

Survival Analysis of and Prognostic Factors for Metastatic Epidural Spinal Cord Compression Compared between Preoperative Known and Unknown Primary Tumors

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ABSTRACT

Objective: To analyze the median survival time of and prognostic factors for metastatic epidural spinal cord compression (MESCC) secondary to preoperative unknown primary tumor (pre-op UPT) compared to MESCC secondary to preoperative known primary tumor (pre-op KPT).

Materials and Methods: This retrospective cohort study reviewed all consecutive MESCC patients who underwent surgical decompression with or without stabilization within 72 hours of admission during 2010 to 2016. Survival was compared between the pre-op UPT and pre-op KPT groups, and preoperative and postoperative prognostic factors for survival were analyzed.

Results: A total of 169 patients (pre-op UPT: 51, and pre-op KPT: 118) were enrolled. The survival rate at 3, 6, and 12 months was 84.3%, 58.8%, and 47.1% in the pre-op UPT group, and 72.0%, 48.3%, and 34.7% in the pre-op KPT group, respectively. The median survival time secondary to lung cancer was significantly longer in the pre-op UPT group (6.0 ± 1.4 months) than in the pre-op KPT group (3.6 ± 0.2 months) ($p=0.031$). Multivariate analysis revealed survival time to be influenced by preoperative known or unknown primary tumor status, revised Tokuhashi score, the adjuvant therapy, and postoperative complications, including myocardial infarction, gastrointestinal bleeding, and urinary tract infection.

Conclusion: MESCC secondary to preoperative unknown primary tumor patients who had the clinical presentation with acute progressive neurological deficits who need urgency spine surgery has comparable survival to MESCC secondary to preoperative known primary tumors.

Keywords: Metastasis; spinal cord compression; unknown primary tumor; survival time; prognosis; urgency decompression (Siriraj Med J 2022; 74: 684-692)

INTRODUCTION

Cancer is one of the leading causes of death.¹ Spinal metastasis was found in seventy percent of cancer death undergoing autopsy, and 10% of spinal metastasis patients developed neurological deficits.^{2,3}

Metastatic epidural spinal cord compression (MESCC) patients who can realize potential benefit from surgical decompression should be urgently treated to improve patient functional status, mental status and to prevent persistent loss of motor and/or sensory function.^{4,5} Surgical

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management is usually considered in patients who have a life expectancy of greater than 3 months.⁶

Survival time prediction has important clinical implications, including decision-making relative to the potential benefit of surgical treatment or palliative cancer therapies. There are many scales/scoring systems for predicting the prognosis of MESCC patients, especially Tomita⁷ and revised Tokuhashi⁸, which are the most widely accepted scoring systems. These assessment tools are useful when standard diagnostic strategy is complete, to include tumor marker, Tc-99m bone scan, positron emission tomography (PET) scan, chest-abdomen-pelvis computed tomography (CT) scan, magnetic resonance imaging (MRI) of the spine with contrast, and tissue biopsy. However, these investigations take time that may delay proper management of spinal metastasis patients who have acute neurological deficit as the first clinical presentation. These patients whose primary tumor was initially not definitively known were described as MESCC with preoperative unknown primary tumor (MESCC with pre-op UPT).

Urgent surgical decompression is quite common in MESCC patients with pre-op UPT. To the best of our knowledge, there is no study that has compared survival time between MESCC with pre-op UPT and MESCC with the preoperative known primary tumor (MESCC with pre-op KPT) in this urgent neurological compromise setting.

Thus, survival analysis of all consecutive MESCC with pre-op UPT or pre-op KPT who underwent surgical decompression was the main objective of this study. The secondly aim was to identify prognostic factors associated with median survival time in both groups.

MATERIALS AND METHODS

This retrospective cohort study reviewed all 193 consecutive MESCC patients who underwent surgical decompression with or without stabilization within 72 hours of admission to Siriraj Hospital during 2010 to 2016. This study was approved by Siriraj Institutional Review Board (SIRB) of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Si 013/2016).

To be eligible for inclusion, MESCC patients who underwent surgical decompression must have had all of the following components of preoperative management: 1) complete medical history and physical examination; 2) standard laboratory analysis, including tumor markers; 3) plain radiography of involved bone and chest X-ray; and, 4) MRI spine with contrast medium, with imaging of the whole spine the sagittal view. MESCC patients with

incomplete data or who died from a non-cancer-related cause were excluded.

Patient survival time was investigated by telephone call and a review of medical records. Preoperative and postoperative assessment parameters were reviewed and recorded, as follows: general demographic data, smoking or nonsmoking, American Spinal Injury Association (ASIA) impairment scale score, site of pathologic spinal level, number of spinal metastases, pre-op KPT, pre-op UPT, final identified primary tumor site, revised Tokuhashi score after complete investigation, adjuvant therapy, operative time and operative complications.

Statistical analysis

Chi-square test was used to compare categorical variables (results shown as number and percentage), and Student's *t*-test was used for continuous variables (results shown as mean plus/minus standard deviation). Survival analyses were performed by Kaplan-Meier method, with subsequent group comparison by log-rank test. Prognostic factors associated with survival time were identified by Cox proportional hazards model. A *p*-value of < 0.05 was considered statistically significant. SPSS for Windows version 18.0 was used for all statistical analyses.

RESULTS

Participants

Of the 193 MESCC patients that were evaluated for eligibility, 24 were excluded. Of those, 19 were excluded for having incomplete patient data or because we could not determine their postoperative status. Another 5 cases were excluded because they died of a non-cancer-related cause (3 suicides, 1 trauma, and 1 murder). The remaining 169 MESCC patients were included in our final analysis (Fig 1).

Descriptive data

The baseline characteristics of the 169 enrolled MESCC patients (101 males, 68 females) were evaluated and compared between the pre-op UPT and pre-op KPT groups. The mean age of study patients was 54.9±12.8 years. Fifty-one cases (30.2%) with preoperative unknown primary tumor site were identified. All MESCC patients presented with incomplete spinal cord lesion, and most (59.2%) had ASIA impairment scale grade D. Almost three-quarters (69.2%) of MESCC patients who underwent urgent spinal decompression presented with more than one level of spinal metastasis, and the most commonly affected spinal region was thoracic spine (50.3%). Regarding the postoperative revised Tokuhashi score after complete

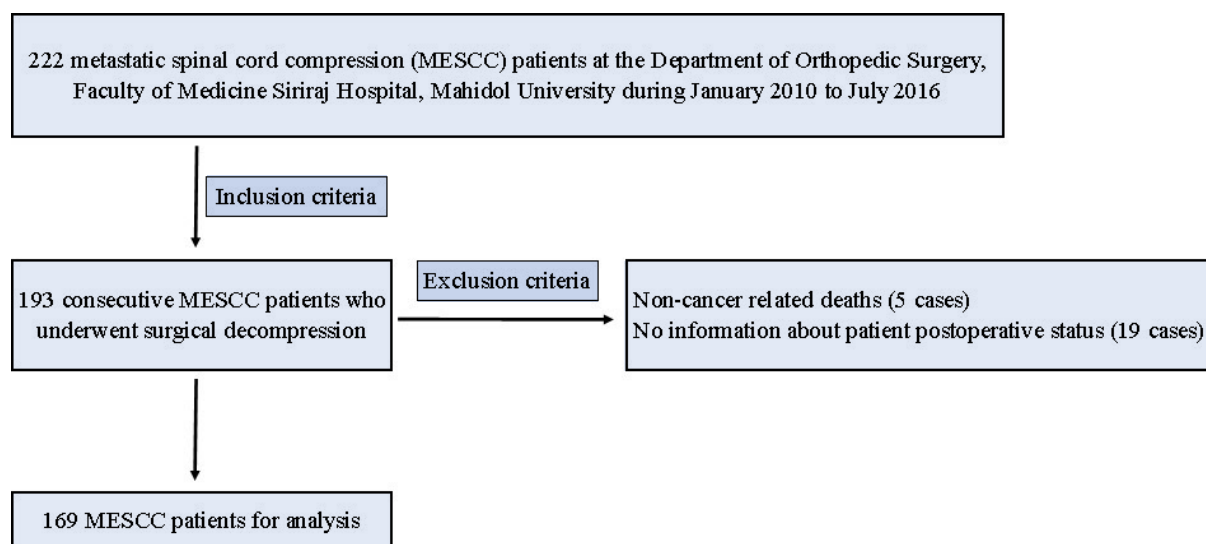


Fig 1. Flow chart describing the patient enrollment process.

investigation according to the standard diagnostic strategy, most patients (55.6%) had a score that fell into the 0-8 group.

The distribution of identified primary tumor site in the pre-op UPT and pre-op KPT groups is shown in Table 2. The most common identified primary tumor site was the lung in both groups. From histological study, eight of nine cases in the cancer of unknown primary site (CUP) patients were adenocarcinoma, and the other was undifferentiated carcinoma.

Survival after surgery

The median survival time between groups was not significantly different, but there was a trend towards longer survival time in the pre-op UPT group (8.4 months, 95% CI: 0.8-16.1) than in the pre-op KPT group (5.1 months, 95% CI: 3.5-6.8) ($p=0.127$). Kaplan-Meier survival method and log-rank test were used to estimate survival and compare the results between groups (Fig 2). The survival rate at 3, 6, and 12 months was 84.3%, 58.8%, and 47.1% in the pre-op UPT group, and 72.0%, 48.3%, and 34.7% in the pre-op KPT group, respectively.

Concerning the lung being the most common primary tumor site in both groups, the median survival time secondary to lung cancer was 3.6 months (95% CI: 3.2-4.0) in the pre-op KPT group, and 6.0 months (95% CI: 3.3-8.7) in the pre-op UPT group ($p=0.031$) (Fig 3).

Prognostic factors associated with survival time

Univariate analysis (Table 3) showed the following prognostic factors to be significantly associated with survival time: American Spinal Injury Association (ASIA) Impairment Scale at presentation, patient smoking status,

number of levels of spinal involvement, revised Tokuhashi score after inclusion of all standard diagnostic data (especially identification of the type of metastatic tumor from histologic finding), adjuvant treatment after surgical intervention, and postoperative complications, including cerebral infarction (stroke), myocardial infarction (MI), gastrointestinal bleeding (GI bleeding), urinary tract infection (UTI), and pressure ulcer.

Multivariate analysis (Table 4) revealed preoperative primary tumor of known or unknown status, adjuvant therapy, revised Tokuhashi score after collection of all standard diagnostic data, and the postoperative complications MI, GI bleeding, and UTI to be independent prognostic factors associated with survival.

DISCUSSION

Interest in the predicted survival time of MESCC patients has increased over the last few years because it is one of the most important factors for guiding decision-making in MESCC patients relative to whether patients with neurological deficit that require urgent care should be given palliative care or operative management. In this study, the prevalence of MESCC patients who presented with acute progressive neurological deficit that indicated for spinal decompression was common with secondary to primary unknown tumor. Moreover, we observed a comparable between median survival time in the pre-op UPT group and in the pre-op KPT group. Regarding lung as the primary tumor site, which was the most common primary tumor site in the pre-op UPT group (37.3%), we found a significantly longer median survival time in the pre-op UPT group than in the pre-op KPT group. This is an interesting finding, especially since patients with

TABLE 1. Demographic and clinical characteristics compared between the preoperative unknown primary tumor site group (Pre-op UPT) and the known primary tumor site group (Pre-op KPT).

Characteristics	Pre-op UPT (n=51)	Pre-op KPT (n=118)	P-value
Gender, n (%)			
Male	39 (76.5%)	62 (52.5%)	0.003
Female	12 (23.5%)	56 (47.5%)	
Age			
Mean age (±SD)	54.9±11.5	54.9±13.3	0.986
ASIA impairment scale			
B	9 (17.7%)	19 (16.1%)	0.418
C	9 (17.7%)	32 (27.1%)	
D	33 (64.7%)	67 (56.8%)	
Pathologic spinal level			
Cervical spine	7 (13.7%)	14 (11.9%)	0.917
Thoracic spine	27 (52.9%)	58 (49.2%)	
T-L junction (T12-L1)	9 (17.7%)	24 (20.3%)	
L2-3 or cord level	8 (15.7%)	22 (18.6%)	
Revised Tokuhashi score			
Score 0-8	28 (54.9%)	66 (55.9%)	0.116
Score 9-11	20 (39.2%)	33 (28.0%)	
Score 12-15	3 (5.9%)	19 (16.1%)	
Number of levels of spinal metastasis			
1 level	19 (37.3%)	33 (28.0%)	0.296
2 levels	15 (29.4%)	31 (26.3%)	
≥3 levels	17 (33.3%)	54 (45.8%)	
Adjuvant therapy			
None	7 (13.7%)	11 (9.3%)	0.092
Chemotherapy (CMT)	2 (3.9%)	3 (2.5%)	
Radiotherapy (RT)	26 (51.0%)	42 (35.6%)	
CMT and RT	16 (31.4%)	62 (52.5%)	

Abbreviation: ASIA indicated American Spinal Injury Association

the lung as the primary tumor site are given the lowest score of 0, the poorest prognosis primary tumor origin category, when using the Tokuhashi scoring system.⁸

MESCC with preoperative unknown primary tumor with acute progressive neurological deficits presents a major decision-making challenge for a spine surgeon, and it makes it difficult for the surgeon to offer the patient accurate information specific to prognosis, survival, and management. These unknowns can lead to surgeon reluctance to perform urgent spinal decompression and

stabilization, but a failure to do so can lead to adverse outcomes for the patient compared to those who receive urgent intervention. The general recommendation is to perform surgery only in patients with a life expectancy of greater than 3 months, and the common survival prediction scoring systems are commonly based on primary tumor, performance status, number of levels of spine metastasis, neurological status, and presence of visceral metastases.⁶⁻⁹ A recent guideline from the Netherlands Comprehensive Cancer Organization relative

TABLE 2. Distribution of identified primary tumor sites compared between the pre-op UPT and pre-op KPT groups.

Identified primary tumor site	Pre-op KPT (n=118)	Pre-op UPT (n=51)
CA Lung	28 (23.7%)	19 (37.3%)
CA Breast	28 (23.7%)	1 (2.0%)
CA Prostate	10 (8.5%)	5 (9.8%)
Hematologic malignancy	10 (8.5%)	9 (17.6%)
CA Nasopharynx	8 (6.8%)	1 (2.0%)
CA Liver	7 (5.9%)	4 (7.8%)
CA Cervix	7 (5.9%)	0 (0.0%)
CA Colon	6 (5.1%)	0 (0.0%)
CA Thyroid	4 (3.4%)	1 (2.0%)
CA Kidney	2 (1.7%)	0 (0.0%)
CA Bladder	1 (0.8%)	0 (0.0%)
Others	7 (5.9%)	2 (3.9%)
Cancer of unknown primary site (CUP)	-	9 (17.6%)

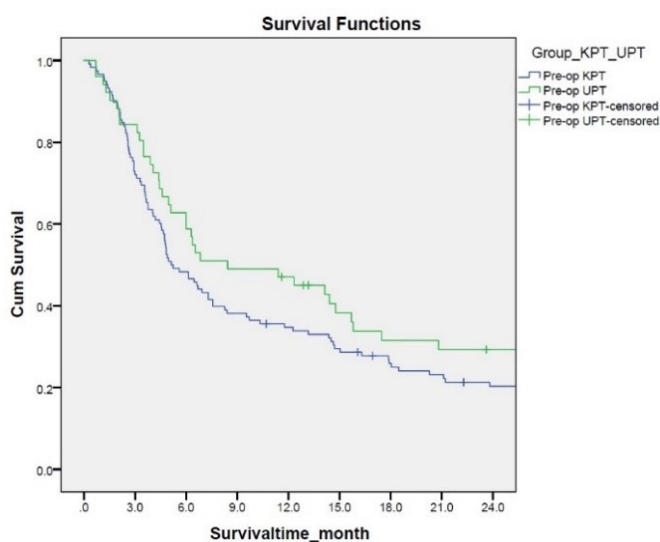
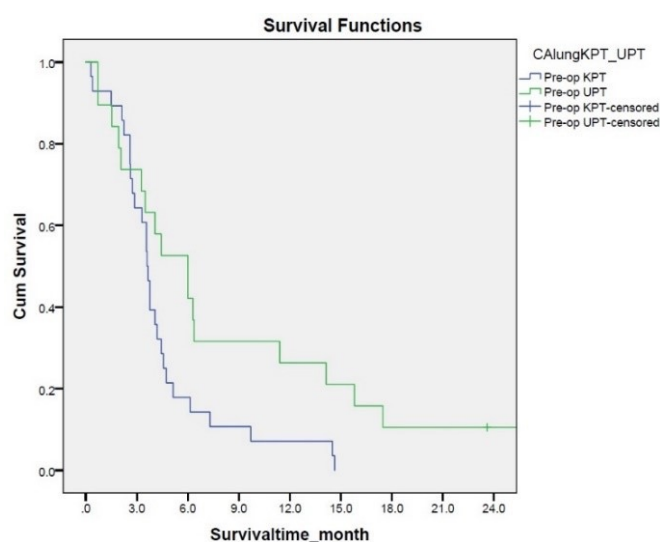
**Fig 2.** Kaplan-Meier survival graphs compared between pre-op unknown primary tumor site group (Pre-op UPT, green line) and the pre-op known primary tumor site group (Pre-op KPT, blue line).**Fig 3.** Kaplan-Meier survival graphs compared between those with pre-op unknown primary tumor site with post-op determination of primary lung cancer (lung CA) (Pre-op UPT, green line) and those with pre-op primary tumor site known to be the lung (Pre-op KPT, blue line).

TABLE 3. Univariate analysis for prognostic factors that predict survival time in MESCC patients who underwent surgical decompression within 72 hours of hospital admission.

Variables	n	Univariate Analysis		
		HR	95% CI	P-value
Preoperative primary tumor				
known	118	1.334	0.920 – 1.933	0.129
unknown	51	1		
Gender: males/females	101/68	1.088	0.777 – 1.523	0.625
Age				
17 – 40 years	26	1.641	0.871 – 3.091	0.125
41 – 50 years	34	1.105	0.595 – 2.054	0.751
51 – 60 years	50	1.206	0.678 – 2.146	0.523
60 – 70 years	39	0.864	0.468 – 1.594	0.640
> 70 years	20	1		
ASIA impairment scale				
B	28	1.998	1.276 – 3.129	0.002*
C	41	1.108	0.737 – 1.664	0.622
D	100	1		
Adjuvant therapy				
None	18	2.344	1.345 – 4.086	0.003*
Chemotherapy(CMT)	5	1.186	0.371 – 3.787	0.774
Radiotherapy(RT)	68	1.092	0.763 – 1.563	0.630
Combined CMT and RT	78	1		
Smoker (+/-)	43/126	1.471	1.010 – 2.142	0.044*
Pathologic level				
Cervical spine	30	1	0.888 – 2.720	0.122
Thoracic spine	21	1.554	0.670 – 2.424	0.460
T-L junction (T12-L1)	85	1.274	0.718 – 2.532	0.353
L2-3 or cord level	33	1.3481		
Spinal related symptom period				
< 1 week	101	0.992	0.450 – 2.190	0.985
1 – 4 weeks	61	0.812	0.362 – 1.820	0.613
>4 weeks	7	1		
Morbidity stage				
ASA 1	7	1		
ASA 2	85	0.990	0.430 – 2.281	0.982
ASA 3	75	1.233	0.532 – 2.858	0.625
ASA 4	2	2.2461	0.449 – 11.233	0.325
Group Tokuhashi score				
Score 0-8	94	5.308	2.909 – 9.686	< 0.001*
Score 9-11	53	1.623	0.862 – 3.053	0.133
Score 12-15	22	1		

TABLE 3. Univariate analysis for prognostic factors that predict survival time in MESCC patients who underwent surgical decompression within 72 hours of hospital admission. (Continued)

Variables	n	Univariate Analysis		
		HR	95% CI	P-value
Number of spinal level involvement				
1 level	52	1		
2 levels	46	1.652	1.063 – 2.567	0.025*
≥ 3 levels	71	1.713	1.141 – 2.572	0.009*
Group operative time (hours)				
< 3 hours	12	1		
3 – 4 hours	60	0.758	0.391 – 1.467	0.410
4 – 5 hours	54	1.028	0.531 – 1.992	0.934
5 – 6 hours	26	1.042	0.501 – 2.170	0.912
> 6 hours	17	1.074	0.491 – 2.345	0.859
Post-op complications				
Cerebral infarction (+/-)	3/166	3.754	1.172 – 12.028	0.026*
Myocardial infarction (+/-)	11/158	2.307	1.209 – 4.402	0.011*
Pneumonia (+/-)	42/127	2.803	1.925 – 4.081	<0.001*
Gastrointestinal bleeding (+/-)	11/158	3.973	2.108 – 7.489	<0.001*
Urinary tract infection (+/-)	68/101	1.650	1.177 – 2.313	0.004*
Thromboembolism (+/-)	18/151	1.590	0.942 – 2.686	0.083
Pressure ulcer (+/-)	54/115	1.521	1.072 – 2.157	0.019*

Abbreviations: ASIA; indicated American Spinal Injury Association, ASA; American Society of Anesthesiologists grade of physical status

to MESCC secondary to preoperative unknown primary tumor recommends that, if it is possible, MRI of the whole spine and PET-CT of the thorax/abdomen should be performed, and that tissue biopsy should be obtained within 1 day.¹⁰ An attempt to complete all recommended investigations and tissue biopsy would delay the critical time needed for recovery of injured neural tissue. The results of our study revealed a survival time of greater than 3 months in 72.0%-84.3% of MESCC patients. Yalamanchili, *et al.* found that rapid progression is common in patients who present with neurological deficit. They found that 30% of patients with weakness could progress to paraplegia within 1 week, and that the likelihood of regaining neurological function was very poor when paraplegia was present for more than 24 hours.¹¹ Preserving the remaining functional neural tissue, increasing the chance of neural tissue injury recovery, and improving ambulatory status all play an important role in patient survival and quality of life and mental status.⁵ A meta-analysis of spinal metastasis by

Luksanapruksa, *et al.* found neurological deficits and ambulatory status to be commonly reported prognostic factors for survival.¹²⁻¹⁵

Cancer of unknown primary site (CUP) was not uncommon (17.6%) in this study, and the most common histopathologic finding was adenocarcinoma. This is similar to previous studies that reported a prevalence of CUP in patients with MESCC of 13.4%-14.5%, and the tissue pathology was usually adenocarcinoma.^{16,17} CUP is usually associated with more aggressive behavior and shorter survival time, which are derived from both biologic condition, such as prior immunoediting and/or featuring a high degree of immunosuppression, and lack of a specific guideline for clinical management.^{17,18}

Our univariate analysis revealed several potential prognostic factors significantly associated with survival time. Subsequent multivariate analysis that included those factors revealed independent prognostic factors for survival time. Among those, we found preoperative primary tumor of known or unknown status to play an important role

TABLE 4. Multivariate analysis for prognostic factors that predict survival time in MESCC patients who underwent surgical decompression within 72 hours of hospital admission.

Variables	n	Multivariate analysis		
		HR	95% CI	P-value
Pre-op primary tumor				
known	118	1.657	1.060 – 2.590	0.027*
unknown	51	1		
ASIA impairment scale				
B	28	0.992	0.583 – 1.689	0.978
C	41	0.752	0.472 – 1.197	0.229
D	100	1		
Adjuvant therapy				
None	18	3.359	1.760 – 6.414	<0.001*
Chemotherapy(CMT)	5	2.401	0.691 – 8.346	0.168
Radiotherapy(RT)	68	0.944	0.616 – 1.447	0.792
Combined CMT and RT	78	1		
Smoker (+/-)	43/126	1.435	0.930 – 2.214	0.103
Pathologic level				
Cervical spine	30	1		
Thoracic spine	21	1.855	0.978 – 3.518	0.058
T-L junction (T12-L1)	85	0.892	0.443 – 1.798	0.750
L2-3 or cord level	33	1.987	0.983 – 4.017	0.056
Group Tokuhashi score				
Score 0-8	94	6.854	3.351 – 14.016	<0.001*
Score 9-11	53	1.892	0.973 – 3.679	0.060
Score 12-15	22	1		
Number of spinal level involvement				
1 level	52	1		
2 levels	46	1.259	0.731 – 2.169	0.407
≥ 3 levels	71	0.937	0.542 – 1.622	0.817
Post-op complications				
Cerebral infarction (+/-)	3/166	1.427	0.354 – 5.752	0.618
Myocardial infarction (+/-)	11/158	3.104	1.450 – 6.648	0.004*
Pneumonia (+/-)	42/127	1.402	0.870 – 2.260	0.165
GI bleeding (+/-)	11/158	3.565	1.702 – 7.465	0.001*
Urinary tract infection (+/-)	68/101	1.519	1.018 – 2.265	0.041*
Thromboembolism (+/-)	18/151	0.960	0.498 – 1.850	0.904
Pressure ulcer (+/-)	54/115	1.262	0.824 – 1.935	0.285

Abbreviation: ASIA indicated American Spinal Injury Association

in survival time. We also found independent association between the revised Tokuhashi score and survival. Similar to other studies^{16,17}, adjuvant therapy was identified as an important prognostic factor for survival; however, differences in survival were reported among different adjuvant treatments and different types of tumors.¹⁹⁻²¹ Lastly, we also found postoperative complications, including myocardial infarction, gastrointestinal bleeding, and urinary tract infection, to be independent prognostic factors to decreased life expectancy. A systematic review by Bakar, *et al.* found a high prevalence of various types of postoperative complications in MESCC patients that ranged in prevalence from 5% to 42.6%.²²

Limitations

This study has some mentionable limitations. First, our study's retrospective design suggests the potential for missing or incomplete data. However, we endeavored to exclude all cases with incomplete data. Second, the small number of each identified primary tumor type except for lung cancer means that Kaplan-Meier survival analysis could only be performed for MESCC secondary to lung cancer. Third and last, the findings of this study could not analyze the decision making for adjuvant treatments in various types of primary tumor and ununiformed optimal chemotherapy in the period of this study with rapid development of chemotherapy.

CONCLUSION

Survival time of MESCC patients who had the clinical presentation with acute progressive neurological deficits depends on multiple prognostic factors, however; the preoperative unknown primary tumor origin is not negative factor for survival in palliative spine surgery.

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Conflict of interest: The authors declare that there is no conflict of interest.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019;69(1):7-34.
2. Rose PS, Buchowski JM. Metastatic disease in the thoracic and lumbar spine: evaluation and management. *J Am Acad Orthop Surg* 2011;19(1):37-48.
3. Jacobs WB, Perrin RG. Evaluation and treatment of spinal metastases: an overview. *Neurosurg Focus* 2001;11(6):e10.
4. Furstenberg CH, Wiedenhofer B, Gerner HJ, Putz C. The effect of early surgical treatment on recovery in patients with metastatic compression of the spinal cord. *J Bone Joint Surg Br* 2009;91(2):240-4.
5. Chavasiri C, Sukprasert N, Chavasiri S. Depression, Social Support, and Coping Strategies in Individuals with Spinal Injury Depression with Spinal Injury Patients. *Siriraj Med J* 2021;73(8): 518-25.
6. Metastatic Spinal Cord Compression: Diagnosis and Management of Patients at Risk of or with Metastatic Spinal Cord Compression. Cardiff (UK); 2008.
7. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine (Phila Pa 1976)* 2001;26(3):298-306.
8. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine (Phila Pa 1976)* 2005;30(19):2186-91.
9. Tokuhashi Y, Uei H, Oshima M, Ajiro Y. Scoring system for prediction of metastatic spine tumor prognosis. *World J Orthop* 2014;5(3):262-71.
10. Bollen L, Dijkstra SPD, Bartels R, Graeff A, Poelma DLH, Brouwer T, et al. Clinical management of spinal metastases- The Dutch national guideline. *Eur J Cancer* 2018;104:81-90.
11. Yalamanchili M, Lesser GJ. Malignant spinal cord compression. *Curr Treat Options Oncol* 2003;4(6):509-16.
12. 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.
13. Pointillart V, Vital JM, Salmi R, Diallo A, Quan GM. Survival prognostic factors and clinical outcomes in patients with spinal metastases. *J Cancer Res Clin Oncol* 2011;137(5):849-56.
14. Tatsui CE, Suki D, Rao G, Kim SS, Salaskar A, Hatiboglu MA, et al. Factors affecting survival in 267 consecutive patients undergoing surgery for spinal metastasis from renal cell carcinoma. *J Neurosurg Spine* 2014;20(1):108-16.
15. Luksanaprukha P, Buchowski JM, Hotchkiss W, Tongsa S, Wilartatsami S, Chotivichit A. Prognostic factors in patients with spinal metastasis: a systematic review and meta-analysis. *Spine J* 2017;17(5):689-708.
16. Paholpak P, Sirichativapee W, Wisanuyotin T, Kosuwon W, Jeeravipoolvarn P. Prevalence of known and unknown primary tumor sites in spinal metastasis patients. *Open Orthop J* 2012; 6:440-4.
17. Wanman J, Grabowski P, Nystrom H, Gustafsson P, Bergh A, Widmark A, et al. Metastatic spinal cord compression as the first sign of malignancy. *Acta Orthop* 2017;88(4):457-62.
18. Aizenberg MR, Fox BD, Suki D, McCutcheon IE, Rao G, Rhines LD. Surgical management of unknown primary tumors metastatic to the spine. *J Neurosurg Spine* 2012;16(1):86-92.
19. Hirsch FR, Scagliotti GV, Mulshine JL, Kwon R, Curran WJ, Wu Y-L, et al. Lung cancer: current therapies and new targeted treatments. *Lancet* 2017;389(10066):299-311.
20. Teo MY, Rathkopf DE, Kantoff P. Treatment of Advanced Prostate Cancer. *Annu Rev Med* 2019; 70: 479-99.
21. Sartor O, de Bono JS. Metastatic Prostate Cancer. *N Engl J Med* 2018;378(7):645-57.
22. Bakar D, Tanenbaum JE, Phan K, Alentado VJ, Steinmetz MP, Benzel EC, et al. Decompression surgery for spinal metastases: a systematic review. *Neurosurg Focus* 2016;41(2):E2.