Surgery Versus Radiation Therapy in Symptomatic Malignant Spinal Cord Compression

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Abstract: Malignant epidural spinal cord compression is an oncologic emergency that often results in pain and neurologic dysfunction, which may be permanent. Few prospective studies have been performed to determine whether surgical intervention confers a significant benefit over radiation therapy. We believe the small amount of existing evidence to support surgical intervention or radiation therapy alone suffers from patient selection bias, and that such bias tends to bear out in practice as well. In addition to the objective benefits achieved by surgical decompression, practitioners need to consider the subjective benefits such as increased ambulatory ability, increased spine stability, and improved pain management provided by timely surgical decompression of metastatic spinal cord lesions.

Keywords: Spinal cord compression, radiation therapy, surgical decompression, spinal metastases.

Malignant epidural spinal cord compression (MESCC) is an emergency that requires prompt evaluation and multi-disciplinary management. More than 20,000 new cases are reported each year [1]. Patients commonly present with pain and rapidly progressive neurologic dysfunction, and a high potential for permanent neurologic impairment exists if treatment is delayed. There is little prospective data to steer management regarding treatment modality. Conclusions from retrospective analysis are mixed.

The benefits of surgical intervention alone were first called into question over thirty years ago when a small prospective study of patients with neurologically-significant compression could not demonstrate a difference in outcomes between radiation therapy and laminectomy plus radiation therapy [2]. Following this, an analysis suggested that laminectomy with or without radiation resulted in lower rates of restored neurologic function and had less benefit for pain relief than radiation alone [3]. In contrast, a later retrospective study showed a significant improvement in neurologic function in patients who received decompressive laminectomy followed by radiation therapy, compared to surgery or radiation alone [4]. Likely due to the move towards direct, selective surgical decompression as opposed to nonselective posterior laminectomy and the subsequent improvement of decompressive surgical techniques, later studies showed that surgery resulted in significant improvement in neurologic function (with the primary outcome of ability to walk) when compared to radiation therapy alone [5].

One prospective study has been performed to evaluate the efficacy of surgery versus radiation with respect to preservation or restoration of ambulatory ability, muscle strength, functional ability, maintenance of continence, and overall survival. Surgical intervention resulted in better outcomes in all categories of assessment [6]. A matched-pair retrospective analysis (using 10/11 conformal prognosticators) subsequently attempted to address the biases of this study and found no differences in outcomes between the surgery plus radiation therapy and the radiation-only group [7]. A systematic review concluded that patients with the ability to walk at the time of diagnosis should be treated with radiotherapy alone, and that surgery is indicated in patients with one region of compression, paraplegia over 48 hours, non-radiosensitive tumors, and a predicted survival of greater than three months [8]. A prospective trial to further examine the efficacy of these two treatment arms is currently recruiting patients (ClinicalTrials.gov identifier: NCT00634426).

Studies to date have measured objective outcomes such as survival, ambulatory ability, and rates of incontinence [2, 6]. Subjective outcomes such as quality of life and degree of independence are less often discussed. We believe these should play a greater role in determining which patients undergo surgery versus which are treated solely with radiotherapy. A survey of MESCC patients performed one month after diagnosis reported a number of

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valuable observations with regard to subjective outcomes. This study reported a correlation between the ability to walk at time of diagnosis and survival (independent ambulators were found to survive 151 days post-diagnosis, versus nonambulatory patients who survived 35 days). There was also a correlation between physical independence and self-reported quality-of-life scores. A significant improvement in reported pain after surgical intervention for MESCC has also been reported, though this study that did not directly compare efficacy to patients who were treated with radiation therapy [9].

Preservation of ambulation is one of the primary goals in treating cord compression, therefore it is important to identify factors that will help select patients for whom the benefits of surgery outweigh the risks. A secondary analysis of the previously mentioned prospective trial showed that 90% of surgically-treated patients who were less than 65 years old maintained the ability to ambulate post-surgery, compared to only 63% in the cohort treated with radiation therapy only (OR=5.14, p=0.002) [2]. Seventy-eight percent of surgical patients over 65 years old were ambulatory post-surgery, versus 55% in the radiation group (not a statistically significant finding). These results suggest that the potential for rehabilitation is lower in the older patient population, and that this could aid in deciding whether a patient should undergo surgical decompression versus treatment with radiation therapy alone.

The data to support radiation therapy alone for palliation of MESCC are somewhat less generalizable. One prospective trial evaluated the benefit of radiation therapy (RT) for back pain, motor capacity, and bladder function, and showed a 54% complete response for back pain with RT alone. Seventy-six percent of these patients maintained full recovery or preservation of their ability to walk [10]. Furthermore, 44% of this population had improvement of sphincter function. All participants in this study were part of an early diagnosis protocol. Half of the included patients had no neurologic deficits at the time of diagnosis, and over half of the patients in this trial had a malignancy with a favorable histologic diagnosis. Because forty-seven percent of patients with MESCC initially present with neurologic symptoms and 90% present with pain [11], we believe it is difficult to generalize these positive outcomes to cases of severe neurologic deficit or more debilitated patients.

The potential for both tumor resection and spinal fixation with direct decompressive surgery lends itself to the improvement of mechanical back pain in addition to tumor-related back pain [11]. Certain surgical techniques offer stabilization of microfractures and ablation of pain receptors which may result in augmented pain relief [12]. Multiple series have been reported with improvement of pain symptoms ranging from 76% to 100% after surgical intervention [13]. We believe this is a relevant response to those who would argue that surgical intervention is not indicated in the absence of neurological motor or sensory deficit. An important consideration is the clinical context of a patient's reported symptoms, and outcomes in patients treated with radiation alone or decompression laminectomy with radiation outside the context of a randomized prospective trial. The multi-institutional trial reported by Patchell, *et al*. [6] is the only reported randomized trial and, as noted above, this study concluded "…direct compression surgery plus postoperative radiation therapy is superior to treatment with radiotherapy alone for patients with spinal cord compression caused by metastatic cancer."

With the emergence of improved surgical techniques such as circumferential decompression and newer stabilization methods, it is increasingly more difficult to apply the existent prospective data to guide decision making when approaching a patient with metastatic spinal cord compression. This is especially true when considering the decreased morbidity associated with newer techniques [12]. Improvements in anterior approach techniques have made it possible to target tumors more directly, as most tumors arise in the vertebral body which laminectomy does not access. In addition, lateral approach *via* thoracotomy has made the lower thoracic vertebrae more easily accessible *via* a less invasive technique. Improvements in laparoscopic techniques have made retroperitoneal access to the lumbar vertebrae possible, more easily enabling both tumor resection and spinal stabilization [12].

Perhaps most importantly, it is imperative to maintain the perspective that a diagnosis of spinal cord compression itself correlates to a decreased life expectancy, thus every effort should be made to provide optimal quality of life for the patient's remaining lifespan. A recent study evaluating the palliative benefit of surgical intervention showed that 40.4% of patients in their cohort experienced an improvement in ECOG performance status, and 43.9% of patients maintained their pre-operative status. Only 15.7% of patients in this

study had a worsening of ECOG score [14]. Post-operative complications were reported as 5.3% (two superficial wound infections and one seroma). Though this was a small study (n=57), it is useful in illustrating the improvements in surgical treatment of metastatic spinal disease.

Considering all of these data together, we propose a lower threshold for surgical intervention in the setting of metastatic spinal cord compression. It is likely reasonable to treat patients with incidentally-discovered cord effacement or patients who have no risk to the stability of their spine with radiation therapy alone. We believe surgical decompression should be pursued for patients with symptomatic neurologic deficits, non-radiosensitive tumors, or any indication of spinal instability. In addition, any patient who would have a significant decline in their quality of life due to the loss of ambulatory ability should be considered for decompression, even if symptoms of impairment have not yet developed. Patients with mild symptoms may benefit significantly from early and urgent decompression, and the deferment of surgical intervention may cost some patients a higher quality of life that they would not experience with more conservative treatment modalities.

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