Predictors of Ambulatory Function after Decompressive Surgery for Metastatic Epidural Spinal Cord Compression

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Received, June 1, 2007.
Accepted, December 14, 2007.

OBJECTIVE: Metastatic epidural spinal cord compression (MESCC) is a relatively common and debilitating complication of metastatic disease that often results in neurological deficits. This study was designed to explore associations with maintaining and regaining ambulatory function after decompressive surgery for MESCC.

METHODS: Seventy-eight patients undergoing decompressive surgery for MESCC at an academic tertiary care institution between 1995 and 2005 were retrospectively reviewed. Fisher's exact analysis was used to compare preoperative ambulatory and nonambulatory patients. Multivariate Cox proportional hazards regression was used to identify associations with either maintaining or regaining the ability to walk.

RESULTS: Patients were followed for 7.1 ± 1.6 (mean ± standard deviation) months after surgery. Preoperative nonambulatory patients required more extensive surgery (increased operative spinal levels and number of laminectomies) and had more surgical site complications (wound dehiscences and cerebrospinal fluid leaks) compared with preoperative ambulatory patients. From the multivariate analysis, preoperative ability to walk (relative risk [RR], 2.320; 95% confidence interval [CI], 1.301–4.416; $P < 0.01$) independently increased the likelihood of ambulation at the last follow-up evaluation 2.3-fold. Pathological vertebral compression fracture at presentation (RR, 0.471; 95% CI, 0.235–0.864; $P = 0.01$) independently decreased the likelihood of ambulation at the time of the last follow-up evaluation 2.1-fold. For patients unable to walk at the time of surgery, preoperative radiation therapy (RR, 0.406; 95% CI, 0.124–0.927; $P = 0.03$) decreased the likelihood of regaining the ability to walk 2.5-fold. Symptoms present for less than 48 hours (RR, 2.925; 95% CI, 1.133–2.925; $P = 0.02$) and postoperative radiotherapy (RR, 2.595; 95% CI, 1.039–8.796; $P = 0.04$) independently increased the likelihood of regaining ambulatory ability 2.9- and 2.6-fold, respectively, by the time of last follow-up evaluation.

CONCLUSION: The identification of these associations with neurological outcome may help guide in the preservation or return of ambulation after surgery for patients with MESCC.

KEY WORDS: Metastatic spine tumors, Outcome, Predictors, Walking

Neurosurgery 62:683–692, 2008 DOI: 10.1227/01.NEU.0000297122.00442.79 www.neurosurgery-online.com

In the United States, there are approximately 500,000 deaths attributable to metastatic disease each year (3). Among osseous sites, the spinal column represents the most common location for metastatic deposits (1). Metastatic epidural spinal cord compression (MESCC) is a debilitating subgroup of these spinal metastases and eventually affects 5 to 10% of patients with cancer (6, 17, 40). These lesions invade the epidural space and compress the spinal cord from its normal position, often leading to paralysis (9, 14, 30).

Treatment for MESCC has historically consisted of corticosteroids and radiotherapy (9, 30). Corticosteroids are believed to delay neurological deterioration by decreasing spinal cord edema and may also have an oncolytic effect on certain tumors, including lymphoma and multiple myeloma (27). Radiotherapy has been shown to be as efficacious as decompressive laminectomy in preserving neurological function and pain control in several retrospective studies (7, 14, 18, 43). However, with recent advances in surgical techniques, neuroimaging, and equipment, direct decompressive surgery has become the standard treatment for metastatic lesions from solid primary tumors (26, 35). In fact, this approach has recently been shown to be superior to radiotherapy in preserving neurological function for metastatic spine tumors that are not significantly radiosensitive (35).

This study was designed to explore associations with maintaining and regaining ambulatory function after decompressive surgery for MESCC. Understanding these factors could promote the development of new therapeutic and surgical strategies as well as aid in clinical decision-making for these relatively common lesions.

PATIENTS AND METHODS

Patient Selection

All patients undergoing surgery for MESCC at an academic tertiary care institution between 1995 and 2005 were retrospectively reviewed. This included a total of 98 patients. Patients at least 18 years old with a tissue-proven diagnosis of solid primary tumor (not of central nervous system origin) and magnetic resonance imaging (MRI) evidence of spinal cord displacement from its normal position in the spinal canal by an epidural mass were eligible for inclusion in this study. The MESCC had to be restricted to a single area, which may include contiguous spinal levels. Patients with multiple, discrete compressive lesions were excluded. Additionally, patients with certain radiosensitive tumors (lymphomas, leukemias, multiple myeloma, and germ-cell tumors), as well as concomitant brain metastases or cauda equina or spinal root compression, were excluded.

The general aim of surgery was to circumferentially decompress the spinal cord, where the approach was dependent on the location of the tumor and the patient's circumstances. An anterior approach was defined as approaching the spine through the vertebral body. A posterior approach was defined as approaching the spine through the posterior elements. In some cases with multidirectional compression, a combined anteroposterior approach was used.

Information recorded for each patient included demographics, clinical presentation, comorbidities, medications prescribed and administered before the day of surgery, preoperative MRI findings, intraoperative recordings including somatosensory evoked potential/motor evoked potential monitoring changes, pathological findings, and postoperative neurological function. Mechanical pain was patient-reported pain that worsened with movement. Radicular pain was pain that followed a dermatomal distribution. Local pain was back pain confined to the region of the spine affected by metastatic disease and did not include diffuse, nonlocalized pain. Sensory deficits were defined as having sensory losses to light touch, temperature, and/or pain confined to a spinal level and/or a nerve root distribution. Patients with multiple presenting symptoms were categorized according to all the symptoms they possessed. Serum glucose, which has been shown to be associated with neurological outcomes (24, 36, 38), was measured on the day before surgery (OD-1), on the day of surgery (OD), and on postoperative Day 1 (OD+1). Serum glucose on OD and OD+1 was measured under fasting conditions. On neuroimaging, a pathological vertebral compression fracture was defined as collapse of the vertebral body secondary to tumor involvement. The direction of compression was defined as the location in which the spinal cord was compressed from its normal position in the spinal canal. The extent of resection (gross total versus subtotal) was determined by evaluating pre- and postoperative MRI scans. Gross total resection was defined as no evidence of residual tumor on postoperative MRI scan. Additionally, spinal recurrence was defined as local recurrence directly adjacent to the resected lesion. Perioperative mortality was defined as death within 30 days of surgery.

Ambulatory Status

The patient's ability to walk at the time of the last follow-up evaluation, even if a cane or walker was needed, was used as the primary endpoint to minimize observer bias and errors associated with retrospective patient classification (35). This endpoint has also been demonstrated to be a critical quality of life indicator, and accurate assessment of this basic functional measurement was uniformly included in all clinical documentation (23). The ability to walk at the time of the last follow-up evaluation included both patients who maintained their preoperative ambulatory status and those who regained the ability to walk postoperatively. Patients who regained the ability to walk are those who were unable to walk preoperatively but could walk at the time of the last follow-up evaluation. Other variables known to affect outcome after MESCC resection were included in the data set and analysis.

Statistical Analysis

Summary data were presented as mean ± standard deviation for parametric data and as median (interquartile range) for nonparametric data. Percentages were compared by Fisher's exact test, and P values less than 0.05 were considered significant. For intergroup comparison, Student's t test was used for parametric data and the Mann-Whitney U test for nonparametric data. Additionally, to identify independent predictors of the ability to walk at the time of the last follow-up evaluation, univariate analysis (JMP 6; SAS Institute, Cary, NC) was first performed to evaluate associations between radiographic, preoperative, operative, and pathological variables and postoperative ambulatory status at the time of the last follow-up evaluation. Variables associated with postoperative ambulatory status ($P < 0.10$) in univariate analysis were then included in a stepwise multivariate Cox proportional hazards regression model (2). Variables in the multivariate analysis with P values less than 0.05 were considered significant (JMP 6). This same model was used to identify independent associations with regaining the ability to walk at the time of the last follow-up evaluation.

RESULTS

Patient Population

The cohort summary data, as well as the comparison between the preoperative ambulatory and nonambulatory patients, are outlined in *Table 1*. Seventy-eight of the original 98 patients met the inclusion/exclusion criteria for this study during the reviewed period. Forty-six (59%) were male, and the mean age at the time of surgery was 56 ± 13 years. Sixty-two (79%) patients presented with pain. Of these, eight (10%), 22 (28%), and 32 (41%) presented with mechanical, local, and radicular pain, respectively. Fifty-four (69%) presented with motor symptoms, 21 (27%) with sensory symptoms, and six (8%) with bowel/bladder incontinence. Twenty-three (29%) patients were unable to walk before surgery. This was secondary to motor weakness in 20 and intractable pain in three. The

TABLE 1. Summary of preoperative characteristics in 78 patients with metastatic epidural spinal cord compression, 55 patients who were able to ambulate preoperatively, and 23 patients who were unable to ambulate preoperatively[a]

Characteristics	Ambulatory preoperatively (%)	Nonambulatory preoperatively (%)	P value
Sex			
Male	30 (55)	16 (70)	0.22
Female	25 (45)	7 (30)	0.22
Age (mean ± standard deviation)	55.7 ± 14.1	57.3 ± 9.3	0.67
Comorbidities			
Smoker	12 (22)	10 (43)	0.07
DM	8 (15)	2 (9)	0.48
CAD	5 (9)	3 (13)	0.60
COPD	2 (4)	1 (4)	0.88
Presenting symptoms			
Pain			
Mechanical	5 (9)	3 (13)	0.60
Local	14 (24)	8 (35)	0.40
Radicular	28 (51)	4 (17)	<0.01
Motor	32 (58)	22 (96)	<0.01
Sensory	13 (24)	8 (35)	0.31
Bowel/bladder incontinence	5 (9)	1 (4)	0.47
Previous treatment			
Previous resection	4 (7)	1 (4)	0.63
Radiation	32 (58)	11 (49)	0.40
Chemotherapy	25 (45)	8 (3)	0.38
Preoperative steroids	19 (35)	10 (43)	0.46
Primary tumor			
Lung	12 (22)	7 (30)	0.42
Breast	10 (18)	3 (13)	0.58
Prostate	11 (20)	4 (17)	0.79
Renal	9 (16)	1 (4)	0.15
Thyroid	2 (4)	1 (4)	0.88
Gastrointestinal	3 (5)	1 (4)	0.84
Sarcoma	3 (5)	3 (13)	0.25
Other	5 (9)	3 (13)	0.60
Radiographics			
Anterior compression	33 (60)	10 (43)	0.18
Lateral compression	10 (18)	5 (22)	0.72
Posterior compression	8 (15)	7 (30)	0.10
Anterolateral compression	3 (5)	1 (4)	0.84
Circumferential compression	1 (2)	0 (0)	0.52
Spinal cord location			
Cervical	13 (24)	2 (9)	0.13
Cervicothoracic	5 (9)	0 (0)	0.14
Thoracic	33 (60)	19 (83)	0.05
Thoracolumbar	3 (5)	3 (13)	0.25
Lumbar	16 (29)	5 (22)	0.50
Pathological compression fracture	13 (24)	12 (52)	0.06
Extracranial extraspinal metastases	23 (42)	13 (57)	0.23

[a] DM, diabetes mellitus; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.

median (interquartile range) duration of symptoms was 0.8 (0.2–2) months.

The pathological findings of the primary tumors are also described in *Table 1*. The most frequent primary tumor location was the lung in 19 (24%), breast in 13 (17%), prostate in 15 (19%), and kidney in 10 (13%). Other sources included thyroid, gastrointestinal, sarcoma, melanoma, and nonrenal genitourinary system. The spinal cord was primarily compressed anteriorly in 43 (55%) patients, laterally in 15 (19%), posteriorly in 15 (19%), anterolaterally in four (5%), and circumferentially in one (1%). The tumor had a cervical component in 15 (19%) patients, thoracic in 52 (67%), and lumbar in 21 (27%). Twenty-five (32%) patients had radiographic evidence of a pathological compression fracture of the vertebral body. Additionally, 36 (46%) had extracranial, extraspinal metastases at the time of presentation.

Preoperative Ambulatory and Nonambulatory Comparison

The results of the Fisher's exact test between preoperative ambulatory and nonambulatory patients are summarized in *Tables 1* and 2. For preoperative variables, patients who were nonambulatory more commonly presented with motor weakness ($P < 0.01$), as would be expected. Preoperative ambulatory patients, however, more commonly presented with signs of radicular pain ($P < 0.01$). Interestingly, preoperative nonambulatory patients, as compared with ambulatory patients, required surgery on more spinal levels ($P < 0.01$), more commonly underwent posterior approaches to their tumor ($P < 0.01$), and subsequently underwent more laminectomies ($P < 0.01$). Additionally, nonambulatory patients incurred more surgery-related, postoperative complications, namely, wound dehiscences ($P = 0.04$) and cerebrospinal fluid leaks ($P < 0.01$). Patients who were able to walk preoperatively more frequently underwent anterior approaches ($P = 0.03$) and spinal fusion ($P < 0.01$) compared with patients who were nonambulatory ($P < 0.01$). No other clinical, imaging, operative, or pathological variables were found to be significantly different between the two cohorts.

Surgical Outcomes

The outcomes after surgery for all patients with MESCC, and the comparison between the preoperative ambulatory and nonambulatory patients, are outlined in *Table 2*. Eight (10%) had gross total resection of their lesion and 62 (79%) underwent spinal fusion. Two (3%) patients died during the perioperative period. This was secondary to a pulmonary embolism in one patient and myocardial infarction in the other patient. Additionally, four (5%) developed wound dehiscence, three (4%) developed postoperative cerebrospinal fluid leak, one (1%) incurred a retroperitoneal hemorrhage, and one (1%) had a pseudomeningocele. Postoperatively, nine (12%), 21 (27%), and 17 (22%) had additional surgery, radiation therapy, and chemotherapy, respectively.

The mean follow-up period was 7.1 ± 1.6 months. After surgical resection, 61 (78%) patients were able to ambulate at their

TABLE 2. Summary of long-term operative outcomes in 78 total patients with metastatic epidural spinal cord compression, 55 patients who were able to ambulate preoperatively, and 23 patients who were unable to ambulate preoperatively[a]

Outcome	Ambulatory preoperatively (%)	Nonambulatory preoperatively (%)	*P* value
Operative			
Anterior approach	24 (44)	4 (17)	0.03
Posterior approach	24 (44)	19 (83)	<0.01
Anteroposterior approach	7 (13)	0 (0)	0.07
Greater than two spinal levels	16 (29)	16 (70)	<0.01
Greater than two laminectomies	13 (24)	16 (70)	<0.01
Monitoring change	2 (4)	0 (0)	0.35
Fusion	48 (87)	14 (61)	<0.01
Gross total resection	7 (13)	1 (4)	0.27
Complications			
Perioperative mortality	1 (2)	1 (4)	0.52
Wound dehiscence	1 (2)	3 (13)	0.04
Cerebrospinal fluid leak	0 (0)	3 (13)	<0.01
Retroperitoneal hemorrhage	1 (2)	0 (0)	0.52
Pseudomeningocele	1 (2)	0 (0)	0.52
Postoperative treatment			
Additional operations	8 (15)	1 (4)	0.20
Radiation therapy	15 (27)	6 (26)	0.91
Chemotherapy	15 (27)	2 (9)	0.07
Spinal recurrence	8 (15)	2 (9)	0.48
Ambulatory outcome			
Ambulate preoperatively	55 (100)	0 (0)	N/A
Ambulate postoperatively	49 (89)	12 (52)	N/A
Maintained ambulation	49 (89)	N/A	N/A
Regained ambulation	N/A	12 (52)	N/A
Lost the ability to walk	6 (11)	N/A	N/A

[a] N/A, not applicable.

last follow-up examination. Of the 55 patients able to ambulate before surgery, 49 (89%) maintained the ability to walk and six (11%) lost the ability to walk postoperatively. This loss of ambulatory status was the result of disease progression in all six patients, of whom five developed motor weakness and one developed intractable pain preventing the ability to walk. Of the 23 patients unable to walk before surgery, 12 (52%) regained the ability to walk. The 11 patients who did not recover remained nonambulatory secondary to motor weakness.

Predictors of Postoperative Ambulatory Ability

In univariate analysis, radicular pain, motor symptoms, preoperative ability to walk, vertebral compression/wedge fracture, preoperative glucose level greater than 180, tumor involving more than two spinal levels, intraoperative monitoring change, and follow-up chemotherapy were associated with the ability to walk at the time of the last follow-up evaluation (*Table 3*). No other clinical, imaging, operative, or pathological variables were found to be associated with postoperative ambulatory ability in this data set.

In multivariate analysis, preoperative ability to walk (relative risk [RR], 2.320; 95% confidence interval [CI], 1.301–4.416; $P < 0.01$) and pathological compression fracture of the vertebral body (RR, 0.471; 95% CI, 0.235–0.864; $P = 0.01$) were found to be independently associated with ambulatory status at the time of the last follow-up evaluation (*Table 4*). Of note, preoperative serum glucose level greater than 180 (RR, 0.562; 95% CI, 0.300–1.072; $P = 0.08$) and follow-up chemotherapy (RR, 2.326; 95% CI, 0.951–10.218; $P = 0.07$) trended toward significance. Patients with preoperative ambulatory function were 2.3-fold more likely to maintain the ability to walk after decompressive surgery. In addition, preoperative imaging showing compressive fracture as well as epidural compression of the thecal sac and/or spinal cord was associated with a 2.1-fold decreased likelihood of walking after decompressive surgery. Among those who were unable to walk at the time of their last follow-up evaluation, five (23%) had serum glucose levels greater than 180, with none of these patients having diabetes and only one being administered preoperative steroids.

Predictors of Regaining Ambulatory Ability

In univariate analyses, preoperative radiotherapy, duration of symptoms for less than 48 hours, metastatic prostate tumor, thoracic component, and follow-up radiation were associated with regaining the ability to walk by the time of the last follow-up evaluation (*Table 5*). No other clinical, imaging, operative, or pathological variables were found to be associated with postoperative ambulatory ability in this data set.

In multivariate analysis, preoperative radiotherapy (RR, 0.406; 95% CI, 0.124–0.927; $P = 0.03$), duration of symptoms less than 48 hours (RR, 2.925; 95% CI, 1.133–2.925; $P = 0.02$), and postoperative radiation therapy (RR, 2.595; 95% CI, 1.039–8.796; $P = 0.04$) (*Table 6*) independently predicted regaining the ability to walk by the time of the last follow-up evaluation. Of note, the thoracic location of the metastatic tumor trended toward being negatively associated with the ability to regain ambulatory ability (RR, 0.003; 95% CI, 0.001–1.113; $P = 0.07$) but did not reach significance. Patients receiving preoperative radiation therapy were more than two times less likely to regain ambulatory function at their last follow-up evaluation. However, postoperative radiation was independently associated with an approximate threefold increased likelihood of recovering ambulatory ability after decompressive surgery. Finally, patients with symptoms for less than 48 hours before surgery were almost three times less likely to regain ambulatory function by the time of their last follow-up evaluation. Patients who regained the ability to walk had symptoms present for an average 18 ± 18 days, whereas patients who failed to regain the ability to walk had symptoms for an average of 48 ± 54 days.

TABLE 3. Univariate associations with the ability to walk after resection of metastatic epidural spinal cord compression[a]

Variable	Univariate relative risk (95% CI)	*P* value
Age older than 70 yr	1.013 (0.975–1.057)	0.53
Female	1.391 (0.823–2.628)	0.23
Comorbidities		
Smoker	1.027 (0.605–1.945)	0.93
Diabetes	0.775 (0.436–1.626)	0.46
Coronary artery disease	0.537 (0.308–1.431)	0.20
COPD	0.645 (0.280–2.771)	0.46
Preoperative symptoms		
Time: symptom to surgery	0.944 (0.718–1.038)	0.39
Pain		
Mechanical pain	1.072 (0.561–2.717)	0.85
Radicular pain	2.371 (1.247–5.994)	<0.01
Local pain	1.002 (0.590–1.901)	0.99
Sensory	0.970 (0.582–1.733)	0.91
Motor	0.534 (0.211–1.013)	0.05
Bowel/bladder incontinence	0.633 (0.324–1.615)	0.29
Ability to walk	2.307 (1.414–3.948)	<0.01
Preoperative steroids	0.949 (0.583–1.622)	0.84
Preoperative treatments		
Chemotherapy	1.143 (0.696–1.961)	0.60
Radiotherapy	0.876 (0.519–1.446)	0.61
Surgical resection	1.085 (0.486–4.618)	0.87
Primary tumor		
Lung	1.829 (0.817–7.796)	0.17
Breast	0.980 (0.551–2.071)	0.95
Prostate	0.681 (0.410–1.214)	0.18
Renal	0.926 (0.486–2.343)	0.84
Thyroid	0.779 (0.347–3.320)	0.65
Gastrointestinal	0.488 (0.214–2.088)	0.26
Radiographics		
Direction of compression		
Anterior location	1.206 (0.730–2.029)	0.46
Lateral location	0.876 (0.526–1.567)	0.63
Posterior location	0.918 (0.538–1.744)	0.77
Spinal cord location		
Cervical	1.344 (0.704–3.409)	0.41
Thoracic	0.632 (0.302–1.119)	0.12
Thoracolumbar	1.039 (0.462–4.431)	0.94
Lumbar	1.697 (0.896–4.285)	0.11
Pathological compression fracture	0.523 (0.314–0.848)	<0.01
Extracranial extraspinal metastases	0.943 (0.573–1.583)	0.82
Operative		
Glucose levels		
OD-1 >180	0.495 (0.279–0.913)	0.03
OD >180	1.026 (0.613–1.782)	0.92
OD+1 >180	0.678 (0.382–1.421)	0.27
More than two spinal levels	0.008 (0.001–1.017)	0.05
More than two laminectomies	0.676 (0.401–1.118)	0.13
Monitoring change	0.465 (0.243–1.182)	0.10
Fusion	1.482 (0.858–2.436)	0.15
Gross total resection	1.550 (0.688–6.623)	0.34
Spinal recurrence	1.567 (0.822–3.969)	0.19
Follow-up surgery	2.003 (0.887–8.565)	0.11
Follow-up chemotherapy	3.345 (1.449–14.447)	<0.01
Follow-up radiation	1.381 (0.807–2.631)	0.25

[a] CI, confidence interval; COPD, chronic obstructive pulmonary disease; OD-1, preoperative Day 1; OD, operative day; OD+1, postoperative Day 1.

TABLE 4. Multivariate stepwise associations with the ability to walk after resection of metastatic epidural spinal cord compression[a]

Variable	Multivariate relative risk (95% CI)	*P* value
Ability to walk	2.320 (1.301–4.416)	<0.01
Pathologic compression fracture	0.471 (0.235–0.864)	0.01
Preoperative glucose (>180)	0.562 (0.300–1.072)	0.08
Follow-up chemotherapy	2.326 (0.951–10. .218)	0.07

[a] CI, confidence interval.

DISCUSSION

In this study of 78 patients with MESCC, 61 (78%) were able to ambulate postoperatively compared with 55 (71%) who were able to ambulate preoperatively. In total, 49 (89%) maintained the ability to walk, 12 (52%) regained the ability to walk, and six (11%) lost the ability to walk after decompressive surgery for MESCC. Preoperative nonambulatory patients more frequently presented with motor symptoms, required more extensive surgery in terms of spinal levels and laminectomies, more commonly underwent posterior approaches, and had more surgical site, postoperative complications, including wound dehiscences and cerebrospinal fluid leaks compared with preoperative ambulatory patients. After uni- and multivariate analysis, preoperative ambulatory ability and vertebral body compression fracture were independently associated with ambulatory status at the time of the last follow-up evaluation. Also, postoperative chemotherapy and preoperative serum glucose levels greater than 180 trended toward significance. Furthermore, in

TABLE 5. Univariate associations with regaining the ability to walk after resection of metastatic epidural spinal cord compression[a]

Variable	Univariate relative risk (95% CI)	*P* value
Age older than 70 yr	1.014 (0.949–1.101)	0.70
Female	1.500 (0.760–3.845)	0.26
Comorbidities		
Smoker	1.201 (0.657–2.355)	0.56
Diabetes	0.771 (0.383–1.993)	0.54
Coronary artery disease	0.914 (0.447–2.374)	0.83
COPD	0.700 (0.292–3.035)	0.54
Preoperative symptoms		
Time: symptom to surgery <48 hr	2.147 (1.103–1.463)	0.03
Pain	1.012 (0.552–1894)	0.97
Mechanical pain	1.531 (0.667–6.566)	0.36
Radicular pain	1.209 (0.521–5.201)	0.71
Local pain	0.669 (0.325–1.494)	0.30
Sensory	1.098 (0.588–2.353)	0.78
Motor	0.001 (0.0001–2.564)	0.41
Bowel/bladder incontinence	0.535 (0.214–2.345)	0.32
Preoperative steroids	1.034 (0.565–2.027)	0.92
Preoperative treatments		
Chemotherapy	1.018 (0.559–1.989)	0.96
Radiotherapy	0.547 (0.255–1.017)	0.06
Surgical resection	0.987 (0.423–4.255)	0.98
Primary tumor		
Lung	1.364 (0.547–5.972)	0.54
Breast	1.531 (0.667–6.566)	0.36
Prostate	0.529 (0.275–1.148)	0.10
Renal	0.700 (0.292–3.035)	0.54
Thyroid	0.987 (0.423–4.255)	0.98
Gastrointestinal	0.311 (0.096–1.444)	0.11
Radiographics		
Direction of compression		
Anterior location	0.854 (0.468–1.595)	0.61
Lateral location	1.103 (0.557–2.833)	0.80
Posterior location	1.102 (0.602–2.165)	0.76
Spinal cord location		
Cervical	1.000 (0.990–1.001)	0.15
Thoracic	0.003 (0.001–0.668)	<0.01
Thoracolumbar	1.227 (0.529–5.275)	0.68
Lumbar	1.736 (0.759–7.438)	0.22
Pathological compression fracture	0.610 (0.310–1.118)	0.11
Extracranial extraspinal metastases	0.950 (0.508–1.739)	0.87
Operative		
Glucose levels		
OD-1 >180	0.645 (0.284–1.738)	0.34
OD >180	0.921 (0.471–2.010)	0.82
OD+1 >180	0.451 (0.140–2.093)	0.25
More than two spinal levels	0.746 (0.291.1.475)	0.43
More than two laminectomies	0.934 (0.622–1.380)	0.73
Fusion	1.328 (0.723–2.498)	0.36
Gross total resection	1.000 (0.99–1.001)	0.30
Spinal recurrence	1.000 (0.99–1.001)	0.35
Follow-up surgery	1.000 (0.99–1.001)	0.30
Follow-up chemotherapy	1.000 (0.99–1.001)	0.30
Follow-up radiation	1.946 (0.966–5.041)	0.06

[a] CI, confidence interval; COPD, chronic obstructive pulmonary disease; OD-1, preoperative Day 1; OD, operative day; OD+1, postoperative Day 1.

TABLE 6. Multivariate stepwise associations with regaining the ability to walk after resection of metastatic epidural spinal cord compression[a]

Variable	Multivariate relative risk (95% CI)	*P* value
Preoperative radiotherapy	0.406 (0.124–0.927)	0.03
Time: symptom to surgery < 48 hr	2.925 (1.133–2.925)	0.02
Thoracic	0.003 (0.001–1.113)	0.07
Follow-up radiation	2.595 (1.039–8.796)	0.04

[a] CI, confidence interval.

a separate analysis, symptoms for less than 48 hours, preoperative radiation therapy, and postoperative radiation therapy were independently associated with regaining ambulatory function at the time of the last follow-up evaluation. In this analysis, thoracic location trended toward significance.

MESCC is a common and debilitating complication of cancer, in which the lesion invades the epidural space and often compresses the spinal cord and nerve roots, often leading to neurological deficits (9, 14, 30). Recently, direct decompressive surgery has become the standard treatment for MESCC caused by solid primary tumors because of its increased efficacy over conventional radiotherapy in preserving neurological function (26, 35). Several studies have evaluated prognostic factors that may affect survival in patients with MESCC, including primary tumor histology and the presence of extraspinal metastases (46–48), but studies focusing on factors that may influence quality of life, namely, the ability to walk, are limited.

Therefore, the aim of this current study was to identify factors that may offer useful insight into improving the quality of life, namely, preserving and/or regaining the ability to walk, in patients surviving with MESCC.

Distinguishing Characteristics of Presenting Patients

Patients who lost the ability to walk before surgery required more extensive surgery in terms of operative spinal levels and number of laminectomies. In addition, these patients also incurred more surgical site complications, including wound dehiscences and cerebrospinal fluid leaks compared with patients who were able to walk before surgery. These findings may reflect the extensive nature of these lesions in patients who were nonambulatory, making it more difficult to decompress the spine and more prone to complications. This may support early surgical intervention in patients with metastatic spine deposits before the patients become nonambulatory and the lesions presumably become more difficult to resect, as suggested in previous studies (15, 19, 20, 22, 34, 35, 42).

Maintaining Ambulatory Ability

The goal of direct decompressive surgery is to preserve and/or recover ambulatory function. In this study, preoperative ambulatory ability was found to be independently associated with postoperative ambulation, in which patients who were able to walk preoperatively were likely to retain the ability to walk. This trend has been described in other studies as well (15, 19, 20, 22, 34, 35, 42). Patchell et al. (35) documented that 32 out of 34 (94%) patients with MESCC retained the ability to walk after surgical resection. Likewise, Fourney et al. (15) reported that 72 out of 74 (97%) patients with metastatic disease, including MESCC, continued to ambulate postoperatively. The analysis in this study confirms these findings statistically and suggests that early surgical intervention may benefit patients before ambulatory function begins to decline.

The presence of a pathological compression fracture was also independently associated with postoperative ambulation in this study. The spine is the third most common site for metastatic deposits, and the vertebral body is the most common site for metastatic growth (2, 16). Because the vertebral body plays a significant role in loadbearing and protection of neural structures, collapse of the vertebral body may lead to paralysis (44, 45). Taneichi et al. (45) reported that impending vertebral body collapse can be predicted by the degree of metastatic involvement of the vertebral body, in which 50 to 60% and 35 to 40% involvement of the thoracic and thoracolumbar/lumbar vertebral bodies, respectively, predicted impending collapse. For this reason, this may advocate for prompt treatment of metastatic disease before the onset of compression fractures, whether such treatment includes vertebroplasty, kyphoplasty, and/or pharmacotherapy, in an attempt to prevent or delay vertebral body collapse and resulting weakness or paraplegia (41, 51).

Additionally, the presence of spinal compression may relate to the destructive nature of some metastatic tumors. Although this study did not find a significant association between tissue pathology and ambulatory outcome, others have suggested the need to stratify such outcomes studies based on tissue type, given the significant differences in tissue biology and lytic versus blastic characteristics (19, 22, 34, 42). This finding of worse functional outcome with compressive lesions may reinforce this suggestion and hint at worse outcomes with those tumors known to be osteolytic.

Interestingly, postoperative chemotherapy trended toward being positively associated with postoperative ambulatory ability. From this study, however, it is difficult to discern which metastatic tumors were more responsive to chemotherapy, because patients with lung, prostate, breast, sarcomas, and renal primary cancers all received chemotherapy. In addition, a potential confounding factor could be that oncologists may introduce a selection bias by selectively administering chemotherapy only to those patients they felt had the best chance for survival. Nevertheless, postoperative chemotherapy may help prevent additional spinal metastases and metastatic growth, thus increasing the likelihood of preserving ambulatory ability. Further studies are needed, however, to clarify the effects of postoperative chemotherapy on preserving ambulatory function after surgery for MESCC.

Serum glucose levels greater than 180 had a trend toward a significant negative association with postoperative ambulation. In other studies, acute hyperglycemia has been associated with increased morbidity and mortality, as well as reduced long-term functional recovery regardless of a patient's previous diabetic status after stroke and traumatic brain injury, among others (4, 5, 49). Elevated serum glucose levels may contribute to decreased neurological outcomes by increasing lactic acid accumulation, worsening tissue acidosis, and increasing free radical production, which may lead to increased tissue ischemia and subsequent infarction (8, 13, 21, 29, 33, 52). Elevated glucose levels may serve as a marker for a more severe disease process and stress response and, thereby, track statistically with worse functional outcomes. This too will require additional studies to elucidate the true effects of preoperative hyperglycemia on neurological outcomes after surgery for MESCC.

Steroids, which have been shown to decrease surgical pain and length of stay, and improve functional outcome after routine spine surgery (28, 31), may also cause hyperglycemia. There was no correlation found among preoperative steroid use, blood glucose levels, and function outcomes in this study. In addition to surgical decompression, corticosteroids may also play a role in recovering ambulatory function. Studies have shown corticosteroids function by decreasing tumor-associated inflammation, decreasing spinal cord edema, and possibly providing an oncolytic effect for some metastatic tumors, including lymphoma and multiple myeloma (11, 12, 50). These effects may show short-term functional benefits, but the long-term benefits are unclear. This study did not show a strong association between preoperative steroid use and 7-month functional outcome.

Regaining Ambulatory Ability

Surgery for MESCC has led to recovery rates that range between 40 and 60% in several series (15, 20, 35), which is consistent with this study. Here, patients who presented with symptoms for less than 48 hours had a significantly increased likelihood of recovering ambulation. This reinforces the adage that "time is function" in neurological injury. This presumably results from direct neural compression causing edema, venous congestion, and demyelination and, with prolonged compression, leads to secondary vascular injury and infarction (16, 35). Thus, prompt surgical intervention before neurovascular injury occurs may alleviate damage to the spinal cord and nerve roots, allowing better recovery of neurological function (26, 35). This may also be why radiotherapy alone, which takes several days to have an effect, is associated with significantly lower recovery rates when compared with surgical intervention (26, 35).

Interestingly, preoperative radiation therapy made it approximately 2.5 times less likely that ambulatory ability would be regained postoperatively, whereas postoperative radiation therapy made it approximately three times more likely. The negative association between preoperative radiation and neurological recovery is likely multifactorial. Direct causes may include radiation-induced myelopathy and/or myelitis (32). Indirect causes may include radiation-induced reactive gliosis and fibrosis, making surgery more difficult by obscuring surgical planes and increasing the risk of injury to adjacent critical neurological structures. Furthermore, radiation can compromise blood supply to the spinal cord, exacerbating spinal cord ischemia during surgical intervention. Postoperative radiation, however, may improve neurological outcomes (35, 41, 51) by limiting local tumor growth, thus preventing tumor progression, vertebral body collapse, and neurological compromise (41, 51). In fact, Patchell et al. (35) reported that only 30% of patients regained the ability to walk when radiation preceded surgical therapy compared with 62% of patients who received postoperative radiation therapy.

Of note, a thoracic location of the metastatic tumor showed a trend toward a significant negative association with regaining ambulatory function after surgery. This parallels other studies of compressive spinal pathology, including tumors, traumatic injury, and degenerative disease, in which the thoracic location is associated with worse functional outcomes (10, 37, 39). This may be because the spinal canal is narrower in the thoracic spine, making the spinal cord more prone to injury in this region. This is also of concern because the thoracic spine is the most common site of metastatic deposits, accounting for as much as 70% of metastatic spine disease in some series (25).

Limitations

Patient selection and differences in surgical skill and judgment between surgeons and over time inherently limit this study. We included patients with evidence of spinal cord compression on neuroimaging with surgery performed at a single institution by our dedicated spine team; patients with very radiosensitive tumors, concomitant brain metastases, and/or cauda equina or spinal root compression were excluded. This was done to select for patients at higher risk of spinal cord-related paralysis and to mirror a recent randomized, prospective clinical trial by Patchell et al. (35), which showed that direct decompressive surgery plus postoperative radiotherapy was superior to radiotherapy alone in patients with MESCC. Therefore, the results of this study do not necessarily apply to patients with very radiosensitive tumors, metastatic involvement limited to osseous structures, and patients with brain metastases. Nevertheless, we feel this study adds to the work done by Patchell et al. (35) by identifying possible predictors of neurological outcome that may serve as a prognostic guide for the preservation or return of the ability to walk for patients with MESCC.

This study is also inherently limited by its retrospective design, and, as a result, it is not appropriate to infer direct causal relationships. We opted to use ambulation as the primary outcome to minimize observer bias and errors associated with retrospective patient classification. This end point is also important because it has been demonstrated to be a critical quality of life indicator, and accurate assessment of this basic functional measurement was uniformly included in all clinical documentation. In addition, we controlled for each variable found to show either a statistical association or known to have a strong clinical relationship with postoperative ambulatory ability. Given this statistical control and a relatively precise outcome measure, we believe our findings offer useful insights into the management of patients with MESCC. Prospective studies, however, are needed to provide better data to guide clinical decision-making.

CONCLUSION

Although a number of factors have been shown to affect survival after surgery for metastatic lesions to the spine, the findings in this study may offer useful insight into those factors that contribute to improved quality of life, namely, preserving and/or regaining the ability to walk, in patients surviving with MESCC. The identification of these associations with neurological outcome may help guide in the preservation or return of ambulation after surgery for these patients.

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COMMENTS

These authors attempt to define important parameters in uni- and multivariate analysis that predict ambulation in patients undergoing decompressive surgery to relieve metastatic epidural spinal cord compression. Many important parameters are addressed in this article, such as, preoperative ambulation status and duration of ambulation deficit. As seen in many earlier studies, patients who ambulate preoperatively have a higher chance of maintaining ambulation than nonambulatory patients. Additionally, patients with a shorter duration of symptoms, here defined as less than 48 hours, have a better chance of recovery. However, in this article, the remainder of outcome variables that show significance suffer from the retrospective nature of the study and limited data availability. Although ambulation is the defined end point, there is no clear delineation of motor, sensory, pain, or systemic complications that led to the inability to ambulate or to recover ambulation. Six patients lost the ability to ambulate postoperatively (11%), but in all patients this loss resulted from local disease progression leading to motor weakness and pain. It is unclear whether the patients had a good surgical outcome and then had progression of disease with no effective adjuvant therapy. Typically, we have found that surgery is excellent for spinal cord decompression, but local disease control is predicated on the ability to control the local tumor with radiation or possibly chemotherapy. The increased probability of nonambulation if a patient undergoes surgery after radiation may simply be related to the lack of effective adjuvant therapy. The fact that tumor progressed through conventional radiation treatment and surgery was required for epidural compression suggests a selection bias for radiotherapy-resistant tumors in the failed preoperative radiation group. Also, patients were not selected for anterior or posterior surgery based on any specific criteria. The fact that posterior surgery has a worse outcome suggests that surgeons chose that approach for multilevel epidural disease or circumferential tumors. A multilevel high-grade epidural tumor is often more effectively decompressed from a posterolateral laminectomy then an anterior vertebrectomy. Ultimately, this article is an interesting analysis but does little to change current practice.

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The authors report on 78 patients who underwent decompressive surgery for metastatic spinal cord compression. These patients were followed for a mean of approximately 7.1 months after surgery. Patients who were nonambulatory before surgery required more extensive surgery that included increased operative spinal levels and a number of laminectomies, and they had more surgical complications such as wound dehiscences and cerebrospinal fluid leaks compared with the patients who were ambulatory before surgery. A detailed analysis nicely showed that the ability to walk independently before surgery increased the likelihood of ambulation at last follow-up by 2.3-fold. Pathological compression fractures at presentation independently decreased the likelihood of ambulation at the last follow-up by 2.1-fold. For patients unable to walk at the time of surgery, preoperative radiation therapy decreased the likelihood of regaining the ability to walk by 2.5-fold, respectively. On the other hand, postoperative radiation increased the likelihood of regaining ambulatory ability by 2.6-fold at the last follow-up.

It is interesting to note that there was no correlation between preoperative steroid use, blood glucose levels, and functional outcomes. The authors report interesting findings, some of which were known previously; however, it is nice to have such good documentation.

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Chaichana et al. present an interesting review on predictors of ambulation after decompressive surgery for metastatic epidural spinal cord compression. They retrospectively review data on 78 patients at a tertiary center and provide detailed analysis of their results. The study reconfirms findings of the landmark paper by Patchell et al. (1) and discusses the relevance of various treatments to postoperative ambulation (their outcome measure). The data concur with previous findings that early decompressive surgery and postoperative radiation/chemotherapy lead to higher likelihood of patient ambulation. Although the surgeon must consider urgent decompression of metastatic epidural spinal cord compression, one must keep in mind the fact that the data refer to nonradiosensitive tumors that were listed in the manuscript. For radiosensitive lesions such as multiple myeloma, patients may fare just as well or better with radiation rather than surgery. Thus, if possible, the surgeon should pursue obtaining a diagnosis because it can guide him or her to the best management plan for the patient.

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1. 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** 366:643–648, 2005.

Since the publication of the recent landmark trial by Patchell et al. (1), which demonstrated the superiority of a combined surgical and radiotherapeutic approach over radiotherapy alone for the treatment of spinal metastases associated with symptomatic epidural cord compression, there has been increased interest in the application of surgical approaches to enhance neurological function and quality of life in patients with spinal metastases.

The current study from Ziya Gokaslan's group at Johns Hopkins involved a retrospective analysis of 78 surgically treated patients with spinal metastases to determine predictors of ambulatory function. Despite the inherent limitations of such a retrospective study, including the lack of detailed neurological assessments and quality of life indicators, this study represents an important contribution to the literature. Of note, preoperative ambulatory status, a brief history (less than 48 hours) of neurological dysfunction, and postoperative radiotherapy were associated with retained ambulation at a mean follow-up of 7.1 months. In contrast, pathological compression fractures and nonambulatory status were negatively correlated with ambulatory status at follow-up. Interestingly, there was a trend (which narrowly missed statistical significance) for poor glucose control to be negatively associated with neurological recovery in this patient population.

The data from the current study highlight the need for early diagnosis and surgical intervention for isolated spinal metastases with cord compression in order to achieve optimum long-term palliation. Of note, studies are still required to examine the impact of palliative spinal decompressive and reconstructive surgery for patients with symptomatic spinal metastases on quality of life and cost utility.

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1. 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** 366:643–648, 2005.