Treatment outcome of bone metastasis : Mahavajiralongkorn Thanyaburi Hospital Experience

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Abstract

Introduction

Bone is a commonly metastatic site from several common cancers such as breast, kidney, lung, multiple myeloma, prostate and thyroid gland. Radiotherapy and medical treatments can relieve pain, prevent complications, improve functioning and quality of life. In Mahavajiralongkorn Thanyaburi Hospital, there is no reported data about management of bone metastasis. This retrospective study is conducted to evaluate the treatment modalities, median survival and overall survival.

Material and methods Retrospective, descriptive study of patients with bone metastasis who received treatment in Mahavajiralongkorn Thanyaburi Hospital between 1 January 2006 and 31 December 2007 and were followed up to 30 July 2010.

Results A total of 111 patients received treatments of bone metastasis; 63 (56.76%) were females and 48 (43.24%) were males. The three most common primary cancer sites were lung (29 patients, 26.13%), breast (26 patients, 23.42%) and thyroid (13 patients, 11.71%). Radiotherapy was the main treatment of our patients. Median follow-up time was 3 months (mean = 8 months, ranged from 0.25-55 months). The overall median survival time was 3.00 ± 0.32 months (95%CI = 2.38-3.61), 1-year and 2- years survival rates were 22% and 12%, respectively. Thyroid cancer had the longest median survival (MS) time (34.00 ± 15.27 months, 95%CI = 4.07-63.93), with 1-year and 2- years survival rate of 77% and 52%, respectively. The factors which effected on MS were bone metastasis at initial presentation versus develop bone metastasis later (MS, 3.00 vs. 7.00 months), primary tumor controlled vs. uncontrolled (MS, 7.00 vs. 3.00 months), patients had symptom from bone metastasis vs. without symptom (MS, 3.00 vs. 6.50 months) and patients had bone metastasis alone vs. multiple organ metastases (MS, 4.00 vs. 2.50 months)

Conclusions Radiotherapy was the main treatment of our bone metastasis patients. Thyroid cancer with bone metastasis patients had excellent clinical outcome. Remarkable poor prognostic factors included bone metastasis at initial presentation, uncontrolled primary tumor, symptomatic bone metastasis and multiple organ metastases.

INTRODUCTION

Bone is a commonly metastatic sites from several common cancer such as breast, kidney, lung, multiple myeloma, prostate and thyroid cancers.[1-3] Vertebral spine is the most common site of bone metastasis. Other common sites are pelvic bone, femur, humerus, ribs, and the skull.[1-3] Bone metastasis has been characterized as osteolytic or osteoblastic. Osteolytic metastasis can cause severe pain, pathologic fractures, spinal cord compression and/or nerve-compression syndrome and life-threatening hypercalcemia. Patients with osteoblastic metastasis have bone pain and pathologic fractures because of poor quality of bone.[4] Coleman reviewed clinical features of metastasis bone disease and risk of skeletal morbidity. Their study showed median survival in bone metastasis cancer patients ranged from 6-48 months, depending on the tumor type.[5] The Rapid Access Palliative Radiotherapy Program (RAPRP), established in 2006, showed that 50% of all cancer patients developed metastasis. About half of those were bone metastasis. Median survival for all histology once bone metastasis was 7.2 months.[6]

Many different treatments can not cure bone metastasis, but can relieve pain, prevent complications, improve functioning and quality of life. There are two types of treatments for bone metastasis. Systemic treatments can reach cancer cells throughout the body, while local treatments treat cancer in the bone directly. Systemic therapies include chemotherapy, hormone therapy, bisphosphonate, radiopharmaceutical and other medicines that are taken by mouth or injected into the blood. Local treatments include external radiation therapy and surgery.

In Mahavajiralongkorn Thanyaburi Hospital, there was no data about management of bone metastasis. This retrospective study was conducted to evaluate treatment modalities and median survival. These results may serve as an overview of our experiences in treatment and provide some information for selection proper management to each patient. Furthermore, these data were the basic information and might be used to improve the treatment of bone metastatic patients in the future.

MATERAIL AND METHODS

We searched the archives of patients with bone metastasis who received treatment in Mahavajiralongkorn Thanyaburi Hospital between January 1, 2006 and December 31, 2007. All patients were followed up to July 30, 2010. The following data were collected: age, sex, primary tumor, clinical manifestation, treatment modalities (surgery, chemotherapy, radiotherapy, hormonal treatment, I-131 treatment and symptomatic and supportive treatment). All treatment outcomes including median survival and overall survival were extracted. We excluded patients who were lost to follow-up and had inadequate data for analysis.

Data were analyzed using SPSS statistical software, version 15 (SPSS Inc.,Chicaco.IL). Descriptive statistic was summarized as number and percentage. Median survival (MS) and overall survival (OS) were analyzed by Kaplan-Meier method. Log-rank test were used to compare between each factor which we interest. A two sided p-value <0.05 was considered statistically significance.

RESULTS

A total of 111 consecutive patients was studied, 63 (56.76%) were female and 48 (43.24%) were male. The mean age was 56.25 (ranged 14-91) years; 54.67 (ranged14-91) years in female and 58.33 (range 32-82) years in male. Three most common primary sites were lung (26.13%), breast (23.42%), and thyroid (11.71%). Details of primary cancer sites are shown in table 1.

Table 2 demonstrates baseline characteristics of metastatic pattern. The majority of patients presented initially with symptomatic bone metastasis and had multiple sites of lesions. Radiotherapy was the main treatment of our patients. Almost half of the patients received radiotherapy alone (48.65%). Six patients (5.41%) received chemotherapy alone, 2 (1.80%) patients received hormonal therapy alone and only 1 (0.90%) patient received surgery alone. Twenty-one patients (18.9%) received combined modalities: radiotherapy and chemotherapy (10 patients; 9.0%), radiotherapy and hormonal therapy (6 patients; 5.4%), radiotherapy and

Table 1 Primary cancer sites

Primary site	No.	%
Lung	29	26.13
Breast	26	23.42
Thyroid	13	11.71
Gastrointestinal	12	10.81
-Esophagus	3	2.70
-Stomach	2	1.80
-Colon	2	1.80
-Rectum	2	1.80
-Liver	2	1.80
-Pancreas	1	0.90
Prostate	8	7.21
Head and neck	7	6.31
-Nasopharynx	4	3.61
-Tonsil	1	0.90
-Oropharynx	1	0.90
-Hypopharynx	1	0.90
Cervix	3	2.70
Non-Hodgkin's lymphoma	1	0.90
Other	3	2.70
-Sweat gland	1	0.90
-Soft tissue	1	0.90
-Melanoma	1	0.90
Unknown primary tumor	9	8.11

chemotherapy and hormonal therapy (4 patients; 3.6%), and radiotherapy and surgery (1 patients; 0.9%). Twelve thyroid cancer patients received I-131 treatment and the other one received only radiotherapy. There were 15 (13.51%) patients received only symptomatic and supportive treatment.

Follow-up time was since the start of treatment of bone metastasis at Mahavajiralongkorn Thanyaburi Hospital until loss to follow-up and/or death. Median follow-up time was 3 months (mean = 8.48 month, ranged from 0.25-55 months). MS for all patients was 3.00 months (95%CI = 2.38-3.61). The 1-year and 2- years OS were 22% and 12%, respectively. Patients with bone metastasis from thyroid cancer had the longest MS 34.00 months (95%CI = 4.07-63.93), while corresponding 1-year and 2- years OS were 77% and 52%, respectively. The MS of bone metastasis from other primary sites were as following; cervical cancer was 9.00 months (95%CI = 0.00-18.60), breast cancer was 5.00 months (95%CI = 1.26-8.74), head and neck cancer was 4.00 months (95%CI = 2.71-5.28), prostate cancer was 3.00 months (95%CI = 1.66-4.34), lung cancer was 2.00 months (95%CI = 1.39-2.61), gastrointestinal cancer was 2.00 months (95%CI = 1.20-2.80) and from other primary tumor (sweat gland, soft tissue and melanoma) was 3.00 months (95%CI = 1.4 - 4.6). In unknown primary

Table 2 Baseline characteristics of the metastatic patterns

Characteristics	No.	%
Status of disease		
Initial presentation with bone metastasis	72	64.87
Primary tumor controlled	7	6.31
Primary tumor uncontrolled	65	58.56
Developed bone metastasis later	39	35.13
Primary tumor controlled	24	21.62
Primary tumor uncontrolled	15	13.51
Symptoms related to bony metastasis		
With symptom	63	56.76
Without symptom (diagnosis by bone scan)	48	43.24
Extension of bony metastasis		
Single bone metastasis	22	19.82
No other organ metastasis	15	13.51
With multiple organ metastases	5	4.51
With cord compression	2	1.80
Multiple bone metastasis	89	80.18
Multiple bone metastases alone	51	45.95
With multiple organ metastases	31	27.93
With cord compression	5	4.50
With cord compression and multiple organ metastases	2	1.80
Site		
Spine metastasis	66	59.46
Non-spine bone metastasis	15	13.51
Spine and non-spine bone metastasis	30	27.03

cancer with bone metastasis, MS was 0.25 months. One patients of bone metastasis from non-Hodgkin's lymphoma was dead in 1 month. (Figure 1 shows survival rate by primary site)

We evaluated the following prognostic factors for their possible impact to survival status of disease, symptom, extension of disease and site of bone metastasis. Poor prognostic factors included initial presentation with bone metastasis, uncontrolled primary tumor, symptomatic bone metastasis and multiple organ metastases. Detailed data are shown in table 3.

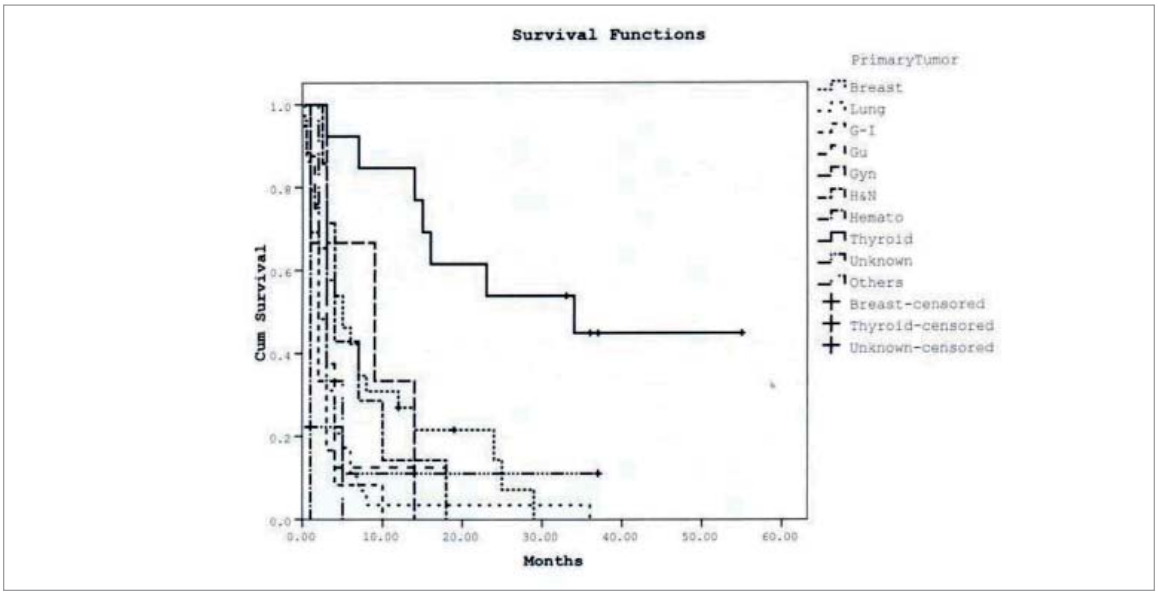
DISCUSSION

This study showed that the most common cancers spread to bone were lung, breast, thyroid and prostate cancer. The median OS was 3 months. In other studies breast and prostate cancer was the common primary site for spread to bone because of the high prevalence of these disease.[5] The median survival for all histology once bone metastasis in The Rapid Access Palliative Radiotherapy Program (RAPRP) was 7.2 months. [6] While International Atomic Energy Agency (IAEA) guideline for palliation of bone metastasis reported median

Table 3 Prognostic factors in univariable analysis

Prognostic factors	MS (months)	1-year OS	2-year OS	p-value
Status of disease				
Initial presentation with bone metastasis	3	8%	6%	<0.001
Progression of primary cancer (developed bone metastasis later)	7	45%	26%	
Status of primary disease				
Primary tumor controlled	7	55%	36%	<0.001
Primary tumor uncontrolled	3	25%	9%	
Symptoms related to bony metastasis				
With symptom	3	10%	3%	<0.001
Without symptom (diagnosis by bone scan)	6.5	37%	20%	
Extension of bony metastasis				
Single bone metastasis	8	32%	17%	0.502
Multiple bone metastasis	3	28%	18%	
No other organ metastasis	4	32%	17%	<0.006
With multiple organ metastases	2.5	20%	0%	
Site				
Spine metastasis	3	14%	10%	0.07
Non-spine bone metastasis	6	32%	20%	

Figure 1 Overall survival by primary tumor



survival range between 2-6 months. [7] Our thyroid cancer patients had the longest median survival. The retrospectively study of 1977 patients with differentiated thyroid carcinoma from 1958-1999 in Pitie-Salpetriere hospital involved 109 patients with bone metastasis. All patients underwent total thyroidectomy then followed by radioiodine therapy. The survival rate at 5 and 10 year were 41% and 15%, respectively and median survival was 3.9 years. [8] In 2011, Wexler revealed the overall 10-year survival rate for patients with differentiated thyroid cancer were 80-95%. Once distant metastasis developed, 10-year survival was 40%. However, 10-year survival of the thyroid cancer with bone metastasis were in the range of 0-34% and mean survival was estimated about 4 years. Nearly all patients received radioiodine, and many patients also underwent adjuvant therapy including surgical excision of bony lesion, external radiotherapy, arterial embolization or chemotherapy. [9]

The MS of bone metastasis from other primary sites in our study was shorter than other studies. Yavas retrospectively analyzed the data of 248 breast cancer patients whose first distant metastasis was in the skeletal. The median survival after bone metastasis was 32 months. [10] Norgaard performed a cohort study of 23,087 patients with prostate cancer from Danish National Patient Registry from 1999 to 2007. One and 5-year survival was 47% and 3%, respectively, in those with bone metastasis. [11] The retrospectively reviewed of 118 patients with bone metastasis from lung cancer treated at Aichi Cancer Center Hospital between 1999 and 2002. The median survival was 7.2 months and the cumulative survival rates were 59.9% at 6 months, 31.6% at 1 year, and 11.3% at 2 years. [12]

Poor prognostic factors in our study included initial presentation with bone metastasis, uncontrolled primary tumor, symptomatic bone metastasis and multiple organ metastases. In Dutch Bone Metastasis Study, the significant predictors for survival were Karnofsky performance score, primary tumor and the absence of visceral metastasis. [13] This is in accordance with the prospectively randomized Dutch Bone Metastasis Study on the effect of a single fraction of 8 Gy versus 24 Gy in six fractions on painful bone metastases, which revealed a good Karnofsky Performance Score, no visceral metastases, and non-opioid analgesics intake as a good prognostic factor for survival. [14] Suguira reviewed prognostic factors in bone metastasis from lung cancer, better prognosis included patients with adenocarcinoma, no evidence of appendicular bone metastases and treatment with an epithelial growth factor receptor inhibitor. [12]

All our patients who received symptomatic and supportive treatment were dead within 4 months and median survival time was 3 months. Other patients who received specific treatment had better survival. Patients who received single modality treatment had shorter survival than multiple modality treatment, except thyroid cancer treated with I-131 treatment. Radiotherapy was our primary therapeutic modality for the treatment of bone metastasis. The median survival time for radiotherapy alone, radiotherapy plus chemotherapy, radiotherapy plus hormonal therapy, radiotherapy plus chemotherapy and hormonal therapy were 3 months, 5 months, 5 months and12 months, respectively. Patients who received specific treatment had better survival than supportive treatment due to performance status and from primary site of cancer. One unknown primary tumor who received radiotherapy plus surgery was still alive more than 3 years.

However, as we described, this study could serve as an overview of our experiences in treatment bone metastatic patients. The result provided some information for selection of proper management in each patient in the future.

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