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Spinal Radiation Before Surgical Decompression Adversely Affects Outcomes of Surgery for Symptomatic Metastatic Spinal Cord Compression

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Study Design. A retrospective chart review was performed.

Objective. To determine whether preoperative spinal radiation increases the number of major wound complications in patients with cancer who have symptomatic spinal cord compression.

Summary of Background Data. Many factors have increased the number of patients hospitalized with symptomatic spinal cord compression after spinal irradiation. The surgical management of metastatic spinal cord compression may be complicated by preoperative radiation.

Methods. A retrospective review of 123 patients admitted with symptomatic metastatic spinal cord compression from 1970 through 1996 was conducted. The final study population of 85 patients was separated into three treatment groups: 1) radiation only, 2) radiation followed by surgery, and 3) *de novo* surgery followed by radiation.

Results. The major wound complication rate for patients who had radiation before surgical decompression and stabilization was 32%, or threefold, higher than the 12% observed in patients who had *de novo* surgery ($P < 0.05$). No other clinical factor or condition predicted the development of a major wound complication. Patients treated initially with surgery had superior functional outcomes in an analysis stratified by Frankel grade ($P < 0.05$). Of the ambulatory patients who underwent *de novo* surgery, 75% remained ambulatory and continent 30 days after treatment, whereas only 50% of those treated with radiation before surgery had similar outcomes.

Conclusions. Spinal radiation before surgical decompression for metastatic spinal cord compression is associated with a significantly higher major wound complication rate. In addition, preoperative spinal irradiation might adversely affect the surgical outcome. [Key words: infection, neoplasm metastasis, outcome, radiation, surgery, spinal cord compression, wound] **Spine 2001;26: 818–824**

Compression of the spinal cord and cauda equina from epidural metastatic disease is a major cause of morbidity in patients with cancer that occurs in approximately 5% of patients with malignant disease.[25] Early detection of disease and prompt institution of treatment favorably affect outcome.[8]

The patients in whom symptomatic spinal cord compression develops often represent a debilitated population with considerable surgical risks.[10] Many patients can safely undergo surgery either anteriorly or posterolaterally with appropriate stabilization procedures. However, a considerable number of these patients are irradiated appropriately, either because there are minimal neurologic symptoms or because an aggressive surgical approach is deemed inappropriate at initial presentation. The widespread use of magnetic resonance imaging (MRI) of the spine to detect metastatic disease in patients with cancer results in the early diagnosis of epidural metastatic disease, which often is irradiated.

For many reasons, therefore, more previously irradiated patients present to the hospital with symptomatic spinal cord compression. The number of major wound complications is high in this population, and the authors hypothesize that radiation before surgical decompression may be a risk factor for the development of a wound complication after surgery for patients with symptomatic spinal cord compression. Therefore, the authors conducted a retrospective study of 123 patients admitted to their institution with symptomatic metastatic spinal cord compression to determine whether preoperative radiation might adversely affect the outcome for patients undergoing spinal decompressive surgery for metastatic spinal cord compression. They also attempted to measure the potential effects of nutritional status and the use of segmental spinal instrumentation on the rate of major wound breakdown in these patients.

Methods

Patients. A retrospective study of 123 patients admitted for evaluation and treatment of metastatic spinal cord compression from 1970 through 1996 was conducted. The study was restricted to adults with a neurologic deficit on admission to the hospital. In addition, only surgical cases approached posteriorly were included. Problems with coding in the medical record department resulted in a lower number of patients being captured by our search. However, the errors in diagnostic coding are a random phenomenon, and therefore do not likely represent any true bias.

The charts of 38 patients were excluded from the study for one or more of the following reasons: insufficient radiologic studies or no cord compression (10 patients), intramedullary disease (4 patients), no objective neurologic deficit (7 patients), consensus among clinicians that only comfort measures should be offered (10 patients), and medical record coding error (7 patients). The resulting 85 patients were separated into three groups depending on patient management: 1) radiation therapy alone (23 patients), 2) radiation followed by surgery (28 patients), or 3) early surgery followed by radiation (34 patients). Of the 28 patients treated with radiation before surgery, 12 were stabilized with instrumentation, and 10 of the 34 patients

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Table 1. Patient Characteristics in Each Treatment Group

Treatment Group	Mean* Age (years)	Location of Disease†			Pathology‡				
		C§	T§	T/L§	Lung§	Breast§	Prostate§	Unknown‖,§	Other§
XRT	55	17	61	22	13	13	26	9	39
XRT/Surg	63	7	82	11	18	21	21	11	29
Surg/XRT	62	6	73	21	15	12	35	9	29

* $P > 0.05$, one-way analysis of variance (ANOVA).
† $P = 0.4$, χ^2 test.
‡ $P = 0.9$, χ^2 test.
§ Percentage of patients.
XRT = patients treated with radiation only; XRT/Surg = patients treated with early radiation followed by surgery; Surg/XRT = patients treated with *de novo* surgery.

treated with *de novo* surgery were stabilized with instrumentation.

Admission Evaluation. In all the study patients, epidural spinal cord compression was confirmed by either myelography or MRI. The location of the compression was recorded. The initial neurologic examination was obtained from the record, and a Frankel Grade was assigned on the basis of the admission history and physical examination. The pathology and any history of prior spinal radiation to the region of pathology were recorded. The management of the patients was determined by the admitting physician and the surgeon in consultation with the patient and family. If a patient deteriorated neurologically during treatment with external radiation, consideration was given to urgent surgery.

Operative Techniques. The patients judged appropriate for surgical decompression underwent urgent laminectomy, generally with posterior and lateral decompression of the spinal cord.[22] At the authors' institution, most cases are managed currently with a single-stage posterolateral decompression and stabilization. Patients who had undergone anterior decompressive procedures were excluded from this study because of small numbers and because wound breakdown has not been observed in these cases.

The use of spinal instrumentation increased in the authors' institution during the 1990s. Individual surgeons selected the type of spinal instrumentation. Intravenous prophylactic antibiotics were used in all cases. Most of the wounds were drained for 24 to 36 hours depending on the amount of drainage and the preference of individual surgeons.

Outcomes. Outcomes were assessed by noting the clinical condition of patients at discharge and at follow-up assessment 1 month after presentation. Patients were judged to have improved or deteriorated neurologically by means of an examination performed by a neurologist or neurosurgeon. Early recovery of ambulatory, bowel, or bladder function as well as a change in Frankel grade was noted. Any readmissions to the hospital in the 6 months after initial treatment were reviewed for evidence of major complications resulting from the treatment strategy selected to manage of spinal cord compression in each patient. The follow-up time was 6 months rather than 2 years because most soft tissue healing has occurred in that time. Latent hardware infections might not manifest themselves during this interval, and more extended follow-up studies (minimum of 2 years) would be important to address this issue.

Statistical Analysis. Appropriate statistical tests were performed to determine whether differences between outcomes in the study patients were significant. The statistical methods included χ^2 analysis, one-way analysis of variance (ANOVA), Cochran-Armitage test, Student's *t* test, Wilcoxon rank sum test, Mantel-Haenszel odds ratio estimation, logistic regression, and ordinal regression tests. Statistical calculations were performed with Microsoft Excel (version 2000), StatXact Turbo (version 2.11; Cytel Software, Cambridge, MA), and S-PLUS (MathSoft, Seattle, WA) functions for ordinal regression written by Dr. Frank Harrell (Hmisc and Design libraries, available from Statlib://lib.stat.cmu.edu). A difference between management groups was judged statistically significant if the *P* value was less than 0.05.

Results

Patient Characteristics

The final study population of 85 patients was separated into three treatment groups: 1) radiation alone (23 patients), 2) early radiation followed by surgery (28 patients), and *de novo* surgery followed by radiation (34 patients). The mean ages in the treatment groups were comparable ($P > 0.05$, one-way ANOVA). Table 1 shows that no significant differences existed between the treatment groups in terms of age, location of pathology, or type of tumor. The admission clinical condition (Frankel grade) for the three treatment groups is shown in Figure 1. Most of patients in the study fell into Frankel Grades C and D. However, more patients in the *de novo* surgical group had lower Frankel grades, as compared with the other two groups. Therefore, all the outcome analyses described in the following sections are stratified by Frankel grade.

Choice of Treatment

The patients' baseline characteristics were analyzed as possible predictors of initial treatment (radiation therapy or surgery). This analysis showed that 15 patients (18%) had received radiation before presentation as a treatment of the primary lesion or another metastasis. These patients were excluded from the analysis to determine the choice of initial treatment.

Almost half of the remaining patients (34/70) underwent surgery as their initial treatment. Poor Frankel grade on admission was a strong predictor of surgery as

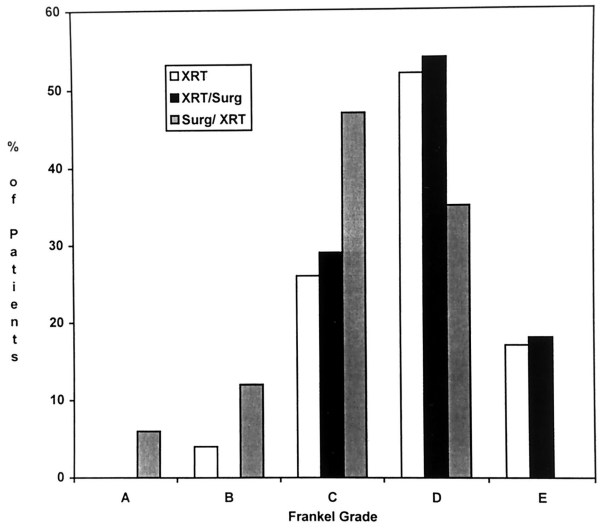

Figure 1. Frankel grade on admission for patients with symptomatic spinal cord compression. **XRT,** Patients (n = 23) treated with radiation only. **XRT/Surg,** Patients (n = 28) treated with early radiation followed by surgery. **Surg/XRT,** Patients (n = 34) treated with *de novo* surgery.

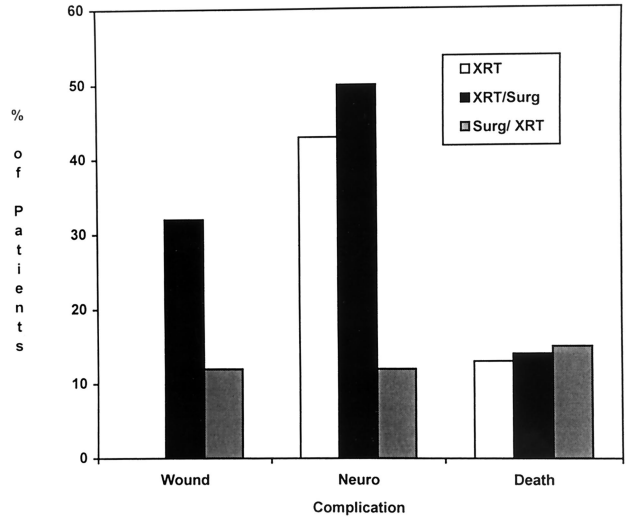

Figure 2. Major clinical complications within 30 days of admission to the hospital for patients with symptomatic spinal cord compression. Patients treated with *de novo* surgery have a significantly lower wound complication rate ($P < 0.05$, χ^2) and significantly fewer neurologic complications than those treated with radiation alone ($P < 0.01$, χ^2) and those treated first with radiation and then with surgery ($P < 0.001$, χ^2). **XRT,** Patients (n = 23) treated with radiation only. **XRT/Surg,** Patients (n = 28) treated with early radiation followed by surgery. **Surg/XRT,** Patients (n = 34) treated with *de novo* surgery.

the initial treatment ($P < 0.001$, Wilcoxon; Table 2). No other factor examined (age, location within the spine, type of pathology, serum albumin, creatinine, or presence of diabetes) was identified as a clinical predictor of the type of therapy selected for each patient in this retrospective analysis.

Major Wound Complications

Figure 2 shows the percentage of patients with major complications in the three treatment groups. A major wound complication was defined as a dehiscence or infection that required intravenous antibiotics, a prolonged hospital stay, and in many cases a wound revision in the operating room. There were 13 major wound complications in the study. *Staphylococcus aureus* was cultured from five of these wounds, and *Enterococcus* from one wound. The remaining seven wounds dehisced, but no organism was cultured from the wound. The rate of wound complications for patients who had radiation before surgery was 32% or threefold more than the 12% seen for patients who had undergone *de novo* surgery. This difference is statistically significant ($P < 0.05$, χ^2).

To understand better the effect of radiation before surgery in these patients, the group was separated into patients treated with radiation in the past (more than 7 days before surgery) and those who received radiation within the week before surgery. In virtually all cases wherein surgery was performed soon after (within 7 days) the onset of radiation therapy, there was neurologic deterioration during the radiation therapy. The results are shown in Table 3. Surgery performed within 7 days of radiation therapy initiation was associated with a wound complication rate of 46%, which is double the 20% seen in patients who had a more remote history of radiation therapy to the spine. A trend toward statistical

Table 2. A Higher Admission Frankel Grade Is Associated with Better Clinical Outcomes*

Treatment Group	Admission Frankel Grade (n)	Outcome: Ambulatory (%)	Outcome: Continent (%)
XRT	B or C (7)	29	29
	D (12)	50	50
XRT/Surg	B or C (8)	13	25
	D (15)	53	47
Surg/XRT	B or C (20)	35	45
	D (12)	83	75

* Greater percentages of ambulatory outcomes occur for patients who present with Frankel Grade D ($P < 0.01$, χ^2 test). There is a trend toward better sphincter function outcome in patients with a higher pretreatment Frankel Grade ($P = 0.12$, χ^2 test).
XRT = patients treated with radiation only; XRT/Surg = patients treated with early radiation followed by surgery; Surg/XRT = patients treated with *de novo* surgery.

Table 3. Radiation Followed by Surgical Decompression Within a Week Is Associated With an Increase in Wound and Neurologic Complications

Treatment Group	No. of Patients	Wound Complication (%)	Neurologically Worse (%)
Remote XRT/Surg	15*	20	33
Urgent XRT/Surg	13	46†	77‡

* Radiation treatment given more than 7 days before decompressive surgery.
† $P = 0.14$, χ^2 test.
‡ $P < 0.05$, χ^2 test.
XRT/Surg = patients treated with early radiation followed by surgery.

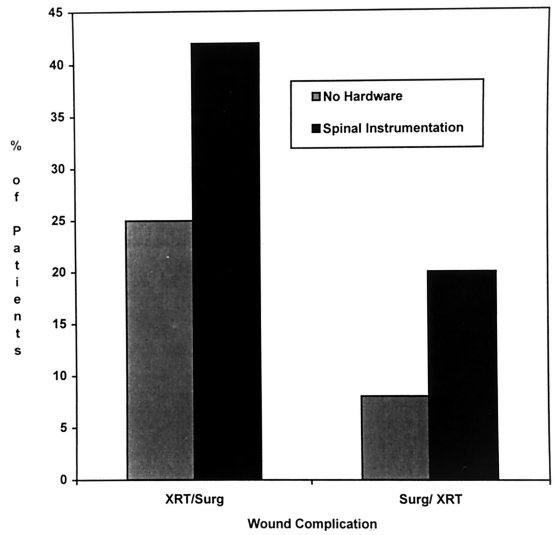

Figure 3. Effect of spinal instrumentation on major wound complication rate. There were more wound complications in patients stabilized with spinal instrumentation. However, the differences were not statistically significant (odds ratio = 2.6, 95% confidence interval = 0.8–9, $P = 0.12$, Mantel-Haenszel odds ratio estimation). **XRT/Surg,** Patients (n = 28) treated first with radiation and then with surgical decompression. Twelve of these patients underwent placement of spinal instrumentation. **Surg/XRT,** Patients (n = 34) treated with *de novo* surgery. Ten of these patients underwent placement of spinal instrumentation.

significance was identified ($P = 0.14$, χ^2). No other factor, including patient age, preoperative albumin, or serum creatinine, was correlated with the development of a major wound complication ($P > 0.3$ for all, logistic regression). The type of primary pathology ($P = 0.6$, χ^2) and the Frankel grade on admission ($P = 0.2$, Cochran-Armitage) were not significant predictors of postoperative wound infections either.

Spinal Instrumentation

To determine whether the use of segmental spinal instrumentation had a significant effect on the rate of wound or other complications, the surgical groups were subdivided into patients with and those without instrumentation and analyzed. The number of patients was small, but it appears that the number of major wound complications was higher in patients who underwent spinal stabilization (Figure 3). In patients treated with radiation before surgery, the wound complication rate was 42% for patients who underwent spinal instrumentation, as compared with 25% for those who had no hardware placed. Patients treated with *de novo* surgery had a 20% wound complication rate when spinal instrumentation was used, as compared with an 8% complication rate when no hardware was used. Despite the small number of patients, these data suggest a trend toward a significant difference ($P = 0.12$, Mantel-Haenszel odds ratio estimation).

Neurologic Deterioration

The rate of neurologic worsening in those patients who had *de novo* surgery (12%) was significantly lower than that seen in the other two treatment groups (Figure 2) ($P < 0.01$ and $P < 0.001$, χ^2). In those patients who were admitted and treated with radiation for symptomatic spinal cord compression and then deteriorated neurologically in the hospital, consideration was given to urgent surgical decompression. In the thirteen cases (Table 3) in which surgery was performed, the results were disappointing. In the majority (77%) of these cases, the lost neurologic function was not recovered.

Functional Outcomes

The most significant factor associated with a good outcome was the pretreatment Frankel grade. Because the Frankel grade on admission was a strong predictor of posttreatment ambulatory status ($P = 0.006$, Cochran-Armitage) and continence ($P = 0.003$), all analyses were stratified by Frankel grade. The odds for posttreatment ambulation and continence were higher when surgery was the initial treatment (ambulation: odds ratio [OR] = 3.8, 95% confidence interval [CI] = 1.06–14, $P = 0.04$; continence: OR = 3.9, 95% CI = 1.2–13, $P = 0.03$). The odds for a better neurologic outcome during treatment also were higher when surgery was the initial treatment (OR = 5.8, 95% CI = 1.9–17, $P = 0.0002$).

In analyses stratified by Frankel grade on admission, age had no influence on any outcome in any treatment group. For ambulatory patients (Table 2), approximately 75% of those treated with *de novo* surgery remained ambulatory and continent, whereas only 50% of those treated with radiation before surgery remained ambulatory and continent ($P < 0.05$, χ^2). Patients with significant neurologic dysfunction on admission had less than a 50% chance of recovering ambulatory function or bowel and bladder function regardless of treatment strategy.

■ Discussion

The objective of therapy in managing the patient with metastatic spinal cord compression and spinal cord dysfunction is to alleviate pain, stabilize or realign the affected motion segments, prevent neurologic decline, and possibly restore lost neurologic function. The optimal result would have patients comfortably ambulating brace-free with normal continence for their remaining life span. The correct management strategy for achieving this goal is not clear from the current literature.[14] Whereas laminectomy alone (without transpedicular decompression for anterior disease) offers no significant benefit, as compared with radiation therapy alone for metastatic spinal cord compression,[26] a number of recent reports demonstrate the efficacy of surgical decompression with appropriate stabilization.[5,6,19,20,24]

Despite these encouraging data, the absence of randomized prospective trials showing the superiority of aggressive surgical treatment likely results in a tendency for many centers to attempt radiation therapy first for many patients unless a tissue diagnosis is necessary.[11,12] The retrospective data presented in this article show that spi-

nal radiation before surgery nearly triples the rate of major wound complications from posterior and posterolateral decompressive surgery for symptomatic spinal cord compression.

Most studies have determined that the rate of major wound complications is high (greater than 10%) for patients undergoing surgery to alleviate metastatic spinal cord compression. The factors influencing wound healing after decompressive surgery for metastatic spinal cord compression have been reviewed recently. McPhee et al[17] found a wound complication rate of 26% in their study of 53 patients. Poor nutritional status and the use of perioperative steroids significantly contributed to the development of major wound complications after surgery in their study. However, in contrast to current findings, the use of preoperative radiation was not found to be a significant factor in McPhee et al's[17] study. Others have found that previous external radiation treatment to the spine does contribute to wound complications in up to 30% of cases,[9,15,23] thus confirming the current finding.

In the current study, the preoperative nutritional status of patients as reflected by the serum albumin value was examined. A low serum albumin level, used as a low-cost indication of malnutrition, was a predictor of surgical morbidity and mortality in a recent national Veterans Administration (VA) study.[4] In the current study, no difference in serum albumin was found between patients in whom wound complications developed (mean albumin, 3.3) and those who had no complications (mean albumin, 3.2; $P = 0.77$, Student's *t* test). The total lymphocyte count[13] also was not a significant predictor of wound infection or dehiscence in the current study or McPhee et al's[17] study.

The biologic effects of ionizing radiation on human tissue might predispose a patient to the development of a wound complication in many ways. Radiation has been shown experimentally to inhibit fibroblasts, which are responsible for the deposition and remodeling of collagen in surgical wounds.[18] Experimental studies also have shown that the tensile strength of wounds is compromised when an incision is made within 1 to 3 weeks after irradiation.[2] In addition, radiation has late effects on human tissue, including dermal and vascular fibrotic changes that might well contribute to increased wound morbidity. Experimental studies show that fibroblasts from wounds previously irradiated grow less well than those isolated from normal subjects.[21] Moreover, in experimental systems, infections develop in irradiated wounds after the introduction of smaller bacterial inoculi.[1] The results presented in this article suggest that surgery within 7 days of irradiation is associated with a much higher wound complication rate than surgery performed after a remote history of external irradiation to the spine (46% *vs* 20%) ($P = 0.14$, χ^2). Further studies with more patients are needed to determine when patients who have undergone radiation are at greatest risk for development of a wound infection. Patients who underwent *de novo* surgery without any history of spinal irradiation had the lowest wound complication rate (12%).

The use of spinal instrumentation in patients with metastatic disease of the spinal column offers the chance to prevent the devastating neurologic consequences of a spine dislocation from a pathologic fracture and likely contributes significantly to pain relief. Cybulski[3] reviewed the situations wherein spinal instrumentation should be used in the surgical management of metastatic spinal disease. The higher rate of wound infections observed by others[16] in patients with segmental spinal instrumentation was noted also in Cybulski's[3] study, although the differences were not statistically significant. The use of spinal instrumentation increases the length of a wound, perhaps increases wound tension, and likely increases dead space, all of which may increase the risk of wound breakdown. Lower-profile instrumentation systems might theoretically be helpful.

Early detection of metastatic spinal cord disease, which often is irradiated before the development of myelopathy, likely prevents many patients from ever requiring any surgical therapy for the metastatic disease. The current study in no way suggests that this practice should be changed. It does raise the possibility that there might be a population of symptomatic patients who could benefit from *de novo* surgery followed by radiation therapy, as Sundaresan et al[23] have proposed.

Recently, Loblaw and Laperriere[14] published an evidence-based set of guidelines for the management of epidural metastatic spinal cord compression. Patients who cannot walk should undergo surgery whenever possible. However, patients admitted with very mild weakness (Frankel Grade D or E) represent a more controversial population. The present study suggests that these ambulatory patients also would benefit from early surgery.

In Figure 4, the outcomes for ambulatory patients treated with either *de novo* surgery or urgent radiation followed by surgery are compared. Almost 80% of the patients treated with surgery were ambulating at discharge, as compared with only 40% of the patients who underwent early radiation followed by surgery. Similar results were obtained considering sphincter outcome. The current study supports the practice of early surgery for patients with symptomatic spinal cord compression.

One significant concern in drawing conclusions from a retrospective study that spans 25 years is that the date of treatment might independently predict specific outcomes attributed to another variable such as preoperative radiation. A logistic regression was performed to address this issue. A trend toward statistical significance was found, suggesting that the past decade of treatment did involve more wound complications ($P = 0.092$, logistic regression). This finding is not surprising, however, because a larger number of patients were treated with radiation before surgery during the past decade. This decade of treatment did not predict sphincter ($P = 0.671$, logistic regression) or ambulatory ($P = 0.700$) outcomes.

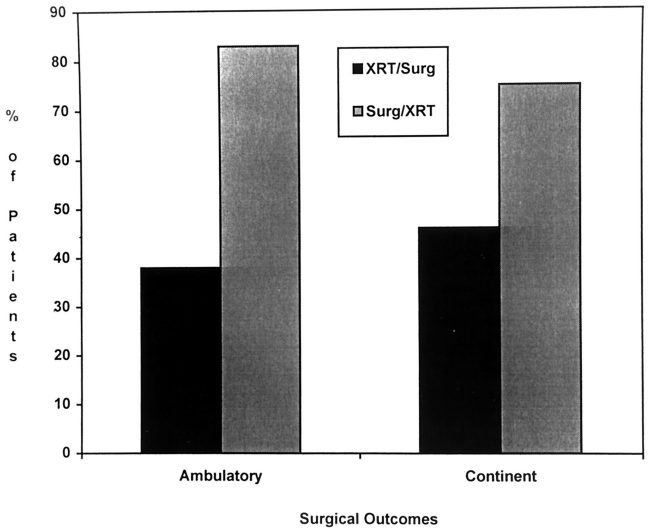

Figure 4. Outcome for ambulatory patients (Frankel Grade D or E) presenting to the the hospital with metastatic spinal cord compression treated with either radiation followed by surgery or *de novo* surgery. When ambulation and continence are independently considered as separate outcome events, the neurologic outcomes are better for patients treated with *de novo* surgery ($P < 0.05$, χ^2). **XRT/Surg,** Ambulatory patients (n = 11) treated first with spinal radiation and then with surgical decompression. **Surg/XRT,** Ambulatory patients (n = 15) treated with *de novo* surgery.

Many patients who have been appropriately irradiated will still need decompressive surgery for cord compression. All of the patients in the current study were treated with intravenous antibiotics (generally a first-generation cephalosporin) before surgery. However, the absence of a cultured organism in most of the wound failures raises the possibility of poor wound healing as a primary problem, with infection as a secondary matter in many cases.

A recent study of 500 patients has demonstrated that increasing supplemental oxygen can substantially reduce surgical wound infections.[7] At the Massachusetts General Hospital institution, the authors have established a practice of making large relaxing incisions to prevent tension in the fascial layer after closure. In addition, a nonabsorbable suture (*e.g.*, prolene) often is used to close the fascia. Finally, the authors believe that careful attention to postoperative nutritional support also is important.

Recommendations

The importance of a coordinated interdisciplinary approach for patients with symptomatic metastatic spinal cord compression should be emphasized at all major medical centers. Most patients with symptomatic spinal cord compression would benefit from surgical decompression and stabilization before the initiation of radiation therapy. The spine surgeon should be involved in the decision to irradiate a patient who has symptomatic disease, and arrangements for careful follow-up assessment must be in place to avoid loss of recoverable neurologic function. Careful consideration should be given to an anterior approach for patients who have had previous radiation. Finally, spine surgeons should consider consultation with plastic surgeons for possible mobilization of muscle flaps at the time of primary closure in previously irradiated patients undergoing posterolateral decompression and stabilization.

■ Key Points

- Retrospective study on metastatic spinal cord compression management was conducted.
- The effect of spinal radiation on wound healing was investigated.
- The effect of preoperative spinal radiation on functional outcomes was studied.
- The effect of spinal instrumentation on wound infections and outcomes was observed.
- Spinal radiation before surgical decompression is associated with a high major wound complication rate and worse clinical outcome.

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