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Treatment of metastatic spinal epidural disease: a review of the literature

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Object. Spinal cord compression is one of the most dreaded complications of metastatic cancer. It can lead to a number of sequelae, including pain, spinal instability, neurological deficits, and a reduction in the patient's quality of life. Except in selected circumstances, treatment is palliative. Treatment options include surgery, radiation, and chemotherapy. The goal of this study was to summarize the existing data on the outcomes of various treatment methods for metastatic spinal epidural disease and to make appropriate recommendations for their use.

Methods. The authors used a search strategy that included an electronic database search, a manual search of journals, analysis of bibliographies in relevant review papers, and consultation with the senior author. There is good evidence, including Class I data, that steroid drugs constitute a beneficial adjunctive therapy in patients with myelopathy from epidural compression. Historically, conventional radiation therapy has been viewed as the first-line treatment because it has been shown to be as effective as a decompressive laminectomy, with a lower incidence of complications (Class II data). Nevertheless, in the last 20 years there has been remarkable progress in surgical techniques and technology. Currently, the goals of surgery are to achieve a circumferential decompression of the spinal cord, and to reconstruct and immediately stabilize the spinal column. Results in a large body of literature support the belief that surgery is better at retaining or regaining neurological function than radiation and that surgery is highly effective in relieving pain. Most of the data on the treatment of metastatic spinal disease are Class II or III, but the preliminary results of a well-designed, randomized controlled trial in which surgery is compared with standard radiation therapy represents the first Class I data.

Conclusions. As the number of treatment options for metastatic spinal disease has grown, it has become clear that effective implementation of these treatments can only be achieved by a multidisciplinary approach.

KEY WORDS • spine • metastasis • radiation therapy • stereotactic radiosurgery

In approximately 50 to 70% of patients with cancer there is evidence of metastatic disease at the time of death.[36] The spinal column is the most common osseous site, and may be involved in up to 40% of patients with cancer.[11,89] Not all spinal metastases will lead to neurological dysfunction, however. Epidural spinal cord compression from metastases occurs in 5 to 10% of cancer patients and in up to 40% of patients with preexisting nonspinal bone metastases.[6,8,15,26,38,89] Of those with spinal disease, 10 to 20% will experience symptomatic spinal cord compression, resulting in more than 25,000 cases per year; this number is expected to grow.[28,50,72]

The thoracic spine is the most common site of disease (70%), followed by the lumbar (20%) and cervical spine (10%).[15,28,29] Metastatic spinal disease can arise from one of three locations: the vertebral column (85%), the paravertebral region (10–15%), and, rarely, the epidural or subarachnoid/intramedullary space itself (< 5%).[15,28,29] The posterior half of the VB is usually involved first, with the anterior body, lamina, and pedicles invaded later.[1] Intradural (including intramedullary) metastases from nonneural primary tumors are extremely rare, but have been reported.[41,73] Multiple lesions at noncontiguous levels occur in 10 to 40% of cases.[15,19,28,29]

Approximately 50% of spinal metastases arise from one of three primary sites: breast, lung, or prostate.[15] These are followed by renal, gastrointestinal, thyroid, sarcoma, and the lymphoreticular malignancies lymphoma and multiple myeloma. Metastases from prostate, breast, melanoma, and lung lesions commonly cause spinal tumors in 90.5, 74.3, 54.5, and 44.9% of patients, respectively.[89] The incidence of neurological deficits caused by epidural spinal cord compression varies, however, with the site of primary disease as follows: 22% of patients with breast cancer, 15% with lung cancer, and 10% with prostate cancer.[28] In the past, neurological dysfunction and spine pain would have been the first manifestation of their cancer in up to 70% of patients.[13,14,79,82] In these cases, the lung was the primary source of malignancy more than 50% of the time.[28,79]

Treatment for spinal metastases is frequently palliative. Only in selected cases, usually with renal cell carcinoma,

Abbreviation used in this paper: VB = vertebral body.

can cure be the goal if the spine is the only known site of disease.[12] Treatment can be broadly categorized as chemotherapy, radiation, and surgery. In this article we summarize the existing data on these treatment modalities and provide appropriate recommendations on their indications.

CLINICAL MATERIAL AND METHODS

Search Strategy

The goal of the search strategy was to identify articles in which the effectiveness of various treatments for metastatic spinal disease, specifically surgery, radiation, and chemotherapy (steroid drugs only) is assessed. The search strategy included an electronic database search, a manual search of journals, analysis of bibliographies in relevant review papers, and consultation with the senior author (M.H.S.). For the electronic search we used Medline (PubMed) to identify articles published between 1966 and August 2003 in which the following terms were used in various combinations: "spine," "metastases," "radiation," "surgery," "steroids," "treatment," "cancer," "decompression," "laminectomy," "stereotactic radiosurgery," and "vertebrectomy." Papers were also found using the "Related Articles" function on PubMed. Articles were reviewed and the data were abstracted by the primary and senior authors (P.K., M.H.S.).

Assessment of Literature Quality and Treatment Recommendations

The quality of the literature and thus the strength of treatment recommendations was assessed using definitions set forth by Woolf, et al.,[90] and used by Loblaw and Laperriere[55] in their review of the literature on the metastatic spine. The definitions of the different classes of evidence denoting literature quality and strength of treatment recommendations are shown in Tables 1 and 2.

Outcome Measures

The primary outcome measure for this literature review was ambulatory status. In most articles this was reported directly, whereas in other articles this number was calculated from the neurological grading schemes that were used, such as the Frankel system (Table 3).[26] Once the ambulatory status before and after treatment was determined, we calculated two further variables in selected studies: the "success" and "rescue" rates. The success rate is defined as the proportion of all patients within the study who retained or regained ambulatory function after treatment. The rescue rate is the percentage of patients who were nonambulatory before treatment, but who regained the ability to walk, either with assistance or independently.

Secondary outcomes included pain, treatment-related morbidity, survival, and autonomic function. These outcomes were not universally reported in the literature reviewed here and will therefore only be mentioned with reference to specific articles.

TABLE 1

Classification of evidence on therapeutic effectiveness of treatments for metastatic spinal disease

Evidence Class	Definition
I	evidence obtained from ≥ 1 properly designed randomized controlled trial
II	evidence obtained from well-designed, controlled trials w/o randomization, such as nonrandomized cohort studies, case-control studies, & other comparable studies, including less well-designed randomized controlled trials
III	evidence from case series, comparative studies w/ historical controls, case reports, & expert opinion, as well as significantly flawed randomized controlled trials

TABLE 2

Classification of recommendations for treatment modalities in metastatic spinal disease

Recommendation	Criteria
A	good evidence (Class I) to support the recommendation that the maneuver be specifically considered as an intervention for the condition
B	fair evidence (Class II) to support the recommendation that the maneuver be specifically considered as an intervention for the condition
C	poor evidence (Class III) to support the recommendation that the maneuver be specifically considered as an intervention for the condition or that it confers no advantage over competing interventions*
D	fair evidence (Class II) to support the recommendation that the maneuver be excluded from consideration as an intervention for the condition
E	good evidence (Class I) to support the recommendation that the maneuver be excluded from consideration as an intervention for the condition

* Considering efficacy of the intervention with regard to primary outcome, and side effects of the intervention. The physician may then want to take into consideration other outcomes, such as cost convenience, resource allocation, and other aspects of feasibility.

RESULTS

Steroid Medications

Best Level of Evidence, Class I; Level of Recommendation, A. There is good evidence to support the use of steroid drugs in patients with newly diagnosed metastatic spinal disease causing spinal cord dysfunction. It should be noted that in patients with no history of cancer who present with an undiagnosed spinal mass, especially younger patients, steroid drugs should be avoided until the diagnosis is made. The reason for this is that for some tumors, particularly lymphomas and thymomas, steroid medications have an oncolytic effect that may cause a delay in diagnosis.[9] Dexamethasone is the most widely used steroid, although methylprednisolone, which is more commonly prescribed in trauma, has also been used. Steroid drugs have been shown to reduce vasogenic edema, protect against lipid peroxidation and lipid hydrolysis, prevent ischemia and intracellular calcium accumulation, and support cellular energy metabolism.[3]

The optimal dosage of dexamethasone in metastatic spinal cord compression is controversial. Loading doses range from 10 to 100 mg, followed by 4 to 24 mg four times a day, tapering down over several weeks.[9,15,29,31.]

TABLE 3

Modified Frankel neurological functional classification

Grade	Description
A	no motor or sensory function
B	preserved sensation only, no motor function
C	nonambulatory, wheelchair-bound, some motor function
a	bowel or bladder paralysis
b	neurogenic bowel or bladder
c	voluntary normal bowel or bladder function
D	ambulatory but w/ neurological symptoms
1	requires walker
2	requires cane
3	can walk independently
a	bowel or bladder paralysis
b	neurogenic bowel or bladder
c	voluntary, normal bowel or bladder function
E	normal neurological function

[57,64,78] Many practitioners use the larger doses for patients who present with severe baseline symptoms or worsening neurological examination. Some advocate using the trauma dose protocol in patients with rapid neurological deterioration.[62] In a well-designed, randomized controlled study in which high-dose dexamethasone followed by radiotherapy was compared to radiotherapy alone, 81% of patients in the steroid treatment group were ambulatory posttreatment compared with 63% of patients treated with radiation alone.[78] In another randomized controlled trial, patients with a complete myelographically confirmed block who received a 100-mg bolus of dexamethasone followed by a standard maintenance dose had no better pain relief, ambulation, or bladder function compared with those who received a 10-mg bolus and the same maintenance therapy.[84] It is clear, however, that higher doses are associated with more complications.[39] Therefore, based on this information, an appropriate regimen of dexamethasone would be an initial bolus of 10 mg followed by 16 mg/day, tapering over several weeks.

Surgery: Posterior Decompressive Laminectomy

Best Level of Evidence, Class II; Level of Recommendation, D. For many years, laminectomy was the only surgical option offered to patients with metastatic spinal disease. In fact, in this context, the term "surgery" is to some extent still equated with laminectomy, contributing to the bias in favor of radiotherapy. One of the reasons laminectomy was the dominant surgical procedure was because of its relative ease. It can be performed quickly by any neurosurgeon with minimal intraoperative risk to the patient, and it does not require spinal column reconstruction or placement of internal stabilization devices. Despite its widespread use, there was no consensus among surgeons regarding its effectiveness. Some thought that it was the only reasonable hope for treating neurological deficits, whereas others found it to be of little value except for obtaining tissue to make a diagnosis and for relieving pain.[10]

Much of the existing literature on decompressive laminectomy consists of uncontrolled cohort studies (Class III). Recorded outcomes usually include ambulatory status before and after treatment, pain relief, and treatment-related complications. As can be seen in Table 4, 14 to 58% of patients who underwent a posterior decompressive laminectomy were ambulatory postsurgery. Not shown in the table, however, are the significant nonneurological complications that follow laminectomy, specifically wound infection/dehiscence and spinal instability. In a review of the literature by Findlay,[23] the incidence of nonneurological complications was found to be approximately 11%.

In a number of articles, including controlled cohort studies (Class II), the efficacy of laminectomy alone has been compared with radiation alone and with laminectomy followed by radiation.[10,18,23,29,58,77,79,92] One of these, by Gilbert, et al.,[29] was a single-institution, retrospective analysis of 235 patients treated with either decompressive laminectomy followed by radiation (65 patients) or radiation alone (170 patients). After treatment, 46% of those who underwent combination therapy were ambulatory compared with 49% of those who underwent radiation alone. Pretreatment neurological function was the most reliable indicator of posttreatment function. There was no significant difference in the rate of neurological recovery

TABLE 4

Ambulatory outcome after various treatments for spinal cord compression

Treatment Authors & Year	No. of Patients	Success (%)*	Mean (%)
posterior decompressive laminectomy alone			30
Barron, et al., 1959	38	29	
Wild & Porter 1963	22	26	
Wright, 1963	21	14	
Brice & McKissock, 1965	139	32	
Smith, 1965	52	25	
Auld & Buerman, 1966	41	42	
Hall & Mackay, 1973	129	30	
Livingston & Perrin, 1978	100	58	
Baldini, et al., 1979	140	30	
Dunn, et al., 1980	104	33	
Stark, et al., 1982	32	16	
Findlay, 1987	80	24	
Sorensen, et al., 1989	105	34	
radiation therapy alone			47
Mones, et al., 1966	41	34	
Khan, et al., 1967	82	41	
Posner, 1971	75	47	
Cobb, et al., 1977	18	50	
Gilbert, et al., 1978	170	49	
Greenberg, et al., 1980	83	57	
Stark, et al., 1982	32	35	
Constans, et al., 1983	108	39	
Martenson, et al., 1985	42	64	
Ruff & Lanska, 1989	41	73	
Sorensen, et al., 1990	149	38	
posterior decompressive laminectomy & radiation therapy			47
Mullan & Evans, 1957	21	43	
Wild & Porter, 1963	23	44	
Wright, 1963	17	47	
Gilbert, et al., 1978	65	45	
Stark, et al., 1982	52	37	
Constans, et al., 1983	465	46	
Martenson, et al., 1985	21	57	
Sherman & Waddell, 1986	111	57	
Sorensen, et al., 1990	91	53	

* "Success" is defined as the ability to walk after the operation (that is, gait was maintained, improved, or regained as a result of the laminectomy).

between the two groups. Of the 22 patients in whom rapidly progressive weakness developed (< 48 hours), nine underwent surgery and 13 received radiation therapy. None of the surgically treated patients improved, but seven of the patients who reveived radiation did. The authors' conclusions were that radiation should be the treatment of choice and that a decompressive laminectomy is indicated in only three situations: 1) to establish a diagnosis; 2) to treat a relapse if the patient is unable to undergo further radiation therapy; and 3) if symptoms progress during radiation treatment.

Despite the obvious need and repeated requests for investigators to conduct a randomized controlled trial, only one has been attempted. Young, et al.,[92] randomized patients who had a symptomatic epidural spinal lesion to groups receiving either laminectomy followed by radiotherapy or radiotherapy alone. Sixteen patients were randomized to the surgical arm, and 13 to the radiotherapy arm. No significant difference was found between the groups with respect to pain relief, ambulatory status, or sphincter function. There were no treatment-related complications for surgery or radiotherapy. The major limitation of their study, as the authors clearly stated, was that the patient group was too small for the au-thors to be able to detect a difference in the treatments. Rather, the major goal of that study was to demonstrate that a properly conducted randomized controlled trial was feasible.

As a result of these articles and others listed in Table 4, laminectomy was viewed as a procedure with minimal neurological benefit and significant morbidity, and it was determined that radiation should assume the primary treatment role. Indiscriminate use of decompressive laminectomy was prone to failure because in most cases the tumor lies ventral to the thecal sac. This makes it impossible to accomplish a meaningful decompression or tumor resection without significant retraction of the thecal sac. Furthermore, a laminectomy can cause or worsen preexisting spinal instability. This can lead to progressive deformity, which in turn can result in pain, more deformity, and neurological compromise. Based on these data, we believe that decompressive laminectomy alone without supplemental internal fixation should not be used in patients with metastatic spinal disease, except in cases in which the disease is strictly confined to the lamina and spinous process. Despite the evidence, however, this procedure continues to be performed by some surgeons.[74]

The results of decompressive laminectomy seem to be improved if internal fixation (for example, pedicle screws) and fusion are performed as well. In a review of 134 patients treated with either a laminectomy (111 patients) or laminectomy with stabilization (23 patients), Sherman and Waddell,[75] found that the latter group had better posttreatment ambulatory status (92 compared with 57%), sphincter function, and pain control, and less recurrent neurological dysfunction. These findings have been supported by others.[7,44,47,62,67,75]

Surgery: Circumferential Spinal Cord Decompression

Best Level of Evidence, Class I; Level of Recommendation, A. With the failure of laminectomy, the primary treatment for metastatic disease has been largely confined to radiation therapy. Nevertheless, a new philosophy on the surgical management of metastatic spinal disease has emerged. In his 1984 article, Findlay[23] reviewed the small amount of data on anterior spinal surgery and found "dramatic results" with regard to neurological function, but warned that ". . . it is unclear as to how often such success could be achieved." As surgeons realized the limitations of the laminectomy, they began to decompress the ventral spinal cord, which is the most common site of metastatic spread. Thus, a new treatment protocol began to emerge—circumferential spinal cord decompression.

To achieve a circumferential decompression, surgical approaches must be tailored to the location of the tumor with respect to the spinal cord. The end result is to free the spinal cord of any malignant compression. Approaches can be broadly classified as anterior (for example, transthoracic or retroperitoneal) or posterior, including posterolateral trajectories (for example, laminectomy, transpedicular, costotransversectomy, or lateral extracavitary). In addition to spinal cord decompression, reconstruction and immediate stabilization of the spinal column form the pillars of surgical management today.

A large amount of literature has emerged over the last 20 years; this is summarized in Table 5. Although the articles on circumferential decompression are generally more detailed than their laminectomy counterparts, they still are uncontrolled cohort studies and thus represent Class III data. In one of the largest reports Sundaresan, et al.,[81] described their results in 80 patients who had solitary metastatic spinal lesions. Depending on the anatomical and radiological findings on the extent of the tumor, they used a variety of approaches: an anterior approach was used in 32 patients, a strictly posterior or posterolateral approach was used in eight, and a combined anteroposterior approach was used in 40. Preoperatively, 48 patients (60%) were ambulatory and 55 (69%) experienced a significant amount of pain. Postoperatively, 78 (98%) were ambulatory, including 94% of those who were initially nonambulatory. Pain was improved in 95%, with 76% reporting complete relief. Although the overall survival duration was 30 months, there was a considerable range among the various tumor types. Patients with breast and renal cell carcinoma had a median survival duration of 36 months, compared with 15 and 12 months for gastrointestinal and unknown primary carcinoma, respectively.

Gokaslan, et al.,[31] reported their results with transthoracic vertebrectomy in 72 patients. Pain was improved in 92% of patients, and 93% were able to walk postoperatively. Of the 13 patients who were nonambulatory preoperatively, 10 regained ambulatory ability after surgery, with three of them regaining normal function. The 1-year survival rate for the entire cohort was 62%. Overall, the data seem to indicate that neurological outcomes are far superior to those that are achieved with decompressive laminectomy and/or radiation. Not surprisingly, the morbidity and mortality rates associated with this more aggressive surgical management are significant (Table 5).

Analogous to the controversy of laminectomy compared with radiation in the "old era," it is clear that a randomized controlled trial is needed to address more adequately the question of the effectiveness of circumferential decompressive surgery compared with radiation in this "new era." At the 2003 annual meeting of the Amer-

TABLE 5

*Literature review of results of circumferential spinal cord decompression in patients with metastasis**

Authors & Year	No. of Patients	Postoperative Results (%)			Complications†	
		Pain (% improved)	Success	Rescue	Type	% or No.
Harrington, 1984	52	NA	85% of those w/ preop neurological deficit had improvement; gait function NA	NA	mortality	11.5%
					morbidity	17.3%
					hardware	5
					surgical	2
					neurological	1
					medical	2
Fidler, 1986	18	NA	78	75	mortality	5.6%
					morbidity	NA
Harrington, 1988	77	NA	73	50	mortality	6.5%
					morbidity	18%
					hardware	5
					surgical	5
					medical	3
					neurological	1
Kostuik, et al., 1988	100	81	72% anterior, 38% posterior	NA	mortality	0%
					morbidity	21%
					hardware	10
					neurological	4
					surgical	3
					medical	4
Moore & Uttley, 1989	26	71	77	63	mortality	31%
					morbidity	7.7%
					surgical	2
Sundaresan, et al., 1991	54	90	94	86	mortality	5.5%
					morbidity	15%
					hardware	1
					surgical	2
					neurological	1
					medical	4
Hammerberg, 1992	56	91	88	71	mortality	3.6%
					morbidity	16.7%
					hardware	3
					surgical	6
Cooper, et al., 1993	33	97	88	25	mortality	3%
					morbidity	42%
					neurological	2
					surgical	1
					medical	11
Akeyson & McCutcheon, 1996	25	80	72	42	mortality	0%
					morbidity	44%
					surgical	7
					hardware	4
Sundaresan, et al., 1996	110	90	82	59	mortality	5%
					morbidity	48%
					neurological	2
					hardware	11
					surgical	45
					medical	10
Gokaslan, et al., 1998	72	92	93	61	mortality	3%
					morbidity	43%
					neurological	6
					surgical	10
					medical	15
Weigel, et al., 1999	76	89	93	90	mortality	7%
					morbidity	24%
					hardware	4
					surgical	6
					medical	4
					neurological	4

TABLE 5, *Continued*

*Literature review of results of circumferential spinal cord decompression in patients with metastasis**

Authors & Year	No. of Patients	Postoperative Results (%) Pain (% improved)	Success	Rescue	Complications† Type	% or No.
Wise, et al., 1999	80	NA	89	41	mortality	2.5%
					morbidity	36%
					surgical	9
					hardware	2
					neurological	2
					medical	16
Bilsky, et al., 2000	25	100	88	0	mortality	12%
					mortality	32%
					surgical	1
					neurological	2
					medical	5
Hatrick, et al., 2000	42	90	86	57	mortality	0
					morbidity	19%
					surgical	3
					hardware	2
					neurological	3
Fourney, et al., 2001	100	87	86	46	mortality	0
					morbidity	65%
					surgical	21
					hardware	3
					neurological	3
					medical	19
Sundaresan, et al., 2002	80	95	98	94	mortality	1.3%
					morbidity	29%
					hardware	4
					surgical	16
					medical	2
					neurological	1

* "Success" is defined as the proportion of patients who were ambulatory after treatment, whereas "rescue" is the proportion of nonambulatory patients who regained ambulatory function, either with assistance or independently. Abbreviations: NA = not available.

† Mortality and morbidity are defined as occurrence of death or complication within 30 days of the operation. Morbidity is the number of complications divided by the number of patients in the study. Thus, overestimates may arise if one patient suffered more than one complication. The number of patients with each type of complication is recorded. Surgical complications include wound infection, hematomas, cerebrospinal fluid leaks, and so on. Examples of hardware complications include broken screws and graft migration/dislodgement. Medical complications are those that are not directly related to the surgery, such as pneumonia, myocardial infarction, deep venous thrombosis/pulmonary embolism, and so on. Patients who suffered new neurological deficits were considered to have neurological complications. Local recurrence and pseudarthrosis were not counted as complications.

ican Society of Clinical Oncology, Patchell, et al.,[63] presented the results of their randomized, controlled trial, in which they compared direct, decompressive resection followed by adjuvant radiation with conventional radiation alone. Both groups were treated with the same steroid protocol and both received the same total radiation dose (30 Gy). There were 50 patients in the surgical arm and 51 in the radiation arm of the study. Patients treated with surgery retained ambulatory and sphincter function significantly longer than patients in the radiation group. Also, 56% of nonambulatory patients in the surgical group regained the ability to walk, compared with 19% in the radiation group. Survival was not significantly different between the two groups.

This landmark study represents the first good Class I data in the metastatic spinal disease literature. Our review of the literature supports a change in the current management protocols for metastatic epidural spinal disease. Traditional indications for surgery include radiation-resistant tumors (sarcoma, lung, colon, and renal cell); obvious spinal instability; clinically significant neural compression secondary to retropulsed bone or from spinal deformity; intractable pain unresponsive to medical treatment; and failure of radiation therapy (progression of deficit during treatment or spinal cord tolerance reached). We believe that surgery should be considered the primary treatment modality in all patients with newly diagnosed metastatic disease who do not have any of the indications for radiotherapy (see *Conventional Radiation Therapy*).

Conventional Radiation therapy

Best Level of Evidence, Class I; Level of Recommendation, A. Indications for radiotherapy are as follows: radiosensitive tumors (lymphoma, multiple myeloma, small-cell lung carcinoma, seminoma of testes, neuroblastoma, and Ewing sarcoma); expected survival less than 3 or 4 months; patient unable to tolerate an operation; total neurological deficit below the level of compression for more than 24 to 48 hours; and multilevel or diffuse spinal involvement. The standard radiation portal involves the diseased level with a 5-cm margin, which effectively includes two VBs above and below.[53] The total radiation dosage is usually 3000 cGy (2000–4000 cGy) and is administered over a 10- to 14-day course, with higher doses delivered in the first few days and then tapered down. Patients with radiosensitive tumors (breast, myeloma, or lymphoma) have a better functional outcome overall than those who have more radiation-resistant tumors (sarcoma, lung, colon, or renal cell). In many patients the disease is isolated in the spine, usually the VB, without epidural compression. For these patients, a single dose (usually 8 Gy) provides good pain relief and is as efficacious as various fractionated regimens.[42,43]

Table 4 depicts the results of radiation therapy during the era in which decompressive laminectomy was the predominant surgical procedure. There have been a number of reports since then, all uncontrolled cohort studies, which are shown in Table 6. One of the largest reports is by Maranzano and colleagues.[51,56,57] They treated 209 patients with radiation (30 Gy) and steroid drugs. Pain was present in 98% of patients and 65% had some degree of neurological dysfunction. The mean follow-up duration was 49 months. Pain improved in 71% of patients, ambulatory function improved in 36%, and bladder function improved in 44%. Overall, 76% recovered or preserved their ability to walk. The median survival duration for the whole group was 6 months, with a 1-year survival rate of 28%. Favorable factors for survival included ambulatory status, both before and after treatment, and histological findings.

Helweg-Larsen[40] followed 153 patients for a median of 2.6 months. Normal gait was present in 60 patients (39%), assisted ambulation in 19 (12%), paresis without gait function was found in 31 (20%), and paraplegia was found in 43 (29%). Neurogenic bladder was present in 57 patients (37%). The total radiation dose was 28 Gy, which was given in fractions of 4 Gy on 7 consecutive days. In total, 21 of the 74 initially nonambulatory patients (12 paretic, nine plegic) recovered some gait function. Seven patients (two with normal gait, five who needed assistance walking) deteriorated to a nonambulatory state because of treatment failure. Of those patients who presented with sphincter dysfunction, 10 (18%) regained bladder function. The median survival duration was 5.4 months.

As stated previously, the recently released results of the first well-designed, randomized, controlled trial comparing stand-alone radiotherapy to surgery with adjuvant radiotherapy show a marked benefit for surgery.[63] Thus, for patients who meet surgical criteria, the role of standard radiotherapy is as adjuvant therapy only. Conversely, there are many patients who either cannot tolerate surgery or in whom it would be inappropriate (for example, in highly radiosensitive tumors in patients with a short life expectancy). In these patients, radiation should still serve as the primary mode of treatment.

TABLE 6

Results of recent radiotherapy trials in patients with metastatic spinal disease

Authors & Year	No. of Patients	Pain (% improved)	Postradiation Results (%) Success	Postradiation Results (%) Rescue
Leviov, et al., 1993)	70	NA	39	4
Maranzano & Latini, 1995	209	71	76	51
Helweg-Larsen, 1996	153	83	61	28
Katagiri, et al., 1998	101	57	64	19
Chamberlain & Kormanik, 1999	108	75	NA	5
Rades, et al., 2002	98	NA	60	NA
Zaidat & Ruff, 2002	139	100	78	47

Nonconventional Radiation Therapy

Best Level of Evidence, Class III; Level of Recommendation, C. With conventional external beam radiation, a significant amount of healthy tissue is exposed to radiation, including the spinal cord, which can lead to radiation-induced myelopathy.[48,83,85] Therefore, if radiation could be delivered to the target while decreasing the amount delivered to healthy tissue, injuries to the spinal cord would theoretically be reduced. Nonconventional radiotherapy, which includes stereotactic radiosurgery and intensity-modulated radiotherapy, is able to do just that. The currently available data represent case series (Class III) evidence.[27,69–71] The follow up is short and outcome measures, such as neurological function, are rarely discussed. The research so far has shown nonconventional radiation therapy to be a safe intervention; however, its effectiveness has not been rigorously tested against other current therapies (surgery or conventional radiotherapy). Such data are needed before a treatment recommendation can be rendered.

CONCLUSIONS

Treatment of metastatic epidural spinal disease has undergone significant changes over the last 20 years. No longer is indiscriminant decompressive laminectomy offered as the only surgical treatment. It carries all the risks associated with an invasive procedure and offers the patient little benefit, unless it is used to remove tumors isolated in the posterior elements. From the existing literature we infer that surgery that frees the spinal cord at the site of compression, in addition to reconstructing and stabilizing the spinal column, is more effective at preserving and regaining neural function, notably ambulatory and sphincter function, than conventional radiotherapy. This type of surgery is also highly effective in relieving pain. The preliminary results of a recent randomized, controlled trial provide the first Class I evidence to support a reversal in the current trend toward primary treatment for many patients with metastatic disease. Conventional radiotherapy has a clearly defined role as adjuvant therapy, as well as primary therapy in those who are unable to tolerate or benefit significantly from surgery. The role of nonconventional radiation therapy, such as intensity-modulated radiotherapy and stereotactic radiosurgery, remains to be elucidated.

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