Surgical Decompression of High-Grade Spinal Cord Compression from Hormone Refractory Metastatic Prostate Cancer

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BACKGROUND: Spine and nonspine skeletal metastases occur in more than 80% of patients with prostate cancer.

OBJECTIVE: To examine the characteristics of the patient population undergoing surgery for the treatment of prostate cancer metastatic to the spine.

METHODS: A retrospective chart review was performed on all patients treated at our institution from June 1993 to August 2014 for surgical management of metastatic spine disease from prostate cancer.

RESULTS: During the study period, 139 patients with 157 surgical lesions underwent surgery for metastatic spine disease. Decompression for high-grade epidural spinal cord compression was required for 126 patients with 143 lesions. Preoperatively, 69% had a motor deficit and 21% were nonambulatory, with 32% due to motor weakness. At surgery, 87% of patients had hormone-refractory prostate cancer (HRPC) and 61% failed prior radiation. Median overall survival for HRPC patients was 6.6 mo (95% confidence interval [CI]: 5.6–8.6) while the median overall survival for hormone-sensitive patients was 16.3 mo (95% CI: 4.0–26.6).

CONCLUSION: The majority of patients undergoing surgery for prostate cancer metastases to the spine were refractory to hormone therapy, indicating that patients with hormone-sensitive prostate cancer are unlikely to develop symptomatic spinal cord compression or spinal instability. A significant number of HRPC patients presented with neurological deficits attributable to spinal cord compression. Vigilant monitoring for the development of signs and symptoms of epidural spinal cord compression and spinal instability in hormone-refractory patients is recommended. Surgical decision making may be affected by the much shorter postoperative survival for HRPC patients as compared to patients with hormone-sensitive cancer.

KEY WORDS: Epidural spinal cord compression, Hormone refractory prostate cancer, Spine metastasis, Prostate cancer, Spinal surgery

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Spine and nonspine skeletal metastases occur in more than 80% of patients with advanced prostate cancer.^{1,2} Metastatic spine disease (MSD) from prostate cancer

may present as a pathological fracture with or without high-grade epidural spinal cord compression (ESCC) or mechanical instability causing pain; in a number of patients, however, MSD may be the presenting feature of newly diagnosed prostate cancer.^{3,4} The osteoblastic lesions typical of metastatic prostate cancer are considered radiosensitive.⁵ Therefore, surgical treatment is reserved for treating symptomatic high-grade ESCC in a previously irradiated field or pathological fractures resulting in mechanical instability.^{6,7} At the time of diagnosis, the majority of prostate cancer is hormone sensitive

ABBREVIATIONS: ADT, androgen deprivation therapy; CEBRT, conventional external beam radiation; CI, confidence interval; CSF, cerebrospinal fluid; ESCC, epidural spinal cord compression; HRPC, hormone-refractory prostate cancer; MRI, magnetic resonance imaging; MSD, metastatic spine disease; OS, overall survival; PSA, prostate-specific antigen; RT, radiation therapy; SRS, stereotactic radiosurgery

and responds well to androgen deprivation. In fact, concomitant hormone therapy with conventional external beam radiation (cEBRT) has been explored as a first line of treatment even for high-grade ESCC from newly diagnosed prostate cancer.⁸ While androgen deprivation is very effective in treating hormone-naïve prostate cancer,⁹ death from prostate cancer typically results from the systemic spread of hormone-resistant cells.^{9,10} A few studies have looked at the effectiveness of surgical decompression in the setting of high-grade ESCC from prostate metastasis with favorable outcomes.^{5,11-16} However, the experience in these studies has been limited due to small sample sizes. In this study, we examine the largest cohort of patients to date who underwent surgical decompression for metastatic prostate cancer to the spine. The purpose of this study was to delineate the patient population requiring spinal surgery for metastatic prostate cancer and to report the surgical outcomes in this patient population.

METHODS

Patient Selection

A retrospective chart review was performed on all patients treated at a single academic medical center from June 1993 to August 2014 for surgical management of spinal metastases from prostate cancer. The review was conducted under IRB Research Protocol #WA0329-14. Patient consent was not required. During this period, all patients with histologically confirmed prostate cancer with MSD causing rapidly progressive neurological deterioration and/or mechanical instability and

who were medically able to tolerate surgery were included in the study. Patients with a life expectancy of less than 3 mo or who were treated with chemoradiation alone were excluded (Figure 1).

Clinical Data

Medical records were reviewed for demographics, diagnosis of primary disease, diagnosis of MSD, time to progression, hormone response status at the time of MSD and spine surgery, prostate-specific antigen (PSA) levels, preoperative treatment, decision making for surgical decompression (neurological, oncologic, or mechanical instability), extent of disease, postoperative treatment (chemoradiation), and follow-up. The degree of ESCC and mechanical instability were noted from available radiographic data and clinical information. For radiation, both the dose and fractionation schemes were recorded. Pathological data included Gleason score and histological variant of prostate cancer. Complications from surgery that required outpatient treatment, readmission, or reoperation, including infection, wound dehiscence, cerebrospinal fluid (CSF) leak, epidural hematoma, and hardware failure, were recorded.

Surgical Decision Making

The need for surgical intervention was dictated by the patient's neurological and oncologic disease burden as well as evidence of mechanical instability, previously described as the NOMS (Neurologic, Oncologic, Mechanical instability, and Systemic disease) framework. The type of surgery, including anterior/posterior decompression, with or without instrumentation, and the number of levels instrumented was documented.

The majority of patients in our study underwent separation surgery. Resection of epidural disease was facilitated by this approach, in which

the laminae, pedicles, and facet joints are removed over the levels affected by the ESCC. In rare instances, the vertebral body disease was lytic rather than sclerotic. In some of those cases, the diseased bone was resected from a posterior transpedicular approach and the vertebral body was replaced with polymethyl methacrylate augmented with Steinmann pins. Posterior segmental fixation was provided with pedicle screws in the thoracic and lumbar spine and with lateral mass screws in the cervical spine.

Postoperative Radiation

The majority of radiation naïve patients underwent postoperative radiation using cEBRT, most commonly 30 Gy in 10 fractions^{17,18} or 24-Gy single-fraction stereotactic radiosurgery (SRS). Patients who failed prior radiation were reirradiated using a high-dose hypofractionated SRS with doses ranging from 18 to 36 Gy in 3 to 6 fractions. In patients undergoing SRS, postoperative computed tomography myelography was performed to delineate spinal cord and dural margins as well as to avoid any radiographic artifact encountered on magnetic resonance imaging (MRI) in the setting of proximate spinal instrumentation. The myelography and simulation were often performed prior to patient discharge following surgery.

Clinical Outcomes

Patients' ambulatory, bowel, bladder, and neurological statuses were recorded pre- and postoperatively. The postoperative assessments were recorded at 3 mo and at the last follow-up visit. Assessment of neurological status included motor or sensory deficits and mechanical pain.

Statistical Analysis

Descriptive statistics such as frequencies, medians, and interquartile ranges were utilized. McNemar's test was used to examine associations of paired pre- and postsurgical data. Overall survival (OS) was calculated from time of surgery to date of last follow-up or date of death. All *P* values were 2-sided and all statistical analyses and graphics were performed in SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Patient Characteristics

One hundred thirty-nine patients underwent 157 spine operations related to MSD due to prostate cancer. The median age at diagnosis of MSD was 65 yr (range: 41-89 yr), while that at surgery was 68 yr (range: 45-90 yr; Table 1). The median overall follow-up from surgery was 6.7 mo (range: 0.3-143.1 mo), while that for survivors was 8.1 mo (range: 1.2-67.2 mo). The median time from MSD diagnosis to surgery was 21.1 mo (range: 0-194.5 mo). The median Gleason score at the time of the prostate cancer diagnosis was 7.5 (range: 5-10), and all but 1 patient had a Gleason score greater than 6. The median PSA level was 18.2 ng/mL (range: 0.2-13 010) at spine diagnosis and 52.0 ng/mL (range: 0.05-3999) at surgery. In terms of responsiveness to hormones, 87% (121/139) of patients were hormone refractory at the time of surgery. Over 95% (133/139) of all patients had prostate adenocarcinoma with classic acinar histology, while 4% (6/139) had nonacinar (small cell) histology.

TABLE 1. Patient Characteristics

		Median	Min-max
Age at MSD diagnosis		65	41-89
Age at spine surgery		68	45-90
Time from MSD dx to surgery	(months)	21.1	0-194.5
Follow-up	(months)	6.7	0.3-143.1
Overall survival	(95% CI)	7.5	6.1-10.2
		n	%
ESCC at MSD diagnosis (n = 157)	Low grade	67	43
	High grade	16	10
	No MRI	74	47
ESCC before surgery (n = 157)	Low grade	14	9
	High grade	143	91

Management of Primary and MSD

In addition to standard hormone depletion therapy, 42% (66/157) of patients also received treatment with bisphosphonates. Surgical orchiectomy was performed in 6% (9/157) of patients. The median time from diagnosis of prostate carcinoma to MSD was 40.8 mo (range: 0-209.7 mo). MSD was single level in 35% (48/139) of patients, involved 2 to 4 levels in 27% (38/139) of patients, and involved >5 levels in 36% (50/139) of patients, while extent of disease was unknown in 2% (3/139). Of the 148 unique lesions, 61% (90/139) received radiation therapy (RT) after diagnosis of MSD. Of these lesions, 86% (77/90) received cEBRT with a median dose of 3000 cGy in 10 fractions (range: 2400-5760 cGy), 7.8% (7/90) received single-fraction SRS with a median dose of 2400 cGy (range: 1800-2400 cGy), 7.8% (7/90) received hypofractionated SRS with a median dose of 2500 cGy in 5 fractions (range: 2000-3900 cGy in 3-5 fractions), and 2% (2/90) received RT of an unknown type at outside institutions.

Hormone Responsiveness at MSD and at Time of Surgery

At the time of MSD diagnosis, 44% (61/139) of patients demonstrated hormone-refractory prostate cancer (HRPC). This number increased to 87% (121/139) at the time of spine surgery. Of patients who received RT prior to surgery, 45% (37/83) had HRPC at the time of MSD diagnosis and 88% (73/83) had progressed to HRPC at the time of surgery. Among patients with high-grade ESCC, 44% (56/126) had HRPC at MSD diagnosis and 89% (112/126) had HRPC at spine surgery (Table 2).

Surgical Decision Making and Patient Characteristics at Time of Surgery

A total of 157 spine operations were performed on 139 patients. Of those, 91% (143/157) were performed for high-grade ESCC, while 9% (14/157) were performed for mechanical instability only. At the time of surgery, 46% (73/157) of lesions caused circumferential spinal cord compression on imaging. Of

TABLE 2. Hormone Responsiveness at Various Stages of Workup

	Hormone sensitive		Hormone refractory	
	n	%	n	%
At MSD diagnosis (n = 139)	78	56	61	44
Preop RT (n = 83)	46	55	37	45
At surgery with preop RT (n = 83)	10	12	73	88
At surgery (n = 139)	18	13	121	87
At surgery with high grade ESCC (n = 126)	14	11	112	89

TABLE 3. Surgical Decision Making

Preoperative		n	%
Motor exam	Intact	45	29
	Deficits	108	69
	Unknown	4	3
Sensory exam	Intact	78	50
	Deficits	70	45
	Unknown	10	6
Ambulatory status	Nonambulatory	33	21
	With assistance	74	47
	Without assistance	49	31
Bowel	Intact	146	93
	Incontinent	10	6
	Unknown	1	1
Bladder	Intact	132	84
	Incontinent	25	16
Mechanical pain	No pain	26	17
	Pain	129	82
	Unknown	2	1

the patients who had received RT to the operated levels, median time from RT to surgery was 352 d (range: 1-5298 d).

Of the 157 clinical presentations, 69% (108) involved motor deficits and 45% (70) involved sensory deficits; 6% (10) were bowel incontinent and 16% (25) were bladder incontinent (Table 3). Overall, 82% (129) had mechanical pain. Nonambulatory patients accounted for 21% (33), while 47% (74) could walk with assistance and 31% (49) were ambulatory without assistance, and the ambulatory status of 1% (1) was unknown at the time of spine surgery. Among the nonambulatory patients, 24% (8/33) were unable to walk due to sensory deficits, 60% (20/33) due to motor deficits, and 12% (4/33) due to a combination of sensory and motor deficits. This information was not available for 1 patient. The majority of the patients were nonambulatory or had difficulty ambulating due to either pain (32%) or weakness (45%).

Surgical Details

Operated levels included 10% (16) cervical, 57% (89) thoracic, 17% (27) lumbar, and 10% (15) spanning junctional

levels (7 cervicothoracic, 8 thoracolumbar; Table 4). Of 157 surgeries, 83% (130) involved separation surgery with instrumentation, 10% (15) involved laminectomy only, 4% (6) involved corpectomy with instrumentation, and 4% (6) had instrumented fixation without decompression. Intraoperative brachytherapy with P³² plaque was given during 6% (9) of operations. Median operative time (including anesthesia time) was 195 min (range: 62-665). Median estimated blood loss was 800 cc (range: 50-9100 cc) with 58.6% of surgeries requiring postoperative transfusion. Median hospital stay was 9 d (range: 2-76 d).

Surgical Outcomes

Surgical treatment significantly improved nearly all measures of preoperative morbidity in patients with MSD requiring surgery (ie, those with symptomatic ESCC or mechanical instability). For 157 lesions in patients in whom both pre- and postoperative data were available, postoperative improvement was noted in 42% (44/105, $P < .0001$) of those with motor deficits, 62% (39/63, $P < .0001$) with sensory deficits, 75% (91/121, $P < .0001$) with mechanical instability pain, 75% (6/8 patients, $P = .16$) with bowel incontinence, and 82% (18/22, $P < .05$) with bladder incontinence. Of nonambulatory patients, 76% (25/33, $P = .003$) regained the ability to walk.

High-grade ESCC accounted for 91% (143/157) of the surgeries performed. In this cohort, surgical decompression significantly improved all measures of preoperative morbidity. Of lesions causing preoperative motor deficits, 42% (40/96, $P < .0001$) were motor intact postoperatively. Of lesions causing sensory deficits, 61% (33/54, $P < .0001$) regained normal sensation postoperatively. Of lesions causing mechanical pain, 72% (79/109) improved postoperatively. Bladder and bowel continence was regained in 80% (16/20, $P = .06$) and 75% (6/8, $P = .06$), respectively. Ambulation was regained in 78% (25/32, $P = .0015$), with 65% (21/32) ambulating with assistance and 12.5% (4/32) ambulating independently ($P = .0004$).

Mechanical instability without high-grade ESCC accounted for 9% (14/157) of surgeries. Of those, 86% (12/14) presented with mechanical pain, all of whom improved after surgical stabilization.

Postoperative Radiation

Postoperatively, 52% (77/148) of unique lesions were irradiated. This included cEBRT in 58% (45) of lesions (median dose: 3000 cGy in 10 fractions) and SRS for 42% (32) of lesions (median dose: 2400 cGy in 3 fractions). The majority of patients who did not receive postoperative RT had been irradiated prior to the evolution of SRS, which allows for reirradiation, or had a large systemic disease burden.

New Postoperative Deficits and 30-d Complications

Of those intact preoperatively, 17% (23/139) of patients experienced at least 1 complication involving new postoperative deficits. This included 1 new case of motor deficits not involving tumor progression. Within 30 d postoperatively, 15.9% (25/157)

TABLE 4. Surgical Details

		n	%
Procedure type performed (n = 157)	Separation surgery	15	10
	Separation surgery with instrumentation	130	82
	Separation surgery with corpectomy	6	4
	Fixation without decompression	6	4
Intraoperative brachytherapy	P32 plaque	9	6
Site of laminectomy	None	10	6
	Cervical	16	10
	Thoracic	89	57
	Lumbar	27	17
	Cervical, thoracic	7	4
	Thoracic, lumbar	8	5
Site of instrumentation	None	18	11
	Posterior only	125	80
	Anterior only	2	1
	Combined	12	8
		Median	Min-max
Number of instrumented levels		6	0-14
Number of laminectomy levels		3	0-7
Number of patients transfused	(%)	92	58
Surgery duration	(minutes)	195	62-665
Operative blood loss	(cc)	800	50-9100

of patients experienced adverse events that required readmission. These included 6 wound infections/dehiscence with 2 requiring washout and repair, 1 case of early hardware failure requiring reoperation, 1 CSF leak requiring operation, 1 epidural abscess requiring drainage, and 2 cases each of pneumonia and urinary tract infection.

Recurrences and Overall Survival

Of 139 patients who underwent 157 operations, 9 procedures were performed for recurrent disease while new lesions accounted for another 9 procedures. At the end of the study period, 21 (15%) patients were still alive. Median follow-up was 6.7 mo for the entire cohort and 8.1 mo for survivors.

Median OS for the entire cohort was 7.5 mo (95% confidence interval [CI]: 6.1-10.2 mo). When dichotomized according to hormone responsiveness at the time of surgery, patients with HRPc had a median OS of 6.6 mo (95% CI: 5.6-8.6), while the median OS of hormone-sensitive patients was 16.3 mo (95% CI: 4.0-26.6; log-rank $P = .06$; Figures 2A and 2B).

DISCUSSION

Prostate cancer is the second most common cause of MSD,¹⁹ with over 95% having adenocarcinoma histology.²⁰ With the advent of routine PSA screening, the incidence of metastatic prostate cancer as the first presentation of disease has fallen to approximately 7%.²¹ Newly diagnosed metastatic prostate cancer is highly sensitive to androgen deprivation therapy (ADT)^{10,20}; for these hormone-naïve cases, ADT along with EBRT has

been proposed as a viable first-line treatment option.⁸ The use of hormone therapy, in contrast to surgical castration, has been in practice in the United States for over 6 decades. Antiandrogen therapy for prostate cancer was first described in the 1960s, with subsequent widespread use of androgen ablation through nonsteroidal antiandrogens starting with the FDA approval of flutamide in 1989.²² With time, however, prostate cancer becomes resistant to hormonal treatment; HRPc¹⁰ is the most common type of prostate cancer with MSD, with significantly increased morbidity and mortality.⁹ The OS of patients with metastatic HRPc is between 2 and 3 yr.²³⁻²⁵ Moreover, long-term ADT can cause osteoporosis^{26,27} and contribute to disease progression in the spine. Spine metastasis from prostate cancer typically presents as a sclerotic lesion ventrally infiltrating vertebral bodies of the thoracolumbar spine.^{28,29} In the absence of high-grade ESCC causing acute neurological morbidity or mechanical instability, these tumors can safely be treated with EBRT or ADT. In prostate cancer patients with MSD who were surgical candidates, surgery was shown to improve functional outcome, ie, recover ambulation^{12,16} and continence^{12,13,16} and reduce the amount of corticosteroid and narcotic use.^{12,13}

Surgical Indications

In the current series, surgical indications included epidural progression of previously irradiated metastases and spinal cord compression causing progressive neurological deficit or mechanical instability. Patients without these surgical indications initially underwent RT or ADT in order to treat MSD. Surgical decompression among patients with symptomatic ESCC

has been shown to provide superior outcomes when compared to RT without surgery.⁷ Therefore, among patients with progressive neurological deficits, decompression is preferred to RT in order to provide rapid spinal cord decompression and to optimize their chances of neurological recovery. In the current series, 69% of patients had motor deficits prior to undergoing surgery, with many additional patients experiencing sensory, bowel, or bladder control deficits. Furthermore, 82% of patients had mechanical pain. Mechanical instability represents an independent surgical indication, as RT and systemic therapy cannot restore mechanical integrity of the spine. Spinal instrumented stabilization effectively restores spinal stability and can be carried out using open or minimally invasive surgical techniques.

Prostate metastases to the spine readily and reliably respond to radiotherapy. In patients without previous radiation or mechanical instability, cEBRT provides effective local control and can be administered in patients without spinal cord compression as well as in patients with spinal cord compression without neurological deficits. In the current patient series, 61% of patients underwent RT as the initial treatment for MSD, with 86% of these patients receiving cEBRT. Among these patients, the median time from RT to local progression requiring surgery was 1 yr. Among patients who underwent RT as the initial treatment, the number of HRPC patients increased from 45% at the time of RT to 88% at the time of surgery, indicating transformation to a more aggressive form of disease. Image-guided spinal reirradiation has been shown to provide effective tumor control, but care must be taken not to exceed safe spinal cord doses. Therefore, in patients with epidural tumor progression in a previously irradiated field, spinal cord decompression should be carried out in order to safely deliver effective reirradiation doses.

As evidenced by the current series, the overwhelming majority of patients with hormone-sensitive prostate cancer do not require spinal surgery. In the current study, 87% of patients undergoing spinal surgery for the treatment of prostate metastases had HRPC. This number was even higher (89%) in patients with high-grade ESCC. Notably, fewer than half of patients had HRPC at the time of MSD diagnosis. Furthermore, a significant number of these patients presented with neurological deficits attributable to spinal cord compression, indicating the aggressive nature of this disease. Transformation to HRPC puts patients at risk for developing symptomatic spinal cord compression and requires careful monitoring for signs and symptoms of spinal tumor progression. HRPC also portends poor survival prognosis for patients undergoing spinal surgery, with patients with hormone-sensitive disease at the time of surgery living much longer than those with HRPC.

Surgical Outcomes and Complications

As expected, surgical treatment significantly improved nearly all measures of preoperative morbidity in patients with MSD requiring surgery (ie, those with symptomatic ESCC or mechanical instability). Forty-two percent of patients with preoperative motor deficits experienced motor improvement, 62% experienced sensory improvement, and 76% of nonambulatory patients recovered ability to ambulate. Furthermore, 75% of patients with mechanical instability experienced significant pain improvement.

The overall 30-d complication rate of 15.9% in our study compares favorably to that reported in the literature.^{5,11,13-16,12} The rate of postoperative motor deterioration was 2% in our study. In a cohort of 678 patients with primary and metastatic spine tumors, the rate of surgical site infection for

metastatic spinal tumors was 9.5%,³⁰ with prior surgery, complex plastics closures, and hospital-acquired infection at the time of previous surgery as significant determinants on multivariate analysis. However, our own experience with reoperation for recurrent ESCC at the same level of prior surgery showed a 5% major complications rate.³¹ Jansson et al¹⁵ reported an overall complication rate of 20% in their cohort of 282 patients (40% metastatic prostate).¹⁵

Limitations

The major limitation of this study lies in its retrospective nature. Additionally, not all patients were diagnosed at our institution, and we also recognize that there may have been others with similar progression who were diagnosed at our institution but sought follow-up treatment elsewhere. The current patient group describes a subgroup of patients with prostate cancer who required spinal surgery. The current results cannot provide conclusive information about the risk of symptomatic spinal cord compression or mechanical instability in patients with prostate cancer as a whole. However, the significant number of patients presenting with motor deficits emphasizes the importance of heightened vigilance in patients with HRPC.

CONCLUSION

Patients with HRPC with MSD are at risk of epidural tumor progression. The purpose of this analysis was to delineate the characteristics of the patient population undergoing surgery for the treatment of prostate cancer metastatic to the spine. Patients with hormone-sensitive prostate cancer constitute a very small proportion of patients undergoing spinal surgery for the treatment of prostate MSD and are unlikely to require spinal surgery. On the other hand, 87% of patients in the current surgical series had HRPC, indicating that these patients represent a group at risk for requiring surgical intervention for the treatment of MSD. The high proportion of patients presenting with motor and sensory deficits emphasizes the aggressive nature of HRPC disease and indicates that this patient population requires close surveillance for the development of signs and symptoms of ESCC and spinal instability. Furthermore, patients with HRPC have significantly shorter postoperative survival when compared to patients with hormone-sensitive cancer, and this may affect surgical decision making and operative planning.

Disclosures

Ilya Laufer and Mark Bilsky serve as consultants for SpineWave, Globus, and DePuy/Synthes. Statistical support for this study was provided by MSK Institutional Core Grant (P30 CA008748). The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Bubendorf L, Schopfer A, Wagner U, et al. Metastatic patterns of prostate cancer: an autopsy study of 1,589 patients. *Hum Pathol*. 2000;31(5):578-583.

2. Mehra R, Kumar-Sinha C, Shankar S, et al. Characterization of bone metastases from rapid autopsies of prostate cancer patients. *Clin Cancer Res*. 2011;17(12):3924-3932.
3. Loblaw DA, Laperriere NJ, Mackillop WJ. A population-based study of malignant spinal cord compression in Ontario. *Clin Oncol*. 2003;15(4):211-217.
4. Mercadante S. Malignant bone pain: pathophysiology and treatment. *Pain*. 1997;69(1-2):1-18.
5. Cereceda LE, Flechon A, Droz JP. Management of vertebral metastases in prostate cancer: a retrospective analysis in 119 patients. *Clin Prostate Cancer*. 2003;2(1):34-40.
6. Klimo P Jr, Thompson CJ, Kestle JR, Schmidt MH. A meta-analysis of surgery versus conventional radiotherapy for the treatment of metastatic spinal epidural disease. *Neuro Oncol*. 2005;7(1):64-76.
7. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet*. 2005;366(9486):643-648.
8. Kato S, Hozumi T, Yamakawa K, et al. Hormonal therapy with external radiation therapy for metastatic spinal cord compression from newly diagnosed prostate cancer. *J Orthop Sci*. 2013;18(5):819-825.
9. Feldman BJ, Feldman D. The development of androgen-independent prostate cancer. *Nat Rev Cancer*. 2001;1(1):34-45.
10. Niraula S, Chi K, Joshua AM. Beyond castration-defining future directions in the hormonal treatment of prostate cancer. *Horm Cancer*. 2012;3(1-2):3-13.
11. Crnalic S, Lofvenberg R, Bergh A, Widmark A, Hildingsson C. Predicting survival for surgery of metastatic spinal cord compression in prostate cancer: a new score. *Spine (Phila Pa 1976)*. 2012;37(26):2168-2176.
12. Ju DG, Zadnik PL, Groves ML, et al. Factors associated with improved outcomes following decompressive surgery for prostate cancer metastatic to the spine. *Neurosurgery*. 2013;73(4):657-666; discussion 666.
13. Williams BJ, Fox BD, Sciubba DM, et al. Surgical management of prostate cancer metastatic to the spine. *J Neurosurg Spine*. 2009;10(5):414-422.
14. Chaichana KL, Pendleton C, Sciubba DM, Wolinsky JP, Gokaslan ZL. Outcome following decompressive surgery for different histological types of metastatic tumors causing epidural spinal cord compression. Clinical article. *J Neurosurg Spine*. 2009;11(1):56-63.
15. Jansson KA, Bauer HC. Survival, complications and outcome in 282 patients operated for neurological deficit due to thoracic or lumbar spinal metastases. *Eur Spine J*. 2006;15(2):196-202.
16. Shoskes DA, Perrin RG. The role of surgical management for symptomatic spinal cord compression in patients with metastatic prostate cancer. *J Urol*. 1989;142(2 Pt 1):337-339.
17. Yamada Y, Bilsky MH, Lovelock DM, et al. High-dose, single-fraction image-guided intensity-modulated radiotherapy for metastatic spinal lesions. *Int J Radiat Oncol Biol Phys*. 2008;71(2):484-490.
18. Yamada Y, Lovelock DM, Yenice KM, et al. Multifractionated image-guided and stereotactic intensity-modulated radiotherapy of paraspinal tumors: a preliminary report. *Int J Radiat Oncol Biol Phys*. 2005;62(1):53-61.
19. Constans JP, de Divitiis E, Donzelli R, Spaziante R, Meder JF, Haye C. Spinal metastases with neurological manifestations. Review of 600 cases. *J Neurosurg*. 1983;59(1):111-118.
20. Bracarda S, de Cobelli O, Greco C, et al. Cancer of the prostate. *Crit Rev Oncol Hematol*. 2005;56(3):379-396.
21. National Cancer Institute. SEER cancer statistics factsheets: Prostate cancer. Available at: <http://seer.cancer.gov/statfacts/html/prost.html>. Accessed June 16, 2015.
22. Denmeade SR, Isaacs JT. A history of prostate cancer treatment. *Nat Rev Cancer*. 2002;2(5):389-396.
23. Halabi S, Small EJ, Kantoff PW, et al. Prognostic model for predicting survival in men with hormone-refractory metastatic prostate cancer. *J Clin Oncol*. 2003;21(7):1232-1237.
24. Svatek R, Karakiewicz PI, Shulman M, Karam J, Perrotte P, Benaim E. Pre-treatment nomogram for disease-specific survival of patients with chemotherapy-naïve androgen independent prostate cancer. *Eur Urol*. 2006;49(4):666-674.
25. Tomioka S, Shimbo M, Amiya Y, Nakatsu H, Murakami S, Shimazaki J. Outcome of patients with hormone-refractory prostate cancer: prognostic

- significance of prostate-specific antigen-doubling time and nadir prostate-specific antigen. *Jpn J Clin Oncol*. 2008;38(1):36-42.
26. Townsend MF, Sanders WH, Northway RO, Graham SD Jr. Bone fractures associated with luteinizing hormone-releasing hormone agonists used in the treatment of prostate carcinoma. *Cancer*. 1997;79(3):545-550.
 27. Collinson MP, Tyrrel CJ, Hutton C. Osteoporosis occurring in two patients receiving LHRH analogs for carcinoma of the prostate. *Calcif Tissue Int*. 1994;54(4):327-328.
 28. Charhon SA, Chapuy MC, Delvin EE, Valentin-Opran A, Edouard CM, Meunier PJ. Histomorphometric analysis of sclerotic bone metastases from prostatic carcinoma special reference to osteomalacia. *Cancer*. 1983;51(5):918-924.
 29. Bridwell KH. Treatment of metastatic prostate cancer of the spine. *Urol Clin North Am*. 1991;18(1):153-159.
 30. Omeis IA, Dhir M, Sciubba DM, et al. Postoperative surgical site infections in patients undergoing spinal tumor surgery: incidence and risk factors. *Spine (Phila Pa 1976)*. 2011;36(17):1410-1419.
 31. Laufer I, Hanover A, Lis E, Yamada Y, Bilsky M. Repeat decompression surgery for recurrent spinal metastases. *J Neurosurg Spine*. 2010;13(1):109-115.

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