Survival Time and Prognostic Factors in Patients with Spinal Metastases:

A retrospective cohort and prognostic study

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Purpose: *To determine the survival time in patients with spinal metastases and identify the factors associated with survival time.*
Methods: *A retrospective cohort study of patients with spinal metastases treated at Maharat Nakhon Ratchasima Hospital between January 2009 and December 2013 was performed. The following assessment parameters were recorded: General demographic data, ambulatory status, the number of involved vertebrae, visceral organ metastases, lung metastases or lung tumor, known or unknown primary sites of metastases, surgical operation, radiotherapy and the survival period. The Kaplan-Meier survival analysis, the log-rank test and Cox proportional hazard regression model were used to determine the survival analysis.*
Results: *There were 119 patients included in the study; 62 were female. The mean age was 61 years old. The most common identified sites of primary tumor were lung, prostate, cervix, breast and multiple myeloma, but 47.9% were from unknown primary sites. The median survival time was 132 days. The multivariate survival analysis revealed statistically significant factors were: type of primary malignancy, evidence of lung metastases or lung cancer.*
Conclusion: *The prevalence of an unidentifiable primary site is high and the most common site is the lungs followed by the prostate. The presence of lung metastases or lung tumor were the factors that associated with poor patient survival.*

Keywords: *Survival Time, Prognostic factor, Spinal Metastases, survival analysis*

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Introduction

Bone is a common site for cancer metastases and the spine is the most common site of bone metastases[1]. The prevalence of patients with symptomatic spinal metastases are increasing because of improvement of the primary cancer treatment that prolong patients survival[2,3]. Bone metastases from lung, liver, breast, cervix and prostate are common in the Thai population[4]. Of patients with bone metastases, 48.9% required therapeutic intervention, including treatment of the spinal cord and nerve root compression, pathological fractures, and bone pain[5].

Choice of treatment in these patients depends on their general condition, presentation and predicting survival of patient. Median survival of spinal metastases patients vary from 5.9-22 months[4-8]. The primary tumor type is one of the most powerful prognostic factors impacting survival when spinal metastases are present[8-13]. Others factors that affect survival are age, gender, ambulatory status, other bone metastases, visceral organ metastases, time to development of motor deficits, number of involved vertebrae and radiation regimen[10,14-16].

Maharat Nakhon Ratchasima Hospital is a referral center in Northeastern Thailand. Patients usually presented with multiple spinal metastases and prolonged neurological deficit. Survival of these patients may be shorter than in other studies. This study aims to determine the survival time in patients with spinal metastases and identify factors associated with poor survival time.

Patients and Methods

A retrospective cohort study was conducted at the Maharat Nakhon Ratchasima Hospital. Patients that were diagnosed with spinal metastases were sorted by ICD-10 (secondary malignant neoplasm of bone (C795), pathological fracture secondary from cancer (M809), spinal cord compression (G952)), from January 1, 2009 to December 31, 2013. Medical records, radiographic and laboratory examinations were reviewed. The

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following parameters included: General demographic data, ambulatory status, number of involved vertebrae, visceral organ metastases, lung metastases or lung tumor, known or unknown primary sites of cancer, surgical operation, radiotherapy and the survival period were recorded.

The data was analyzed and survival analyses were performed using the log-rank test and the Cox proportional hazard model. Statistical analysis was performed using STATA, version 12.0 (College Station, TX) and Wizard, Version 1.8.23 (199). The threshold to keep the variable for model selection with p-value equal to or less than 0.2 and p-value less than 0.05 was considered statistically significant. This study was approved by the Institutional Review Board of Maharat Nakhon Ratchasima Hospital.

Results

There were 119 patients included in the study (62 females, 57 males). The mean age was 61 (range 28-88 years). The primary site of tumor is shown in Table 1. The most commonly identified sites of primary tumor were lung, prostate, cervix, breast and multiple myeloma however 47.9% were unknown primary sites. There were 63 patients (52.9%) that presented with neurological deficits and disability. Amongst the spinal metastases patients, 68 (57.1%) had multiple spinal segment involvement (>2 segments), 45 (37%) had visceral metastases and 57 (47.9%) had lungs metastases. Only 19 patients (16%) were treated with surgical decompression and fixation, but 64 (53.8%) were treated with radiation therapy.

There were 115 patients that died during the follow-up period; median survival time was 132 days (95% CI = 96-166) (Fig. 1). The overall survival rates at 3, 6, 9, 12, and 24 months were 61.7%, 40%, 22.6%, 15.7% and 9.7%, respectively. Median survival time and overall survival rate of spinal metastases patients with each type of primary tumor are shown in Table 2.

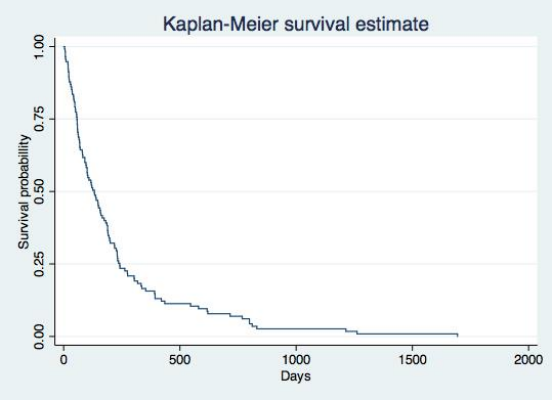

Fig. 1 Kaplan Meier curves of survival patterns

The univariate analysis with the log-rank test indicated that the primary carcinoma site and lung metastases were the only statistically significant factors (Table 3). The multivariate survival analysis with the Cox proportional hazard model found that lung metastases was a statistically significant factor (Table 4).

Table 1 Type of primary tumor

Primary tumor type	Numbers of patients	percent
Lung	15	12.6
Prostate	11	9.2
Breast	9	7.6
Cervix	9	7.6
Myeloma and hematologic malignancy	7	5.9
Thyroid	3	2.5
Rectum	3	2.5
Esophagus	2	1.7
Liver	1	0.8
Colon	1	0.8
Ovary	1	0.8
Unknown primary	57	47.9
Total	119	100

Table 2 Median survival time and overall survival rate of spinal metastases patients with each type of primary tumor

Primary tumor type	**Median survival time** (day)	**Overall survival** (%)			
		3rd month (95%CI)	**6th month** (95%CI)	**9th month** (95%CI)	**12th month** (95%CI)
Lung	104	53.3 (26.3-74.4)	33.3 (12.2-56.4)	13.3 (2.2-34.6)	6.7 (0.4-26.0)
Prostate	189	81.8 (44.7-95.1)	54.6 (22.9-78.0)	45.5 (16.7-70.7)	27.3 (6.5-53.9)
Breast	333	88.9 (43.3-98.4)	77.8 (36.5-93.9)	55.6 (20.4-80.5)	44.4 (13.6-71.9)
Cervix	189	88.9 (43.3-98.4)	55.6 (20.4-80.5)	11.1 (0.6-38.8)	-
Unknown primary	109	56.1 (42.4-67.8)	31.6 (20.1-43.7)	15.8 (7.8-26.3)	14.0 (6.6-24.4)
Overall	132	61.7 (52.2-69.9)	40 (31.0-48.8)	22.6 (15.5-30.6)	15.7 (9.7-22.9)

** others tumor type not show in this table due to small number of patients

Table 3 Univariate Survival Analysis Using the Log-Rank Test

Univariate Analysis (Log-Rank Test)	***P*-value**
Primary tumor type	0.024*
Female vs. male	0.774
Age<65 vs Age>65	0.357
Multiple spinal segment metastases >2 level vs. single spinal lesion	0.168
Ambulatory vs. non ambulatory	0.336
Visceral organ metastases vs. No visceral organ metastases	0.056
Lungs metastases vs. No lungs metastases	0.035*
Surgery vs. non surgery	0.881
Radiation therapy vs. non radiation therapy	0.909

Table 4 Multivariate Survival Analysis Using the Cox Proportional Hazard Model

Multivariate Analysis (Cox Proportional Hazard Model)	**HR**	**95%CI**	***P*-value**
Multiple spinal segment metastases >2 level vs. single spinal lesion	1.33	0.91-1.95	0.138
Visceral organ metastases vs. No visceral organ metastases	1.43	0.97-2.10	0.071
Lungs metastases vs. No lungs metastases	1.53	1.05-2.23	0.027*

Discussion

Many studies report overall median survival of spinal metastases patients vary from 5.9-22 months[4-8]. The most commonly identified primary tumor type in spinal metastases patients are the lungs, breasts, the prostate, kidneys, thyroid and hematopoietic system. Only 10-20% of primary tumor type was unidentifiable after performing a thorough investigation (history and physical examination, laboratory tests, CXR, CT chest and abdomen, and Tc-99m bone scan)[2,5,9].

From this study, more than 50% of spinal metastases patients presented with paraplegia and multiple spinal segment metastases that affected shorter overall median survival period (4.4 months) than other study and only 52.1% of the primary tumor types can be identified. The five most commonly identified primary tumor types were the lungs, prostate, breast, cervix and myeloma and hematologic malignancy. Because of the patient and their family deciding not to complete the investigation and perform tissue biopsy, the unknown primary tumor type proportion is higher than in other studies.

Besides the primary tumor type, the survival prognosis for spinal metastases is affected by many factors such as gender, age, pre-treatment non-ambulatory status, postoperative non-ambulatory status, systemic disease, extra-spinal bone metastases, number of spinal metastases, abnormal blood test, comorbidities, previous chemotherapy, time to development of motor

deficits, visceral metastases and treatment protocol[17].

Leithner et al,[10] evaluate seven preoperative prognostic scoring systems and factor affected survival for spinal metastases. They found that rapid growing primary tumor, visceral organ metastases were a statistically significant factor with Hazard ratio 6.03 and 2.42, respectively.

Lee et al,[18] reviewed 577 cases of spinal metastases and reported significant factor affected survival were female, internal organ metastases, primary type of tumor and adjuvant therapy with Hazard ratio 1.303, 1.349, 3.217 and 1.378, respectively.

In the survival analysis of this study, it was discovered that hazard rate of survival was varied across the primary tumor type and presentation of lungs metastases. But multivariate survival analysis showed only lung metastases was a statistically significant factor (Hazard ratio = 1.53, 95%CI = 1.05-2.23)

The limitations of this study are: 1.) this study is a retrospective study and suffers a few problems from the quality of the medical record; 2.) there were a small number of spinal metastases patients; 3.) because of the small numbers of some primary tumor types, the survival analysis using the Kaplan-Meier curve could not be performed; 4.) many patients decided not to undergo full investigation and tissue biopsy, which may cause under-diagnosis of the primary tumor type and other metastases sites.

Conclusion

The overall median survival of these patients is shorter than in other studies. The prevalence of an unidentifiable primary site is high and the most common site is the lungs followed by the prostate. The presence of lung metastases or lung tumor were the factors that associated with poor patient survival.

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อัตราการรอดชีพ และปัจจัยที่ส่งต่ออัตราการรอดชีพของผู้ป่วยโรคมะเร็งแพร่กระจายมาที่กระดูกสันหลัง

อุรวิศ ปิยะพรมดี, พบ, วรินธร อดุลยานุโกศล, พบ

วัตถุประสงค์: *ศึกษาถึงอัตราการรอดชีพ และปัจจัยที่ส่งต่ออัตราการรอดชีพของผู้ป่วยโรคมะเร็งแพร่กระจายมาที่กระดูกสันหลัง*

วิธีการศึกษา: *การศึกษาการศึกษาย้อนหลังของผู้ป่วยโรคมะเร็งแพร่กระจายมาที่กระดูกสันหลัง รักษาที่โรงพยาบาลมหาราชนครราชสีมาระหว่างเดือนมกราคม 2552 และธันวาคม 2556 ปัจจัยที่นำมาวิเคราะห์ ได้แก่ ข้อมูลประชากรทั่วไป, สถานะผู้ป่วยในการช่วยเหลือตนเอง จำนวนกระดูกสันหลังที่เกี่ยวข้องกับการแพร่กระจาย การแพร่กระจายของอวัยวะอวัยวะภายใน การแพร่กระจายของเนื้องอกมาที่ปอด การผ่าตัด การได้รับรังสีรักษา*

ผลการศึกษา: *ผู้ป่วย 119 ถูกรวบรวมเข้าในการศึกษา เป็นเพศหญิง 62 ราย อายุเฉลี่ย 61 ปี ชนิดของมะเร็งที่พบมากที่สุดคือมะเร็งปอด, มะเร็งต่อมลูกหมาก, มะเร็งปากมดลูก, มะเร็งเต้านมและโรคมะเร็งทางโลหิตวิทยา ตามลำดับ แต่พบว่า ร้อยละ 47.9 ไม่สามารถตรวจวินิจฉัยพบมะเร็งต้นกำเนิดได้ เฉลี่ยระยะเวลาการอยู่รอดของผู้ป่วยคือ 132 วัน และปัจจัยที่มีนัยสำคัญทางสถิติต่ออัตราการอยู่รอด คือชนิดของมะเร็งต้นกำเนิด และการแพร่กระจายของเนื้องอกมาที่ปอด*

สรุป: *ผู้ป่วยที่ไม่สามารถตรวจวินิจฉัยพบมะเร็งต้นกำเนิดได้ยังอยู่ในอัตราส่วนที่สูง แต่มะเร็งที่ตรวจพบและเป็น สาเหตุหลักของโรคมะเร็งแพร่กระจายมาที่กระดูกสันหลังคือ มะเร็งปอดและมะเร็งต่อมลูกหมาก การตรวจพบการแพร่กระจายมะเร็งไปที่ปอดจะเป็นปัจจัยที่มีนัยสำคัญทางสถิติต่ออัตราการอยู่รอดของผู้ป่วย*