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Effect of Orthopedics Promotional Activities on Multidisciplinary Management of Patients with Bone Metastases

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Background: The rapid aging of the Japanese population is leading to an increase in the number of patients with bone metastases. Since 2014, our orthopedics department has promoted multidisciplinary hospital activities, including offering lectures to hospital staff on multidisciplinary approaches for bone metastases and holding regular cancer board meetings on bone metastases. This study investigated whether these activities were effective in promoting multidisciplinary approaches and improving outcomes of patients with bone metastasis.

Methods: To investigate the effects of changes in medical practice on patients with bone metastases, we compared patient clinical characteristics after (January 2014 through December 2017) and before the start of the activities (January 2011 through December 2013).

Results: The semiannual numbers of first-visit, referral, and orthopedic surgical patients, the number of patients with slower growing primary cancers, and the number of patients with milder pain were significantly higher post-activity than pre-activity. The number of patients without paralysis was higher after the start of the activity than before the activity, but the difference was not significant. Survival after the first visit to the orthopedics department was significantly longer after the start of the activity than before the activity.

Conclusions: The potential demand for a multidisciplinary approach to bone metastases is high, and orthopedic specialists should actively participate in this approach.

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Key words: multidisciplinary approach, bone metastases, orthopedic, cancer

Introduction

Because of population aging, almost half of Japanese will develop cancer. Cancer incidence in 2012 was 2.5 times that in 1985[1]. Bone metastasis is a sequela of cancer that greatly impairs patient activities of daily living (ADL) and worsens prognosis. In recent years, treatments for bone metastases have substantially improved and now include development of molecularly targeted anti-cancer drugs and bone-modifying drugs. The importance of multidisciplinary management has also been emphasized for patients with bone metastases[2–7].

General orthopedic surgeons are inevitably involved in treating bone metastases, because it is difficult to centralize patients who present with bone metastases at a specialist hospital; however, patients with much rarer sarcomas can be centralized[8]. The recent rapid rise in the number of patients with bone metastases has increased the role of orthopedic surgeons in their treatment.

In 2014, the orthopedics department at our hospital began promoting multidisciplinary approaches for bone metastases. These include lectures to the hospital's medical staff and regular cancer board meetings focusing on bone metastases. This study investigated if these activities were effective in promoting multidisciplinary approaches and improving outcomes of patients with bone metastasis.

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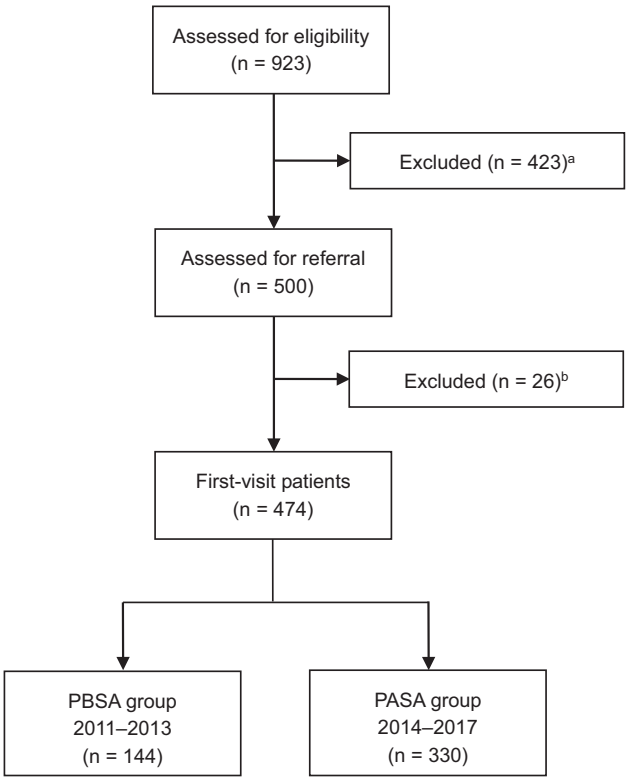

Fig. 1 Flowchart of patient enrollment.
[a]exclusion criteria: patients without bone metastases, patients receiving clinical treatment in orthopedic surgery for conditions unrelated to bone metastases, and patients with sarcoma originally treated in the orthopedics department.
[b]exclusion criterion: patients who initially visited the orthopedics department for bone metastases before 2011. PBSA: period before the start of the activity, PASA: period after the start of the activity.

Materials and Methods

This retrospective study was conducted in the orthopedics department of a university hospital. It was approved by the hospital institutional review board and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from the study participants, in accordance with the information disclosure procedure for retrospective observational research at Nippon Medical School (opt-out). This retrospective review analyzed the medical records of consecutive patients with bone metastases at the authors' hospital.

Hospital Characteristics

In 2017, the hospital comprised 42 departments and 897 beds, and 20,177 patients were newly hospitalized, of whom 6,514 (32.3%) were newly hospitalized cancer patients. In addition, 97,827 outpatients with cancer were assessed[9]. The Japanese Ministry of Health, Labour and Welfare recognizes this hospital as a designated cancer hospital[10].

Patients

Using disease name registrations, we searched the hospital records for patients treated in the orthopedics department for bone metastases during the period from January 1, 2011 through December 31, 2017. **Figure 1** shows a flowchart outlining the patient enrollment process. Computerization of the hospital medical charts began in 2011, and the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) was used to classify diagnoses[11]. A total of 923 patients with a diagnosis coded as C79.5 were initially selected. This code corresponds to secondary malignant neoplasms of the bone and bone marrow in the ICD-10. The patients had all undergone examination for bone metastases at the orthopedics department as outpatients or inpatients. A careful review of the medical charts of these patients led to exclusion of 423, because they did not have bone metastases, their clinical treatment in the orthopedics department was not related to bone metastases, or they were originally treated for sarcoma in our department. The remaining patients (n = 500) were enrolled for evaluation of their referral to the orthopedics department. Subsequently, 26 patients with initial visits before 2011 were excluded, and data from the remaining 474 patients with first visits to the orthopedics department for bone metastases were analyzed. The affected bones were the lumbar spine (n = 142), thoracic spine (n = 110), femur (n = 46), iliac bone (n = 45), cervical spine (n = 36), sacral bones (n = 21), humerus (n = 20), and others (n = 54). The sites of primary cancer were the lung (n = 134), prostate (n = 72), hematopoietic system (n = 49), breast (n = 42), kidney (n = 35), others (n = 129), and unknown (n = 13) (**Table 1**).

In 2014 the orthopedics department began activities to intensively promote a multidisciplinary hospital approach for bone metastases. To investigate the effects of changes in medical practice on patients with bone metastases, patient clinical characteristics were compared after (January 1, 2014 through December 31, 2017) and before the start of the activities (January 1, 2011 through December 31, 2013). Patient medical charts were reviewed to ascertain patient status, namely, patients with bone metastases undertaking first visits (first-visit patients) to the orthopedics department, patients referred from other departments for treatment of bone metastases in the orthopedics department, and patients who underwent orthopedic surgery for bone metastases, excluding biopsies. First-visit patients were classified as inpatients from the

Table 1 Patients' characteristics and primary cancers

Characteristics	All patients	PBSA	PASA	p value
Period	2011-2017 (n = 474)	2011-2013 (n = 144)	2014-2017 (n = 330)	
Median age, years (range)	68 (17-93)	68.4 (32-92)	67.7 (17-93)	0.68
Sex				0.91
Male, n (%)	278 (58.6)	85 (59.0)	193 (58.5)	
Female, n (%)	196 (41.4)	59 (41.0)	137 (41.5)	
Primary cancer				
Lung, % (n)	28.3 (134)	29.2 (42)	27.9 (92)	0.62
Prostate, % (n)	15.2 (72)	14.6 (21)	15.5 (51)	0.81
Hematopoietic system, % (n)	10.3 (49)	7.6 (11)	11.5 (38)	0.20
Breast, % (n)	8.9 (42)	6.3 (9)	10.0 (33)	0.19
Kidney, % (n)	7.4 (35)	9.7 (14)	6.3 (21)	0.20
Colon, rectum, and appendix % (n)	4.2 (20)	4.9 (7)	3.9 (13)	0.65
Liver, bile duct, and gall bladder % (n)	4.0 (19)	5.6 (8)	3.3 (11)	0.26
Pancreas, % (n)	3.6 (17)	6.3 (9)	2.4 (8)	0.04
Stomach, % (n)	3.0 (14)	3.5 (5)	2.7 (9)	0.62
Thyroid, % (n)	3.0 (14)	1.4 (2)	3.6 (12)	0.18
Esophagus, % (n)	2.1 (10)	0.7 (1)	2.7 (9)	0.16
Bladder and ureter, % (n)	2.1 (10)	2.1 (3)	2.1 (7)	0.98
Uterus, % (n)	1.9 (9)	2.8 (4)	1.5 (5)	0.35
Other, % (n)	3.4 (16)	3.5 (5)	3.3 (11)	0.94
Unknown, % (n)	2.7 (13)	2.1 (3)	3.0 (10)	0.56

PBSA: period before the start of the activity, PASA: period after the start of the activity.

same hospital, outpatients from the same hospital, and patients from other hospitals or clinics. First-visit patients were also categorized according to the location of the primary cancer (ie, cancers commonly associated with bone metastasis (lung, prostate, and breast) vs other primary cancers). Referrals were classified as inpatient or outpatient and according to clinical purpose. Patients who underwent orthopedic surgery were investigated in relation to whether they were referred from the same hospital.

Several additional characteristics were investigated, namely, age, sex, primary cancer type and rate of growth, bone affected, ADL, Eastern Cooperative Oncology Group performance status (PS), pain, pathological fractures, spinal cord compression, invasive treatment comprising surgery and/or radiation, and duration of survival after a first visit to the orthopedics department. The annual numbers of hospital-registered cancer patients were also recorded. The rate of growth of the primary tumor was classified as rapid, moderate, and slow, in accordance with the Katagiri method for predicting the prognosis of patients with bone metastases[12]. The slow-growth group included hormone-dependent breast and prostate cancers, thyroid cancers, multiple myeloma, and malignant lymphomas. The moderate-growth group included lung cancers treated with molecularly targeted drugs, hormone-independent breast and prostate cancers, renal cell carcinomas, endometrial and ovarian cancers, sarcomas, and others. The rapid-growth group included lung cancers not treated with molecularly targeted drugs, colorectal cancers, gastric cancers, pancreatic cancers, head and neck cancers, esophageal cancers, other urological cancers, melanomas, hepatocellular carcinomas, gall bladder cancers, cervical cancers, and cancers of unknown origin. The affected bones were categorized as spine and others. Using the classification developed by Fukuhara et al.[13], we defined three ADL categories: can walk independently, can move with a wheelchair, and cannot move. Pain was graded as 1 to 3 during the patient's first visit to the orthopedics department by using the World Health Organization's Pain Relief Ladder[14]. Pathological fracture did not include impending fracture. Spinal cord compression was graded according to the Frankel classification[15]. In addition, we determined if invasive treatment, that is, surgery and/or radiotherapy, was performed after the first visit to the orthopedics department.

Activities in Orthopedics Department

The orthopedics department began intensively promoting multidisciplinary approaches for bone metastases in the hospital in 2014. Four lectures on multidisciplinary approaches were given to hospital medical staff, and a cancer board specializing in bone metastases (BMCB) met

Table 2 Numbers of patients in the orthopedics department

Characteristics	PBSA	PASA	p value
Period	2011-2013 (n = 144)	2014-2017 (n = 330)	
Mean semiannual number of first-visit bone metastases patients, n (range)	24.0 (18-30)	41.3 (26-53)	0.0023
Inpatients from same hospital, n (range)	13.2 (8-17)	16.1 (0-25)	0.18
Outpatients from same hospital, n (range)	7.2 (5-10)	17.0 (11-26)	< 0.001
Patients from other hospitals, n (range)	3.7 (1-5)	8.1 (5-12)	0.0013
Mean semiannual number of first-visit bone metastasis patients, by primary cancer, n (range)			
Common cancers	12 (8-17)	22 (14-34)	0.0063
Others	12 (6-18)	19 (11-22)	0.0043
Mean semiannual number of referrals from other departments, n (range)	31.2 (22-41)	54.6 (31-86)	0.0080
Inpatients, n (range)	22.7 (15-31)	31.4 (20-52)	0.065
Outpatients, n (range)	8.5 (5-13)	23.3 (11-38)	< 0.001
Mean semiannual number of referrals from other departments, by reason for referral, n (range)			
Diagnosis, with or without treatment	16.7 (12-21)	27.9 (13-38)	0.013
Treatment	6.8 (4-9)	13.4 (7-30)	0.0073
Assessment of required load-restriction	1.2 (0-4)	5.6 (1-18)	0.014
Others	6.5 (2-10)	7.8 (5-13)	0.64
Mean semiannual number of surgical cases, n (range)	2.0 (0-4)	6.1 (3-13)	0.0090
Patients from same hospital, n (range)	1.5 (0-4)	4.1 (0-13)	0.32
Patients from other hospitals, n (range)	0.5 (0-1)	2.0 (0-5)	0.26

PBSA: period before the start of the activity, PASA: period after the start of the activity.

regularly. Three of the four lectures were given during hospital-wide cancer board meetings, and one was given during a palliative care meeting. The BMCB meetings were held in the hospital about once a month. They lasted for approximately 1 hour and were attended by approximately 20 participants, including physicians specializing in orthopedics, rehabilitation, palliative care, and radiology; representatives from departments in charge of patients to be discussed; physical therapists; occupational therapists; speech therapists; pharmacists; nurses; and medical social workers. During BMCB meetings, patient information was shared and treatment goals and priorities were discussed. The number of patients discussed during a single BMCB meeting was 1 to 4.

Statistical Analysis

The Mann-Whitney U test was used to compare patients before and after the start of the activities in relation to the semiannual numbers of first-visit patients with bone metastases in the orthopedics department, first-visit patients in relation to primary cancer type, referrals from other departments, referrals in relation to reason for referral, and patients requiring orthopedic surgery, as well as the annual numbers of hospital-registered cancer patients. The Welch t test was used to compare the groups in relation to age, and the chi-square test was used to compare the groups in relation to sex, primary cancer type and growth rate, bones affected, ADL, PS, pain, pathological fractures, and invasive treatment. Kaplan-Meier analysis was used to analyze survival after the first visit to the orthopedics department. A two-sided p-value of <0.05 was considered statistically significant. All statistical analyses were performed with BellCurve for Excel, version 2.15 2017 (Social Survey Research Information Co., Ltd., Tokyo, Japan).

Results

The numbers of patients with common primary cancers, including lung, prostate, and breast cancers, and other cancers, were higher after than before the start of the activities (**Table 1**). However, except for pancreatic cancer, the proportions of primary cancers did not differ between groups (**Table 1**). The semiannual numbers of first-visit, referral, and orthopedic surgical patients were all significantly higher after than before the start of the activities (**Table 2**, **Fig. 2〜4**). Regarding the numbers of first-visit patients, the numbers of outpatients from the same hospital and patients from other hospitals or clinics were significantly higher after than before the start of the activities, but the numbers of inpatients from the same hospital did not significantly differ. The number of out-

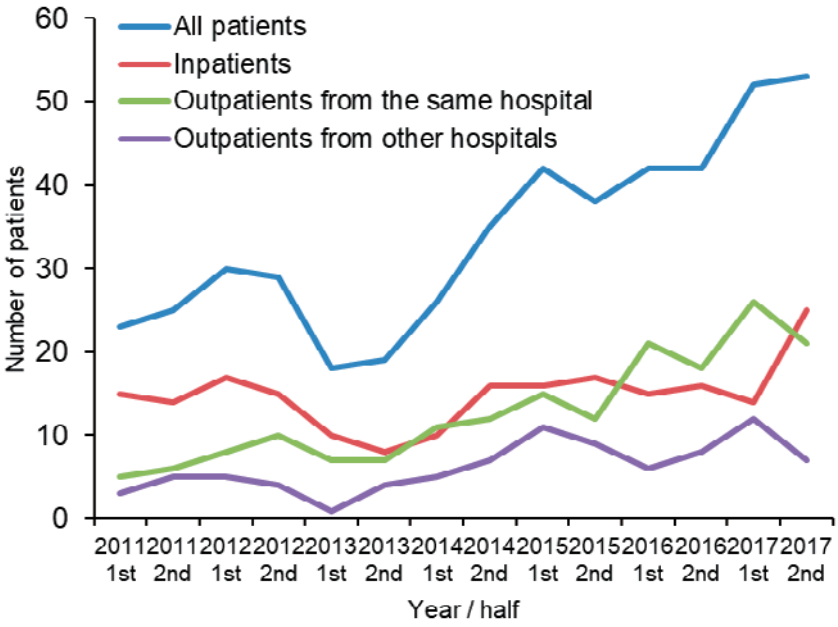

Fig. 2 Semiannual numbers of new patients with bone metastases in the orthopedics department.

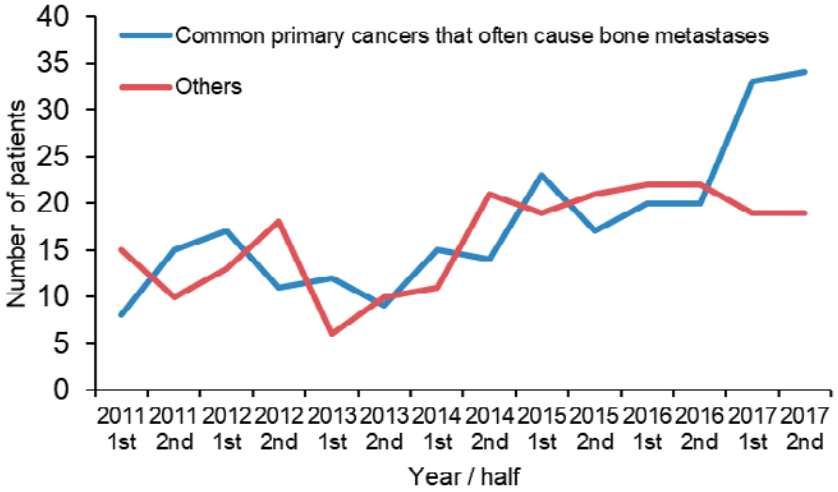

Fig. 3 Semiannual numbers of new patients with bone metastases treated in the orthopedics department, by primary cancer. Common cancers are lung, prostate, and breast cancer.

patient referrals was significantly higher after than before the start of the activities, but the numbers of inpatients did not differ. The semiannual numbers of referrals for diagnosis (with or without treatment), treatment, and assessment of the required load-restrictions were significantly higher after than before the start of the activities (**Table 2**, **Fig. 5**). There were no differences between groups in the numbers of referrals for other purposes, including orthoses prescriptions, biopsies, and medical certificates issued for people with disabilities (**Table 2**, **Fig. 5**).

The number of patients with slow-growing primary cancers was significantly higher after than before the start of the activities; this was true for the patients overall and among patients with primary cancers for which Katagiri scores changed because of sensitivity to molecularly targeted agents or hormones, namely, lung, breast, and prostate cancers (**Table 3**). The number of patients with milder pain was significantly higher after than before the start of the activities (**Table 3**). Regarding spinal cord compression, the number of patients without paralysis tended to be higher after than before the start of the activities. In addition, survival was significantly longer after than before the start of the activities. There

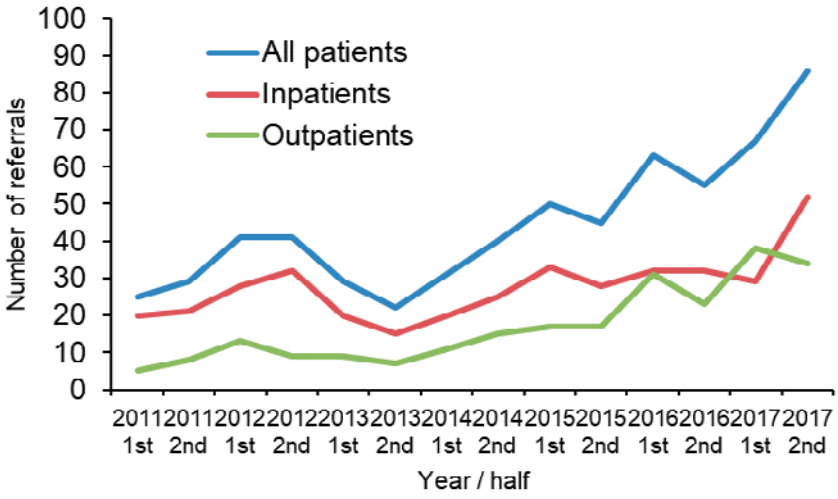

Fig. 4 Semiannual numbers of referrals of patients with bone metastases to the orthopedics department.

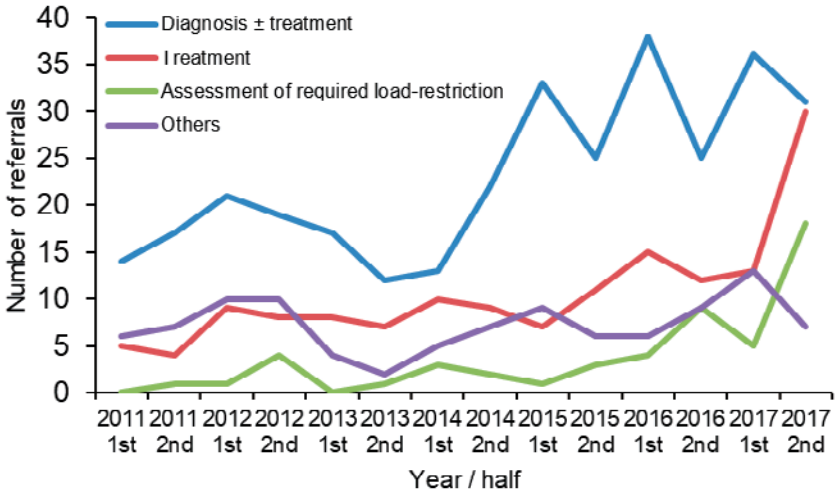

Fig. 5 Semiannual numbers of referrals of patients with bone metastases to the orthopedics department, by reason for referral.

was no significant difference between groups in ADL or PS (**Table 3**). The mean annual number of hospital-registered cancer patients was 2,706 (range 2,468-3,088) from 2011-2013 and 3,102 (range 2,908-3,158) from 2014-2017; the difference was not significant ($p = 0.23$).

Discussion

The most important finding of this study was that promotional activities, eg, hospital lectures on bone metastases and frequent BMCB meetings, improved referral of bone metastasis patients to the orthopedics department from other departments, which suggests a high demand for orthopedic clinical practice when using multidisciplinary approaches for bone metastases. For specialists who manage primary cancers, decision-making regarding treatment of bone metastases, including assessments of instability in the affected bone and indications for surgery and radiotherapy, may be too specialized. By attending the lectures, specialists managing primary cancers understood the importance of bone metastases and the expertise required for their management, which led to patient referrals to the orthopedics department. The BMCB meetings were beneficial for patients because they addressed patient problems by using an interdisciplinary approach, which may have improved identification of bone metastases by hospital medical staff and contributed to the knowledge and experience of core members.

An important finding was that, after the activities began, patient referrals to the orthopedics department occurred earlier. In addition, associated rates of skeletal

Table 3 Characteristics of bone metastasis patients in the orthopedics department

Characteristics	PBSA	PASA	p value
Period	2011-2013 (n = 144)	2014-2017 (n = 330)	
Growth rate of primary cancer			0.018
Rapid, n (%)	63 (43.8)	103 (31.2)	
Moderate, n (%)	49 (34.0)	121 (36.7)	
Slow, n (%)	32 (22.2)	106 (32.1)	
Growth rate of lung, breast, prostate cancers			0.016
Rapid, n (%)	34 (47.2)	50 (28.4)	
Moderate, n (%)	19 (26.4)	69 (39.2)	
Slow, n (%)	19 (26.4)	57 (32.4)	
Affected bones			0.51
Spine, n (%)	97 (67.4)	212 (64.2)	
Others, n (%)	47 (32.6)	118 (54.5)	
Activities of daily living score			0.73
1, n (%)	99 (69.7)	218 (66.1)	
2, n (%)	31 (21.8)	79 (23.9)	
3, n (%)	12 (8.5)	33 (10.0)	
ECOG performance status			0.98
0-2, n (%)	94 (66.2)	218 (66.1)	
3-4, n (%)	48 (33.8)	112 (33.9)	
Pain grade (WHO ladder)			0.040
1, n (%)	90 (63.8)	220 (66.7)	
2, n (%)	7 (5.0)	35 (10.6)	
3, n (%)	44 (31.2)	75 (22.7)	
Pathological fracture			0.16
Yes, n (%)	72 (50.0)	142 (43.0)	
No, n (%)	72 (50.0)	188 (57.0)	
Spinal cord compression			0.095
Frankel grade A-D, n (%)	28 (29.2)	43 (20.5)	
Frankel grade E, n (%)	68 (70.8)	167 (79.5)	
Surgery and/or radiation			0.31
Yes, n (%)	77 (59.2)	171 (53.9)	
No, n (%)	53 (40.8)	146 (46.1)	
Duration of survival			< 0.001
1 year	0.39	0.55	
3 years	0.16	0.39	

PBSA: period before the start of the activity, PASA: period after the start of the activity, ECOG: Eastern Cooperative Oncology Group, WHO: World Health Organization.

events such as severe pain, pathological fracture, and spinal paralysis at the first visit to the orthopedics department decreased after the activities began. Survival after a first visit to the orthopedics department also improved significantly after the activities began, perhaps because of increases in the proportions of slow-growing primary cancers among the patients overall and among patients with primary cancers for which Katagiri scores changed because of sensitivity to molecularly targeted agents or hormones. Another reason for the significant increase in survival after the first visit to the orthopedics department following the start of the activities could be the ongoing development of new drugs for cancer[16–18]. Survival of patients with non-small cell lung cancer was significantly increased by the introduction of a new class of antineoplastic agents, two decades ago[16].

The absence of improvement in ADL and PS after the start of the activities may indicate that orthopedic surgeons are unable to intervene effectively unless ADL and PS decline to particular levels[19]. Assessment and decision-making regarding treatment of bone metastases are unfamiliar to specialists managing primary cancers. Therefore, when possible, patients with bone metastases should be referred to orthopedics departments at an early stage, and orthopedic specialists should follow these patients in parallel with specialists managing the

primary cancers. To ensure such cooperation among specialists, those who manage primary cancers must recognize the importance of early referrals, and orthopedics departments must readily accept patients with bone metastases.

Multidisciplinary medical systems for bone metastases should consider the size and other characteristics of hospitals. Some large cancer centers offer weekly multidisciplinary outpatient clinics for patients with bone metastases[2,7]. Addressing the limited resources of small and medium-sized hospitals will enable orthopedic clinics and orthopedic specialists to play more substantial roles. The present results also highlight specific requirements for treatment of bone metastases in orthopedics departments. Orthopedics has essential and far-reaching roles in multidisciplinary approaches, including diagnosis, treatment involving surgery, assessment of required load restrictions, orthoses prescriptions, biopsies, and issuing medical certificates for people with disabilities.

The present study has some limitations. First, it was a single-center retrospective observational study. Second, although use of a disease registry seemed to identify most patients, not all patients were identified. Third, the reasons for increases in the numbers of new patients with bone metastases in, and referred to, the orthopedics department are multifactorial. Changes in treatment policies or human resources in other departments may have affected referrals to the orthopedics department. Fourth, patient quality of life and patient-based outcomes were not assessed. Despite these limitations, the study had several strengths. To our knowledge, this is the first study of the processes used to promote multidisciplinary approaches for bone metastasis management by, and from the perspective of, orthopedic specialists. The results shed light on methods to prevent complications in patients with bone metastases.

In conclusion, the present results suggest a high demand for orthopedics in multidisciplinary approaches for bone metastases and that orthopedic specialists should actively participate in these approaches. Future research should focus on patient benefits from orthopedics-led multidisciplinary approaches, including prevention and exacerbation of complications, maintenance of ADL, PS, and quality of life, and extension of survival.

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