Patients With Cervical Metastasis and Neoplastic Pachymeningitis are Less Likely to Improve Neurologically After Surgery

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Abstract

Background Although many patients with cervical spine metastases are treated surgically, it is unknown whether certain subsets achieve better pain relief and improvement of neurologic function.

Questions/purposes (1) Does tumor removal with reconstruction improve the neurologic status? (2) Is any subset of patients more likely to have neurological recovery from palliative surgery? (3) What is the rate of surgery-related complications?

Patients and Methods We retrospectively reviewed 46 patients who had palliative surgery for metastatic solid tumor metastases of the subaxial cervical spine. Indications were neurologic deficits, life expectancy longer than 6 months, and a Karnofsky Performance Score of 50 to 70. Surgery consisted of anterior tumor removal and reconstruction with titanium mesh cages and/or tricortical iliac crest allograft plus plate fixation or of a combined procedure

with adjunctive posterior decompression and stabilization with lateral mass screw fixation. Postoperatively, neurologic Frankel score grade, Karnofsky Performance Score, and complications were recorded.

Results Five of 18 nonambulatory patients (Frankel B/C) became ambulatory again (Frankel D). No patients were Frankel Grade E preoperatively, whereas 19 of 46 gained Frankel Grade E after surgery. One patient worsened neurologically and died 4 months after surgery. Patients with neoplastic pachymeningitis had less neurologic recovery than those without. Complications included dural tears (three), wound infection (three), and tumor relapse at the same or an adjacent level (four). Two of these four patients had instrumentation-related complications.

Conclusions Surgery improved clinical and neurologic status according to Frankel score; patients with neoplastic pachymeningitis are likely to experience less neurologic recovery.

Level of Evidence Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that all investigations were conducted in conformity with ethical principles of research.

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Introduction

The spine is the most common site of localization of bone tumor metastases [15], and nearly 5% to 10% of patients with systemic cancer have spinal metastases [34]; moreover, between 30% and 70% of patients with cancer will have spinal metastases at autopsy [18]. Nearly 10% of patients with spinal metastases develop neurologic compromise such as intense pain, sensory loss, weakness, and sphincter dysfunction as a result of either pathologic fractures of the vertebral bodies or direct extension of a tumor mass from the vertebral body directly within the spinal

cord and/or the nerve roots [5, 21]. The treatment of spinal metastasis is typically multidisciplinary, including chemotherapy, radiation, and surgery. Currently, there is a consensus on considering palliation the first choice for patients with a life expectancy of less than 6 months and poor general status [12]. On the other hand, surgery is generally considered reasonable when localized spinal metastasis is the only secondary site and the patient has a tumor with a good prognosis and a life expectancy of greater than 6 months. In these patients, spinal metastasis is treated as one might a primary tumor with complete excision [1, 12, 15]. Surgery can also be considered as palliative care to control pain and to maintain mobility, thus improving the quality [13] of remaining life [26]. Surgery in these patients is associated with an increased number of complications [8], particularly related to the surgical approach, general status of the patient, and to the presence of neurologic deficits. These three factors are also related to overall patient complications and survival [36].

The cervical spine is the least common site of spinal metastasis [6, 33], and relatively little is published about surgery in metastasis to the cervical spine; a recent systematic review on surgical decision-making in cervical spine metastases surgery [16] identified only 13 papers addressing surgery at the subaxial cervical spine, although the authors found relatively more published about the treatment of tumors at the occipitocervical (20 papers) and cervicothoracic (18 papers) junctions. Most data can be derived from papers generically dealing with metastatic lesions at the whole spine [3, 27, 35].

Most surgeons currently recommend that patients with high-grade epidural spinal cord compression from solid tumor metastases undergo decompressive surgery and instrumentation (moderate quality evidence) to improve neurologic function or prevent progression of neurologic deficits [17]. It has also been suggested that patients with segmental kyphosis and collapse involving any region of the cervical spine should have surgery to stabilize the spine [17]. The higher the general health status assessed by the Karnofsky Performance Score, the better will be the

clinical and neurologic recovery [24]. However, it is unclear whether it is possible to predict neurologic recovery after surgical decompression in patients affected by cervical spine metastasis.

We therefore posed three questions: (1) Does tumor removal with reconstruction improve the neurologic status? (2) Is any subset of patients more likely to experienced neurological recovery after surgery than others? (3) What is the rate of surgery-related complications?

Patients and Methods

We retrospectively reviewed 213 patients (96 males and 117 females) with a mean age of 52 (range, 44–78 years) who underwent palliative surgery for spinal metastasis in any location between 1994 and 2008. Of these, 46 patients had a tumor located in the subaxial cervical spine. There were 28 females and 18 males with an average mean age of 63 years (range, 47–73 years). Neck pain or radicular pain was present in all patients before surgery. At the time of review, five of the 46 patients were alive. All other patients but one had died by that time as a result of causes related to the primary neoplasm; in one patient, death was related to postoperative complications. In 12 of 46 patients (26%), no other evidence of extraskelatal metastatic disease (eg, lung or liver) was found before surgery (Table 1). The primary tumors were breast carcinoma (13 patients), renal cell carcinoma (11), gastrointestinal tract carcinoma (eight), lung carcinoma (four), prostate carcinoma (four), thyroid (three), and malignant tumors at other sites (three). Mean postoperative survival time was 27 months (range, 4–52 months). The highest survival rates were seen in patients with renal cell carcinoma (47 months) and breast carcinoma (41 months). The poorest survival rates were seen in patients with lung carcinoma (5.6 months).

The indications for surgery were (1) neurologic deficit; (2) life expectancy longer than 6 months; and (3) a Karnofsky Performance Score [29] of 50 to 70. Patients with brain metastases or Karnofsky Performance Score less

Table 1. Study population characteristics

Primary tumor	Total (N = 46)	Male (N = 18)	Female (N = 28)	Average survival 27 months (4–52 months)
Breast	13	NA	13	41 months (2 still alive)
Lung	4	3	1	5.6 months
Gastrointestinal tract	8	3	5	44 months (1 still alive)
Renal	11	8	3	52 months (1 still alive)
Prostate	4	4	NA	36 months (1 still alive)
Thyroid	3	1	2	32 months
Others	3	1	2	11.1 months

NA = not applicable.

than 50 were not treated surgically. Spinal angiography with tumor embolization was performed in all patients within 24 to 48 hours before surgery to reduce intraoperative blood loss [11, 14]. All patients were operated on by the same surgeon (VD) with a uniform treatment algorithm according to current surgical standards (Fig. 1). Surgery consisted of anterior tumor removal; bone loss reconstruction with titanium mesh cages filled with bone allograft or properly shaped tricortical iliac crest allograft alone stabilized with plate fixation through an anterior approach in 31 patients (Fig. 2A–C); or by combined anterior and posterior procedures with adjunctive posterior decompression and stabilization with lateral mass screws

fixation systems in the remaining 15 patients (Fig. 3A–D). Intraoperative homologous blood was not collected or transfused to avoid possible tumor cell contamination; allogeneic blood was transfused when needed.

Postoperative mobilization was initiated in 24 hours with the use of a cervical collar when compatible with neurologic status of the patient. Not all the patients received the same postoperative protocol, in particular, time and entity of postoperative mobilization were determined by neurologic status and above all stability of the instrumentation construct. Patients with stable constructs had a soft collar, whereas patients with poorer bony anchorage were managed with occipito-chin-cervicothoracic orthoses. Physical

Fig. 1 An algorithm for management of patients with spinal metastases and neurologic deficits is shown. RT = radiotherapy.

Fig. 2A–C (A) A sagittal T2 MRI shows vertebral collapse of C7 and partial involvement of C6 and T1 (arrow) compressing the spinal cord resulting from metastatic biliary tract tumor. (B) Surgery consisted of C7 corpectomy and partial corpectomy of C6 and T1, full spinal cord decompression, and reconstruction with titanium mesh filled with iliac crest allograft and plate fixation, as shown on lateral radiographs. (C) AP radiograph showing vertical alignment of mesh and plate.

Fig. 3A–D (A) A sagittal T1 MRI shows vertebral collapse of C7 (arrow) compressing the spinal cord and posterior compression of the spinal cord at C5–C6 resulting from metastatic melanoma. (B) Surgery consisted of C7 corpectomy and reconstruction with titanium mesh filled with iliac crest allograft and C6–T1 plate fixation plus a

posterior decompression at C5–C6 with posterior C5–C7 instrumentation with lateral mass screw fixation reinforced with C5–C7 interspinous metal wiring (arrows), as shown on AP radiographs. (C) Lateral radiograph showing postoperative sagittal alignment. (D) Lateral radiograph with magnification of instrumentation system.

therapy was performed three times per day and consisted of assisted ambulatory reeducation; in case of patients on bed rest, mobilization of the major joints and respiratory exercises were performed. No patients underwent radiotherapy before surgery. Radiation and chemotherapy were performed after surgery in 39 patients. The remaining seven patients received no additional radiation therapy for various reasons (eg, low radiation therapy response of the neoplasm, poor general health status, or complications) and were treated by chemotherapy ($n = 4$) or hormone therapy alone ($n = 3$).

Postoperatively patients were evaluated in an integrated assessment from both the orthopaedic surgeon and the oncologist. Patients were evaluated 2 weeks after discharge, then 1 month after and each month later. The imaging followup consisted of standard radiographs taken each month and CT scan every 3 months. MRI was performed in case of suspected recurrence of neural involvement. Intraoperative and perioperative complications in this patient population were recorded.

The Karnofsky Performance Score [29] was used to assess the patient's general health; the Frankel score [19] was used for neurologic function. The Karnofsky Performance Score includes individually weighted items to evaluate whether the patient is able to perform normal activities independently or required assistance [29]. The Karnofsky Performance Score calculates functional impairment of the patients. In general, the lower the score, the worse the survival. It gives a score from 0 (dead) to 100% (normal), and patients can be divided into three ranges of classes. In the score from 10 to 40, patients are unable to care for themselves and require the equivalent of institutional or

hospital care. Patients with scores ranging from 50 to 70 are usually able to work and live at home. These patients can care for most personal needs but could require varying amounts of assistance. Patients above the score of 70 are able to carry on normal activity and to work and do not require special care. According to the Frankel score, a complete lesion (paraplegia) was classified as Frankel A, presence of only sensory function as Frankel B, motor function present but of no practical use (nonambulatory) as Frankel C, motor function present and sufficient to allow walking (ambulatory) as Frankel D, and no neurologic signs or symptoms as Frankel E. Patients were further divided depending on the presence or absence intraoperatively of neoplastic pachymeningitis as evident from surgical reports; obtained results were correlated to neurologic recovery and analyzed to ascertain which patients could benefit more from surgery.

Descriptive statistics were calculated. The unpaired t test was used to compare preoperative and postoperative values in regard to Karnofsky Performance Score. The chi square test was performed to compare preoperative and postoperative-reported data in relation to Frankel score. An additional chi square test was used for evaluation of intergroup difference (presence or not of neoplastic pachymeningitis) in incidence of neurologic improvement. Statistical analysis was performed with the SPSS software package, Version 11.0 (SPSS, Chicago, IL).

Results

The mean Karnofsky Performance Score did not change ($p = 0.078$) from pre- to postoperatively (65% and 73%,

Table 2. Pre- and postoperative Frankel score

	Frankel score					Total patients
	A	B	C	D	E	
Preoperative	2	5	13	26	–	46
Postoperative						
A	1				–	1
B	1	2	1		–	4
C		2	8		–	10
D		1	4	7	–	12
E				19	–	19

Table 3. Perioperative complications

Type of complications	Patients (N = 46)
Dural tears	3
Wound infection	2
Instrumentation related complications	2*
Recurrent disease at the same or adjacent level	4
Neurologic worsening and death	1

* These two patients belong to the recurrent disease group.

respectively). Patients experienced improved neurologic status compared with the preoperative condition (chi square = 24.9; $p < 0.001$) (Table 2). Five of 18 (27.8%) nonambulatory patients (Frankel B/C) became ambulatory again (Frankel D). No patients (according to inclusion criteria) were Frankel Grade E preoperatively, whereas 19 of 46 gained Frankel Grade E after surgery.

Patients with intraoperative findings of neoplastic pachymeningitis had less (chi square = 34.73; $df = 1$; $p < 0.001$) neurologic recovery compared with the others. Two of the 21 patients with intraoperative findings of neoplastic meningitis improved postoperatively, whereas all but one patient without pachymeningitis improved.

Perioperative complications occurred in 10 of 46 patients (Table 3). There was one surgically related postoperative death; this patient developed an acute ischemic lesion at the spinal cord as confirmed by a contrast-enhanced MRI, and the patient began to deteriorate neurologically after 24 hours. The patient developed quadriplegia and eventually died of respiratory failure 4 months after surgery. Dural tears occurred intraoperatively in three patients and were treated by direct surgical repair. Two patients had superficial wound infections that resolved with intravenous antibiotic therapy alone. In four patients, newer tumor growth at the same or at an adjacent level occurred. In these, local tumor recurrence was associated with brain or other site metastases and worsening of overall prognosis. Two of those four patients experienced

some instrumentation failure (plate mobilization and screw pullout). No revision surgery was performed in either case as a result of poor general conditions. Treatment consisted of external bracing and radiotherapy and/or chemotherapy.

Discussion

Few papers address surgery for metastasis exclusively at the cervical spine [3, 27, 35]. Surgery in these patients is usually associated with an increased number of complications related to the surgical approach, general status of the patient, and presence of neurologic deficits, factors that could also lead to reduced survival [26, 36]. Patients with normal neurologic function at admission have a higher rate of survival with respect to those with Frankel Grades A to D [26]. However, it is unclear whether it is possible to predict neurologic recovery after surgical decompression in patients affected by cervical spine metastasis [7]. We therefore posed three questions: (1) Does tumor removal with reconstruction improve the neurologic status? (2) Is any subset of patients more likely to experience neurological recovery after surgery than others? (3) What is the rate of surgery-related complications?

We recognize some limitations in our study. First, this is a retrospective study, and the lack of prospective data recall did not allow us to identify precise risk factors (ie, role of adjuvant therapies, timing of decompressive surgery) related to surgery except for neoplastic pachymeningitis. Second, with the available data, we could not explore any correlation between the timing of surgery and neurologic improvement or between tumor histology and neurologic status of the patient after surgery. Nonetheless, this group represents one of the largest series of patients with cervical spine metastases.

Our observations confirm those from the literature suggesting tumor removal with reconstruction improves neurologic status and an increased rate of surgery-related complications with respect to surgery performed in non-neoplastic patients. In the presence of neurologic deficits, palliative surgery represents the best option to improve recovery. In a trial on 121 patients affected by spinal metastasis with spinal cord compression, and treated with surgery plus radiotherapy or radiotherapy alone [31], surgery resulted in better maintenance of bladder continence, muscle strength, functional ability, and survival compared with radiotherapy alone. In the study by Shehadi et al., cervical involvement was reported in 15 of 87 patients [32], but data were not available for the separate spinal segments. In that study, the majority of patients (85%) maintained or improved the Frankel score from preoperatively to up to 1 year after surgery. In the study by Bilsky et al. [4] on 41 patients affected by metastatic (33) and

primary tumors (eight) located at the cervical spine, neurologic recovery was dependent on preoperative neurologic picture, and patients with more severe deficits improved less after surgery. Preoperative neurologic status is also related to overall survival [26]; in particular, normal neurologic function at admission predicts higher survival and patients with Frankel Grade E at admission have a higher median survival compared with those with Frankel Grades A to D. Hosono et al. also showed a correlation between patient preoperative neurologic status or prognosis and survival [25].

Nonetheless, not all patients tend to recover neurologically in the same fashion after palliative surgery when affected by metastatic epidural spinal cord compression [7, 23]. In general, metastatic epidural spinal cord compression can occur acutely after vertebral collapse or slowly after impairment of venous drainage leading to intramedullary vasogenic edema and eventually irreversible spinal cord necrosis. This latter condition is related to the presence of a reactive inflammatory-like tissue called neoplastic pachymeningitis [8]. We found the presence of such peridural tissue was related to less neurologic improvement with only two of 21 patients improving postoperatively. Our observations are consistent with those of Chaichana et al. [7] who found in a study on 162 patients that patients with neurologic injury and without vertebral body fracture tended to be less likely to regain ambulation postoperatively. These data could help guide monitoring and treatment paradigms for patients with primary cancer and help predict neurologic improvement after palliative surgical decompression.

Palliative surgery in patients affected by spinal metastasis is also related to an increased rate of complications with respect to surgery in nonneoplastic patients. This can be directly related to the surgical approach (wound infections, cerebrospinal fluid leaks, and fistulae) and to the use of spinal instrumentation [2] (breakage, mobilization, and migration) as well as medical and neurologic complications (ie, pneumonias worsening or new neurologic deficits) [9, 10, 28]. In our previous report on 73 patients affected by cervical spine metastasis with a poor prognosis and treated either nonoperatively or surgically [9], seven patients developed infection at the surgical site (one with dehiscence at the surgical wound related to adjuvant radiotherapy), nine patients had neurologic deterioration postoperatively, and 13 died of causes related to the primary disease within 6 months after surgery. In the study of Bilsky et al. [4], complications occurred in 10 of 41 patients (24.4%). One patient developed bilateral vocal cord paralysis undergoing an extended exposure at the C6–C7 level, eventually requiring tracheostomy and gastrostomy. Another patient developed unilateral recurrent laryngeal nerve palsy. Preoperative irradiation determined adhesions of the pharynx that could not be mobilized from

the spine; in both cases, the anterior approach was suspended and tumors were then excised through a posterolateral approach. Cerebrospinal fluid leak occurred in a patient with intradural tumor extension. Medical complications (ie, deep venous thrombosis and two pneumonia) also occurred in four patients. Three of our patients experienced instrumentation failure after an anterior approach and underwent revision surgery with a combined AP approach. Several factors can contribute to an increased risk of intra- or postoperative complications. Among these, radiotherapy in the week before surgery, malnutrition, and chronic use of steroids are acknowledged [22, 30]. Because patients with tumors at the cervical spine usually have poor general health status, with clinical pictures difficult to standardize, the surgeon should work hard to decrease the incidence of the most common complications.

Most of our patients improved clinically and neurologically after surgery, although those with neoplastic pachymeningitis were less likely to improve neurologically after surgery. Prospective multicentric cohort studies are required to confirm these findings and identify prognostic factors. Neoplastic pachymeningitis can be suspected preoperatively by the use of current imaging modalities such as contrast-enhanced MRI [20] and by medical history of a slowly progressive neurological impairment in absence of vertebral collapse [23], but both the surgeon and the patient should be aware that the diagnosis is more often performed intraoperatively. Appropriate statements about the risk of neurologic worsening or absence of recovery could be added to the informed consent and improve patient awareness of complications related to palliative surgical decompression.

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References

1. Asdourian PL, Weidenbaum M, DeWald RL, Hammerberg KW, Ramsey RG. The pattern of vertebral involvement in metastatic vertebral breast cancer. *Clin Orthop Relat Res*. 1990;250:164–170.
2. Bauer HC. Posterior decompression and stabilization for spinal metastases. Analysis of sixty-seven consecutive patients. *J Bone Joint Surg Am*. 1997;79:514–522.
3. Bauer HC, Wedin R. Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. *Acta Orthop Scand*. 1995;66:143–146.
4. Bilsky MH, Boakye M, Collignon F, Kraus D, Boland P. Operative management of metastatic and malignant primary subaxial cervical tumors. *J Neurosurg Spine*. 2005;2:256–264.
5. Brihaye J, Ectors P, Lemort M, Van Houtte P. The management of spinal epidural metastases. *Adv Tech Stand Neurosurg*. 1988;16:121–176.
6. Campanacci M. Metastatic bone disease. In: Campanacci M, ed. *Bone and Soft Tissue Tumors*. New York, NY: Springer-Verlag; 1999.

7. Chaichana KL, Pendleton C, Wolinsky JP, Gokaslan ZL, Sciubba DM. Vertebral compression fractures in patients presenting with metastatic epidural spinal cord compression. *Neurosurgery*. 2009;65:267–274.
8. Denaro L, Di Martino A, Longo U, Denaro V. Cervical spine bone tumor surgery. In: Denaro L, D'Avella D, Denaro V, eds. *Pitfalls in Cervical Spine Surgery (Avoidance and Management of Complications)*. Heidelberg, Germany: Springer; 2010.
9. Denaro V. Treatment of metastasis and systemic tumors of the cervical spine. *Neuro-Orthopedics*. 1988;6:101–110.
10. Denaro V, ed. *Stenosis of the Cervical Spine: Causes, Diagnosis and Treatment*. Berlin, Germany: Springer; 1991.
11. Denaro V, Denaro L, Papalia R, Marinuzzi A, Di Martino A. Surgical management of cervical spine osteoblastomas. *Clin Orthop Relat Res*. 2007;455:190–195.
12. Denaro V, Di Martino A. The role of orthopaedic surgery in bone metastases: Guidelines, Italian Society of Medical Oncology (AIOM) 2008. In: Santini D, ed. *Treatment of Bone Metastases* [in Italian]. Como, Italy: Tecnografica Edizioni Lomazzo; 2009.
13. Denaro V, Di Martino A, Ippolito M, Papalia R. Surgical team in the management of bone metastasis. *Supp Pall Cancer Care*. 2006;2(Suppl):17–23.
14. Di Martino A, Vincenzi B, Denaro L, Barnaba SA, Papalia R, Santini D, Tonini G, Denaro V. 'Internal bracing' surgery in the management of solid tumor metastases of the thoracic and lumbar spine. *Oncol Rep*. 2009;21:431–435.
15. Durr HR, Maier M, Pfahler M, Baur A, Refior HJ. Surgical treatment of osseous metastases in patients with renal cell carcinoma. *Clin Orthop Relat Res*. 1999;367:283–290.
16. Fehlings MG, David KS, Vialle L, Vialle E, Setzer M, Vronis FD. Decision making in the surgical treatment of cervical spine metastases. *Spine*. 2009;34:S108–S117.
17. Fisher CG, Andersson GB, Weinstein JN. Spine focus issue. Summary of management recommendations in spine oncology. *Spine*. 2009;34:S2–S6.
18. Fornasier VL, Horne JG. Metastases to the vertebral column. *Cancer*. 1975;36:590–594.
19. Frankel HL, Hancock DO, Hyslop G, Melzak J, Michaelis LS, Ungar GH, Vernon JD, Walsh JJ. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. I. *Paraplegia*. 1969;7:179–192.
20. Fukui MB, Meltzer CC, Kanal E, Smirniotopoulos JG. MR imaging of the meninges. Part II. Neoplastic disease. *Radiology*. 1996;201:605–612.
21. Galasko CS. Spinal instability secondary to metastatic cancer. *J Bone Joint Surg Br*. 1991;73:104–108.
22. Ghogawala Z, Mansfield FL, Borges LF. Spinal radiation before surgical decompression adversely affects outcomes of surgery for symptomatic metastatic spinal cord compression. *Spine*. 2001;26:818–824.
23. Hamamoto Y, Kataoka M, Senba T, Uwatsu K, Sugawara Y, Inoue T, Sakai S, Aono S, Takahashi T, Oda S. Vertebral metastases with high risk of symptomatic malignant spinal cord compression. *Jpn J Clin Oncol*. 2009;39:431–434.
24. Heidecke V, Rainov NG, Burkert W. Results and outcome of neurosurgical treatment for extradural metastases in the cervical spine. *Acta Neurochir (Wien)*. 2003;145:873–880.
25. Hosono N, Ueda T, Tamura D, Aoki Y, Yoshikawa H. Prognostic relevance of clinical symptoms in patients with spinal metastases. *Clin Orthop Relat Res*. 2005;436:196–201.
26. Ibrahim A, Crockard A, Antonietti P, Boriani S, Bunger C, Gasbarrini A, Grejs A, Harms J, Kawahara N, Mazel C, Melcher R, Tomita K. Does spinal surgery improve the quality of life for those with extradural (spinal) osseous metastases? An international multicenter prospective observational study of 223 patients. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2007. *J Neurosurg Spine*. 2008;8:271–278.
27. Kocalkowski S, Webb J. Metastatic spinal tumours: survival after surgery. *Eur Spine J*. 1992:43–48.
28. Li H, Gasbarrini A, Cappuccio M, Terzi S, Paderni S, Mirabile L, Boriani S. Outcome of excisional surgeries for the patients with spinal metastases. *Eur Spine J*. 2009;18:1423–1430.
29. MacLeod CM. Evaluation of chemotherapeutic agents. In: Karnofsky DA, Burchenal JH, eds. *The Clinical Evaluation of Chemotherapeutic Agents in Cancer*. New York, NY: Columbia University Press; 1949.
30. McPhee IB, Williams RP, Swanson CE. Factors influencing wound healing after surgery for metastatic disease of the spine. *Spine*. 1998;23:726–732.
31. Patchell RA, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, Mohiuddin M, Young B. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet*. 2005;366:643–648.
32. Shehadi JA, Sciubba DM, Suk I, Suki D, Maldaun MV, McCutcheon IE, Nader R, Theriault R, Rhines LD, Gokaslan ZL. Surgical treatment strategies and outcome in patients with breast cancer metastatic to the spine: a review of 87 patients. *Eur Spine J*. 2007;16:1179–1192.
33. Suen KC, Lau LL, Yermakov V. Cancer and old age. An autopsy study of 3,535 patients over 65 years old. *Cancer*. 1974;33:1164–1168.
34. Sundaresan N, Digiacinto GV, Hughes JE. Surgical treatment of spinal metastases. *Clin Neurosurg*. 1986;33:503–522.
35. Weigel B, Maghsudi M, Neumann C, Kretschmer R, Muller FJ, Nerlich M. Surgical management of symptomatic spinal metastases. Postoperative outcome and quality of life. *Spine*. 1999;24:2240–2246.
36. Wise JJ, Fischgrund JS, Herkowitz HN, Montgomery D, Kurz LT. Complication, survival rates, and risk factors of surgery for metastatic disease of the spine. *Spine*. 1999;24:1943–1951.