary problems, skin problems—that's what leads to death in many of these cases, even more so than the progression of the tumor itself.*

Delay in diagnosis of spinal cord compression results in loss of mobility,[16,17] bladder dysfunction,[16] and decreased survival.[18-22] Because therapy is usually well tolerated in ambulatory patients (even those with very limited overall prognoses),[23] the diagnosis of spinal cord compression should always be considered urgent.

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Magnetic resonance imaging is the gold standard in detecting epidural metastatic disease and frank spinal cord compression[4,19,24,25] (sensitivity 93%, specificity 97%, overall accuracy 95%).[26] Plain spine radiographs have inadequate sensitivity and a false-negative rate of 10% to 17%.[3] No validated predictive models suggest that clinicians can omit an MRI in a patient with known cancer and back pain.[27]

Finding unsuspected lesions is not unusual.[5,28,29] In 45% of patients, MRI findings altered the radiation therapy field.[30] An MRI of the entire spine is therefore required, including T1-weighted sagittal images with T1- or T2-weighted axial images in areas of interest.[3,19,31] Because patients with prostate cancer who have had more than 20 bone metastases and who have taken hormone therapy for several years have a 44% incidence of spinal epidural disease, MRIs might be considered even before the development of symptoms of spinal cord compression.[4]

Treatment of Spinal Cord Compression

Ms H: *All I care about is walking and living my life.*

DR O: *For many patients, reasonable goals are improvement of pain, improvement of quality of life, improvement of independence. For [other] patients, the goal is to improve survival. Understanding exactly what the patient's goals are and understanding the clinical scenario are important for an appropriately guided treatment.*

Pain Management and Symptomatic Measures

TABLE 1 lists common opioids and adjuvants that control neuropathic and bone pain from vertebral metastases and spinal cord compression.[3,6,34,35] Opioid dosages shown are for opioid-naïve patients; those already taking opioids may need substantially higher dosages. Patients who have moderate or severe pain often benefit from a continuous intravenous infusion of opioids delivered through a patient-controlled analgesia device, which allows the patient to self-administer rescue doses should the initial basal rate chosen be inadequate or should pain occur with movement (so-called incident pain). A consensus document from the American Pain Society offers algorithms for safe titration of intravenous opioids.[35] Corticosteroids, effective for both neuropathic and bone pain, are discussed below. The anticonvulsants gabapentin and pregabalin have been shown to decrease the paresthesias and the burning, shooting, "toothache" pain that arises from peripheral nerve or spinal cord injury,[6,33,36,37] although no studies have specifically investigated patients with malignant spinal cord compression. To minimize sedation, both agents should be started at a low dose and titrated to effect (Table 1). Tricyclic antidepressant agents, which putatively act via a different mechanism than anticonvulsant agents,[33] can be used at bedtime because most induce sedation.[6,33] Although no randomized trials have investigated the effects of anticonvulsants in patients with

Table 1. Pharmacologic Management of Pain in Opioid Naïve Patients With Malignant Spinal Cord Compression[a]

Drug	Initial Dose for Opioid	Comments
Opioids		
Morphine[b]		
Immediate release	15-30 mg orally every 2 h as needed	Titrate to relief
Sustained release	15 mg orally every 8-12 h	Increase every 24 h based on need
Oxycodone[b]		
Immediate release	10-20 mg orally every 2 h as needed	Titrate to relief
Sustained release	10 mg orally every 12 h	Increase every 24 h based on need
Hydromorphone		
Immediate release	4-8 mg orally every 4 h as needed	Titrate to relief; add sustained release opioid or fentanyl for basal relief
Fentanyl	12-25 µg/h transdermally every 72 h	Add immediate release opioid as needed every 2-4 h
Neuropathic pain adjuvants		
Dexamethasone[12,32]	10 mg orally or intravenous load 4-6 mg orally or intravenously every 6 h	Current practice; in patients with symptomatic compression, evidence favors higher doses (see text for discussion)
Gabapentin[33bc]	100 mg orally twice a day; 300 mg at bedtime	Can cause somnolence, edema, myoclonus
Pregabalin[33bc]	75 mg orally twice a day	More reliable oral absorption than gabapentin
Amitriptyline, nortriptyline[33d]	10-25 mg orally at bedtime	Second-line therapy, anticholinergic adverse effects
Bone pain adjuvants		
Zoledronic acid[12]	4 mg intravenously every 3-4 wk	Hypocalcemia occurs in patients with vitamin D deficiency
Pamidronate[12]	90 mg intravenously every 3-4 wk	May have less renal toxicity
Acetaminophen	1000 mg orally every 6-8 h	
Bowel regimen medications[e]		
Docusate plus senna	1-2 orally twice a day	Use in most patients taking opioids
Polyethylene glycol	17-34 g orally at bedtime as needed	Used when no stool in 48 h
Bisacodyl or glycerin suppository	Daily, scheduled	To empty bowel in patients with severe autonomic dysfunction, suppository followed by enema as needed

Abbreviations: IR, immediate release; SR, sustained release.
[a] Decrease doses in elderly patients. Table is based on Schiff,[3] Abrahm,[6] Schmidt et al,[32] and Dworkin et al.[33]
[b] Decrease doses for creatinine clearance less than 50 mL/min.
[c] No studies in gabapentin or pregabalin have been reported in patients with malignant spinal cord compression.
[d] A randomized trial of amitriptyline in patients with spinal cord injury (from unspecified causes) showed no benefit over placebo.
[e] Goal: soft daily or every-other-day stool without need for Valsalva maneuver.

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malignant spinal cord compression, a single randomized controlled trial involving patients with spinal cord injury (from unspecified causes) showed that amitriptyline was no more effective than placebo.[38]

Aggressive treatment of constipation due to autonomic dysfunction, inactivity, or opioids will prevent increased pain from use of the Valsalva maneuver.[3,6,35] For patients who retain sphincter control, a typical initial regimen would include a stool softener, a stimulant, and an osmotic laxative, to promote soft stooling at least every 1 to 2 days (Table 1). For patients who cannot eliminate stool on their own, a regimen of polyethylene glycol and a daily stimulant suppository is effective.[6]

Bisphosphonates such as zoledronic acid and pamidronate decrease bone pain.[6,12] Nonsteroidal anti-inflammatory agents are safest for younger patients who have no history of gastrointestinal bleeding and normal renal function. They may be added for patients who poorly tolerate opioid-induced adverse effects.[6,34,35] Physical therapy will not diminish the pain related to tumor or pathological fracture and may accentuate fracture pain, so it should not be used before radiation or surgery. Braces, however, may improve comfort by providing external support.

Patients with paraparesis or paralysis frequently experience anxiety and depression.[39] Patients whose core self-image and sense of self-esteem are predicated upon physical activity and independence may find themselves feeling out of control, helpless, and hopeless. They and their families need referrals to social workers, psychologists, psychiatrists, or spiritual leaders.

Glucocorticoid Therapy

Glucocorticoids reduce injury from traumatic spinal cord injury[40] presumably through their antioxidant or antioxidantlike activity, reducing the release of total free fatty acids and prostanoids, and preventing lipid hydrolysis and peroxidation.[40] Dexamethasone inhibits prostaglandin E_2[41] and vascular endothelial growth factor production and activity[42] and therefore decreases vasogenic edema, which is partially mediated by increased levels of prostaglandin E_2[43] and vascular endothelial growth factor.[44] Animal models indicate a dose-dependent response of vasogenic edema and improved neurological function with corticosteroids, even without radiation therapy.[45-47]

Although some experts believe that dexamethasone does not benefit asymptomatic ambulatory patients receiving radiation therapy,[19,23,48,49] the general consensus is that corticosteroids are beneficial.[12,23] Prospective studies suggest an initial dexamethasone dose of 96 or 100 mg of intravenous bolus followed by 24 mg taken orally 4 times daily for 3 days, tapered over 10 days.[10,50] Of patients so treated, 64% reported substantial relief on day 1 and 82%, overall relief.[10] In a randomized single-blind trial, 57 patients receiving radiation therapy were randomized by diagnosis (breast cancer or other) and gait function (preserved or not) to receive either high-dose or no doses of dexamethasone. At the end of therapy, 22 of 27 patients taking dexamethasone were ambulatory compared with 19 of 30 who did not ($P = .046$).[50]

High-dose dexamethasone to promote posttreatment ambulation was a grade A recommendation from a 1998 evidence-based guideline.[48] However, the guideline acknowledged that the optimal dose of dexamethasone is unknown.[19,24,51] This remains the case a decade later, but given the anxiety, restlessness, and delirium that high doses of dexamethasone can induce,[52] an initial dexamethasone dose of 24 to 40 mg/d orally or intravenously (eg, 6 to 10 mg every 6 hours), with a taper during or immediately after completion of radiation is reasonable.[12,32]

Even at these lower doses, 5% of 21 patients receiving less than 3 weeks of therapy experienced tremulousness, insomnia, delirium, and hyperglycemia.[51] Toxicity increased when the total dose exceeded 400 mg and when treatment extended for more than 3 weeks.[51] Fourteen of 38 patients (37%) on the prolonged steroid course developed oral or esophageal *Candida* infections.[51] If a prolonged course of dexamethasone is planned, simultaneous trimethoprim and sulfamethoxazole to prevent *Pneumocystis jiroveci* infection[53] and 100 mg of fluconazole taken orally daily to prevent thrush and esophageal candidiasis should be considered.

Radiation Therapy

Radiation therapy is directed at vertebral metastatic sites that are painful or are associated with significant epidural involvement or thecal sac indentation (ie, subclinical spinal cord compression). Prospective observational studies have shown that 60% to 90% of patients achieve pain relief with radiation therapy and dexamethasone.[2,20,54,55] From 60% to 100% of patients who are ambulatory before radiation therapy maintain the ability to walk.[2,10,18,19,54] Patients with lung cancer are least likely to remain ambulatory.[2,3] Pooled studies indicate that 36%[29-31,33-43] to 40%[31,33-50] of paraparetic patients become ambulatory after radiation therapy.[18,20] Restoration of full ambulation and sphincter function ranges from 13%[7-20] to 15%[8-23] of paralyzed patients.[18-20] More than 50% of patients with lung cancer and 40% with prostate cancer remained paralyzed vs 10% of patients with breast cancer ($P = .003$).[18]

Radiation therapy ports extend 1 or 2 vertebral bodies above and below the site of compression.[15] Myelosuppression can occur if multiple spinal sites are treated.[56] Dosing schedules are designed to have a less than 5% chance of inducing radiation myelopathy (ie, hemiparesis, spasticity, and loss of pain and temperature sensation). Standard external beam radiation therapy usually consists of 30 Gy in 10 fractions[48]; regimens of more than 30 Gy do not improve outcomes.[57] However, treatment regimens can be more prolonged (25-40 Gy in 10-20 fractions over 2-4 weeks)[15]; treatment courses can also be shorter (4 Gy/d for 7 days)[18,32]; or much shorter (8 Gy once or 4 Gy for 5 sessions, or 8 Gy for 2 sessions 1 week apart).[56 58,59] After balancing significant pretreatment prognostic factors, no regimen has been shown to be superior in preserving ambulation.[19,24,60]

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No late radiation-related toxicities have been reported using short courses,[18,59-61] but patients develop more infield recurrences, less bone recalcification,[60] and shortened survival compared with patients receiving longer courses.[62,63] Nevertheless, shorter courses are safe and effective and may be particularly appropriate for patients with shorter life expectancy who can achieve pain control and preserve their ambulatory status.

A new score, derived from a retrospective analysis of more than 1800 patients with metastatic spinal cord compression, estimates 6-month survival following radiation therapy.[63] Variables associated with a short prognosis include primary tumors other than breast, prostate, or myeloma and lymphoma; other bone or visceral metastases; nonambulatory status before therapy; interval from tumor diagnosis of less than 15 months; and motor deficits developing less than 14 days before therapy.[62,63] Estimates of 6-month survival vary from 4% for patients with all the negative prognostic factors to 99% for those with none.[63] Patients not likely to live long enough for a recurrence or for bone recalcification are the best candidates for single fraction or short course radiation therapy.

Overall, 10% of patients treated with standard radiation therapy develop recurrences in the short term (median time to recurrence, 4.5 months),[18] but 50% of 2-year survivors and almost all 3-year survivors develop recurrences.[3] For patients who initially received a short course of therapy, a repeat course of external beam radiation therapy (or stereotactic radiosurgery as described below) can be considered.[19] Patients who experience a recurrence have a median survival of 4.2 months, but of those who survive, 88% remain ambulatory at 6.5 to 35 months. Radiation-induced myelopathy rarely develops (eg, 1 of 13 long-term survivors[59]), with a median latency of 1 to 2 years.[64] Therefore, for patients likely to survive less than 1 year, the benefits of reirradiation likely exceed the risks.

High-Precision Radiotherapy Techniques

Advances in radiation therapy techniques show promise both for primary treatment and for patients with recurrent disease. With the evolution in computed tomography and MRI capabilities, conformational radiation therapy plans are now 3-dimensional, and, with the advent of intensity-modulated radiotherapy (IMRT) (the ability to vary dose delivery during a treatment session), higher radiation doses can now be delivered to the target, sparing normal spinal and paraspinal tissues.[65] Image guidance with IMRT is a further refinement.[66] Tomotherapy is a third high-precision technique that uses a rotating linear accelerator to deliver IMRT.[65]

Stereotactic radiosurgery (eg, the CyberKnife[65] or the Novalis Shaped Beam Surgery[64]) can be used alone or following external-beam radiation or surgery, as it was for Ms H.[67] Patients receive 1 large dose (eg, 6-8 Gy) to a localized tumor with the precisely shaped radiation beam that comes as close as 1.36 mm to the simulation isocenter.[68] Patients must be able to tolerate staying in the same position for the 90 minutes of the treatment.[69]

When used alone (without spinal tumor resection), radiosurgery provided pain relief in 74%[70] to 89%[71,72] of patients followed up prospectively for 14 to 48 months.[71] None developed spinal instability or neurological defects, even though 12% later required surgery for progressive tumor.[71] One prospective cohort study of 500 patients followed up for a median of 21 months (range, 3-53 months) analyzed the outcomes of radiosurgery in patients without "bony compression of neural elements or overt spinal instability."[72] Long-term pain control was achieved in 86% overall, in 96% of patients with breast cancer or melanoma, and in 93% of patients with lung cancer. Tumor progression was halted in 90% of the 65 patients receiving radiosurgery for primary treatment (100% of breast, lung, and renal cell carcinoma and 75% of melanoma) and in 90% of the 51 patients treated after failure of conventional irradiation (100% of breast and lung carcinoma, 87% of renal carcinomas, and 75% of melanomas).[72] Few studies to date have directly compared the efficacy and toxicity of radiosurgery and conventional radiation therapy. One retrospective matched-pair analysis of patients with spinal metastases from metastatic breast cancer showed similar ambulation, performance status, and pain control in 18 patients with initial spinal disease who received CyberKnife radiosurgery and 17 patients reirradiated for recurrent disease.[73]

Insurance coverage for radiosurgery is generally available for patients requiring reirradiation but may be more problematic for initial therapy. Further studies comparing radiosurgery to traditional radiotherapy are needed to determine its effectiveness and the highest tolerable doses.[68,74]

Surgery

DR O: *[O]ur goal was to improve her pain and deformity. . . . We can reliably stabilize the spine and that will improve pain, as well as stance and alignment of the spine. . . . She'd already had her maximum tolerable dose of radiation, and despite radiation, she had progression of tumor. . . . The deformity would continue to get worse over time. . . . In this setting, with the tumor in the epidural space and a revision surgery, we're unable to get all the tumor out. By getting a majority of the tumor out, . . . we were able to accurately localize where to go with radiation using the CyberKnife. It's important to recognize that there is a role for a multidisciplinary approach to the patient. . . . We have neuroradiologists who put together some of the imaging. We have medical oncologists and radiation oncologists. We have our orthopedic team who does complex reconstructions. . . .Having all of these components integrated in a setting where we are discussing cases and learning from each other is very valuable.*

Debate is ongoing regarding the merits of radiotherapy alone vs surgical therapy followed by radiation for selected patients with spinal cord compression. Despite finding "few papers of high methodological quality,"[24] a 2005 evidence-

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Table 2. Tokuhashi Revised Scoring System for Preoperative Prognosis of Metastatic Spinal Tumors[a]

Parameter	Score
General condition	
Poor	0
Moderate	1
Good	2
No. of extraspinal metastases	
≥3	0
1-2	1
0	2
No. of vertebral body metastases	
≥3	0
2	1
1	2
Metastases to the major internal organs	
Nonremovable	0
Removable	1
None	2
Primary site of cancer	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gallbladder, unidentified	1
Others	2
Kidney, uterus	3
Rectum	4
Thyroid, breast, prostate, carcinoid	5
Palsy or myelopathy	
Complete	0
Incomplete	1
None	2

[a]The information in this table is based on Tokuhashi et al.[76] The lower the score, the worse the prognosis. Those scoring from 0 to 8 have a prognosis of less than 6 months to live; a score of 9 to 11, between 6 and 12 months; and a score of 12 to 15, more than a year.

based review recommended radiation for ambulatory patients without spinal "instability," bony compression, or paraplegia on presentation; it recommended surgery for patients with progressive neurological deficits, vertebral column instability, radioresistant tumors (lung, colon, renal cell), and intractable pain unrelieved by radiation therapy.[18,24,48,75]

Physicians must weigh the patient's health, ability to tolerate surgery, and goals of therapy. Surgeons generally agree that a life expectancy of more than 3 months is required for spinal surgery and use the scoring system developed by Tokuhashi et al[76] to predict it (**TABLE 2**). Several trials have confirmed the accuracy of this scoring system, including patients with metastatic breast or renal cell cancers.[77,78] The prognostic scoring system developed by Rades et al,[63] developed from patients receiving radiation therapy, might be applicable as well.

Prior to the 1980s, laminectomy was the generally accepted surgical approach, but it not only inadequately decompresses the spinal canal, it potentially compromises vertebral column stability.[79] Currently, surgeons use anterior (transthoracic and retroperitoneal) and posterolateral approaches (costotransversectomy, lateral extracavitary) for surgical decompression with reconstruction. In observational studies, 80% to 94% of patients obtained pain relief,[75,80-82] 68% to 75% of nonambulatory patients regained ambulatory status,[75,82] and 50% of severely paraparetic patients became completely ambulatory.[75]

In 2005, Patchell et al[79] published the first prospective, randomized trial comparing direct decompressive surgery followed by radiotherapy with radiotherapy alone in a carefully selected subset of patients. Patients had to have MRI evidence of metastatic epidural spinal cord compression restricted to a single contiguous area to be eligible, although they could have other noncompressive areas of epidural disease. Patients had to have a cancer origin other than CNS or spinal column, no prior history of cord compression or preexisting neurological disease, at least 1 neurological symptom (eg, pain) or sign, and, if totally paraplegic, for no longer than 48 hours before study entry.

Fifty patients were randomized to initial surgery; 3 patients who completed surgery did not receive postoperative radiation; 51 patients were randomized to initial radiation therapy (30 Gy in 10 fractions), 1 of whom required surgery because of deterioration of strength during radiotherapy. The study was discontinued at its mid point due to the superior response of the group randomized to decompressive surgery plus radiation therapy. The posttreatment ambulation rate in those randomized to combination treatment was 84% vs 57% in those randomized to radiation therapy alone ($P=.001$; odds ratio [OR], 6.2; 95% confidence interval [CI], 2.0 -19.8]). Patients who were randomized to surgery plus radiotherapy retained ambulation for a significantly longer period than patients who were randomized to radiation alone (122 vs 13 days, $P=.003$), and 94% of patients who were ambulatory before surgery plus radiotherapy remained ambulatory, while only 76% of patients who were randomized to radiation alone did so. Maintenance of continence, functional scores, and survival were also significantly greater in the group randomized to surgery before radiation therapy. Importantly, the efficacy of radiation therapy alone in the study by Patchell et al was far less than that seen in unselected patient series. Suggested explanations included exclusion of patients with highly radiosensitive tumors from the study,[83] inclusion of fewer patients with more fast-growing and potentially radiosensitive tumors in the radiotherapy group,[84] and a higher proportion of patients with vertebral body collapse or with nonneurological morbidity in the radiotherapy group.[85] The authors later provided data refuting the latter 2 explanations.[86]

Rates of surgical complications (wound breakdown, failure of spinal stabilization, infection, excessive blood loss, respiratory failure, intra-abdominal vascular or visceral injury, or cerebrospinal fluid leak) range from 23% to 50%.[75] Complication rates are significantly ($P<.001$) related to age older than 65 vs younger than 65 years (71% vs 43%), history of prior radiation therapy (67% vs 33%),[79,81,87] and paraparesis vs ambulatory status (64% vs 39%).[79,81,87]

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A recent meta-analysis confirmed that patients with symptomatic spinal cord compression who underwent surgery (with or without preoperative or postoperative adjunctive radiation therapy) were 1.3 times more likely to be ambulatory (crude risk ratio [cRR], 1.28; 95% CI, 1.20-1.37; $P<.001$) than patients treated primarily with radiation.[88] Although radiation remains the therapy offered to most patients,[89] surgery is increasingly being offered to patients with metastatic spinal cord compression who fulfill the strict criteria of the study by Patchell et al. Given that these patients commonly require urgent surgery, the surgical teams at the tertiary cancer centers who perform these procedures may need to develop new systems to enable them to fit these complex reconstructive procedures into their surgical schedules.[90]

Chemotherapy and Hormonal Therapy

Because the epidural space is on the systemic side of the blood brain barrier, chemotherapy and hormonal therapies have been used in individual patients with spinal cord compression from Hodgkin and non-Hodgkin lymphomas,[91,92] germ cell tumors,[93] breast or prostate carcinomas, or neuroblastomas.[3] In these individual case reports, the compression completely resolved in 5 of the 7 patients reported. No large case series or randomized controlled trials have been reported.

Prognosis of Patients With Spinal Cord Compression

DR O: *The outcomes are different for patients with solitary metastases vs patients with widely metastatic disease. For somebody with widely metastatic disease, in general, our focus is on improving health-related quality of life. . . .We're not affecting the natural history of the tumor. We improve mortality by improving ambulation and the comorbidities that can occur with progressive loss of function.*

MS H: *I know that cancer is going to get me eventually. I have a nodule in my lung that I'm not even thinking about right now. I'm not worrying about it right now. I just don't get into that prognosis stuff. All I care about is walking and living my life. I'm more interested in quality than quantity.*

Pretreatment ambulatory status and time from development of motor deficits to radiotherapy are the most important predictors of ambulation after treatment.[60,94-96] Overall, 75% to 100% of ambulatory patients remain ambulatory,[3,19,54] and 50% of those who survive 1 year are still ambulatory.[3] About 14% to 35% of paraparetic and 15% of paralyzed patients regain useful function after radiation therapy.[4,19]

Median survival after spinal cord compression depends on the patient's tumor type, ambulatory status, and number and site of metastases.[62,94-96] Patients with a single metastasis, a radiosensitive tumor, or with myeloma, breast, or prostate cancer have the longest survival,[3,18,58,97] while patients with multiple metastases, visceral or brain metastases, or lung or gastrointestinal cancers have the shortest.[3,18,75] Even patients with responsive tumors, such as myeloma, lymphoma, and breast cancer, have relatively short median survivals of 6.4, 6.7, and 5 months, respectively; survival of patients with prostate or lung cancer is only 4 and 1.5 months, respectively.[1] One-year survival rates for patients with spinal cord compression due to multiple myeloma, lymphoma, and breast and prostate cancers were 39%, 38%, 27%, and 22%, respectively, while that of lung cancer patients was 4%.[1]

Retrospective and prospective observational studies demonstrate that median survival for patients who could walk after the completion of therapy was 7.9 to 9 months, but median survival for nonambulatory patients was only 1 to 2 months.[18,20,21] Patients with cancer who develop spinal cord compression spend twice as many days in the hospital during the last year of life compared with those without spinal cord compression.[1]

The medical oncology team can help patients with spinal cord compression decide which mode of therapy, if any, is appropriate for them by exploring the patient's goals, the likely outcomes of each therapy (eg, pain relief or preservation or return of function), the beneficial and adverse effects of therapy, the likely duration of inpatient and rehabilitation stays, and the estimated survival times with and without therapy. For patients, like Ms H, aggressive palliative surgery plus radiation therapy will markedly improve the quality of the time remaining. Arranging a multidisciplinary consultation with a radiation oncologist and a surgeon can help patients and families make their best choice.

Rehabilitation

DR O: *It's important to help the patient make informed choices, and understand exactly what kind of effect this surgery is going to have on their life and what their needs will be after surgery. They will need immediate rehabilitation. We try to identify what kind of resources the patient will have among family and friends, and try to mobilize those resources and try to optimize what's available to the patient.*

MS H: *I had gone through surgery before and I was fine. I just tootled along. So, this time I was surprised at how weak I was and [at] my inability to walk afterwards. . . . At first, I couldn't even get over to the commode by myself. . . . By the time I left the rehab unit, I [could] climb 8 steps and . . . walk about 100 feet, then sit down and rest, then walk further.*

Rehabilitation is helpful whether the patient is treated with radiation, surgery, or both. Critical to the success of rehabilitation efforts is integration of patient and support group and family efforts with those of the multidisciplinary team. In rehabilitation units, paraplegic patients with bowel and bladder incontinence receive instruction in transfers, incentive spirometry, nutrition, bowel and bladder care, and skin care.[98] Ambulatory patients receive strength and mobility training. Along with this improved strength, the multilevel fixation achieved by modern spinal instrumentation has made postoperative bracing optional[99]; it does not lead to a higher spinal fusion rate or improve pain relief.

Observational studies have shown that patients with spinal cord compression who receive rehabilitation have increased satisfaction with life, less depression, and persistent

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decreases in pain.[98,100] In 1 study, average length of inpatient rehabilitation was 27 days; 84% of patients were discharged to home; and mobility, ambulation, self-care, and transfer abilities persisted for at least 3 months following discharge.[101]

Palliative Care

Oncologists and palliative care clinicians can also help patients and families begin to explore and cope with changes in self-image, independence, roles in the family and community, and living arrangements. Questions to help the clinician understand the patient better include the following:

Help me understand what a typical day at home (work, school, etc) was like for you before the (pain, weakness, numbness) started. What are the things you need to get done? What do you really enjoy doing?

Have you ever needed help to take care of yourself before, or has it happened to anyone close to you? How did you deal with that? Did you see a counselor? Did your clergyman or religious community support you?

Do you know anyone who had to use a cane or a wheelchair to get around? How did you feel about that? How do you think it might make you feel?

If you weren't able to walk on your own, what would it take for you to be able to stay at home? Who is there to help during the day and overnight?

For patients with limited prognoses, clinicians should also help the patient and family identify health care proxies and delineate preferences regarding cardiopulmonary resuscitation. Questions to help in doing this include:

Whom do you regularly consult about important issues? Is there one person who really understands what is important to you and how you make your choices about treatments?

If, at sometime in the future, you weren't able to tell us directly what you wanted, should we talk with them? They would be what we call a health care proxy. We would ask them to tell us what they think you would want us to do.

Given their short median survival, this work is especially important for patients with spinal cord compression due to lung or gastrointestinal cancers (especially those with multiple metastases), or any patient who is nonambulatory after surgery or radiation therapy. By refocusing efforts from disease-oriented therapies to creating legacies and bringing closure to their personal relationships, oncology teams can reassure patients and their families that they will not be abandoned. Oncologists can remain the patient's physician in hospice programs, and for patients whose needs exceed those that hospice programs can provide, palliative care teams can help oncology teams provide care and comfort during the final months.

CONCLUSION

Diagnosis of epidural spinal cord compression is an emergency. Survival and quality of life are directly related to the patients' pretreatment ambulatory status. Emergency MRI and immediate initiation of specific therapy may preserve function. Although all patients benefit from identification of their goals, counseling, and symptomatic treatment and although most receive corticosteroids, advances in radiation and surgical techniques and refinements of prognosis are beginning to enable individualization of specific therapy to maximize quality and length of life. Radiation therapy alone is offered to the majority of patients. Even patients with a very limited prognosis may be appropriate candidates for single-fraction external-beam radiation therapy or radiosurgery to decrease their pain, preserve their ambulation and their ability to transfer, and maintain bowel and bladder function. These patients may also be appropriate for referral to palliative care or hospice programs, as are patients who are not ambulatory after radiotherapy. Patients meeting the Patchell criteria should be considered for surgery followed by radiation therapy. Whichever path is chosen, multidisciplinary teams remain central to providing support and care for patients with spinal cord compression and their families.

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Web Resources for Cancer Care

PATIENT INFORMATION ABOUT MALIGNANT SPINAL CORD COMPRESSION

http://www.cancerbackup.org.uk/Resourcessupport/Symptomssideeffects/Othersymptomssideeffects/Malignantspinalcordcompression

Cancerbackup's "mission is to give patients with cancer and their families up-to-date information, practical advice, and support they need." This user-friendly Web page provides specific information about spinal cord compression.

CANCER CARE

http://www.cancercare.org

Cancer Care is an organization of social workers who provide free telephone group counseling for patients and caregivers.

PEOPLE LIVING WITH CANCER

http://www.plwc.org

People Living With Cancer is supported by the American Society for Clinical Oncology; its Web site includes information about pain, palliative care, care giving, and coping.

SPINAL CORD INJURY WEB SITES

http://www.spinal-cord.org; http://www.aascipsw.org; http://www.makoa.org

These sites are for patients with spinal cord injuries and their families.

UNITED KINGDOM INFORMATION

http://www.beatson.scot.nhs.uk/assets/pdf/education/MSCC%20Literature%20Review.pdf

Patient-oriented information regarding malignant spinal cord compression from the United Kingdom, emphasizing rehabilitation as an important part of the management.

NATIONAL CANCER INSTITUTE

http://www.cancer.gov/clinicaltrials/results/spinal-cord-compression0603

Results of the trial comparing surgery to radiation therapy for malignant spinal cord compression written in patient-centered language.

LITERATURE REVIEW REGARDING MALIGNANT SPINAL CORD COMPRESSION.

http://www.supportiveoncology.net/journal/articles/0205377.pdf

Review through 2003 of diagnosis and management of malignant extradural spinal cord compression.

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