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Prognostic factors and survival rate in patients with metastatic bone disease at universi sains malaysia 8 years review

Mahmoud Abumarzouq[1*], Umar Zayyanu Usman[2], Wan Faisham Wan Ismail[1], Mohd Imran Yusof[1]

[1]Department of Orthopedic, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia [2]Department of Physiology, College of Health Sciences, UDUS, Sokoto, Nigeria

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

SUMMARY

Background: Surgical intervention for metastatic bone lesions has shown to have a satisfactory outcome. However, several factors can affect the survival of patients with metastatic bone disease. This review aims to evaluate the prognostic factors that affect the survival of patients with bone metastatic disease.

Methods: A retrospective study was conducted on 40 patients with bone metastatic disease who underwent surgical treatment between 2007 and 2015 at the oncology unit of the orthopaedic department at Hospital Universiti Sains Malaysia. Prognostic factors affecting the median survival rate were evaluated. The performance status questionnaire of the Eastern Cooperative Oncology Group (ECOG) was used to assess the patient's quality of life at three, six, and twelve months post-operatively. The survival rate was calculated using the Kaplan-Meier method.

Results: After evaluating 250 patient folders with metastatic bone disease, 40 cases met the inclusion criteria for this study. The study population consisted of 29 females and 11 males, with 70% of patients being under 60 years of age. The majority of patients were Malays (36 patients) and Chinese (4 patients). The most common primary tumour was breast cancer (42.5%), followed by thyroid cancer (17.5%, n=7).

The median survival for all patients was 36 months. Survival analysis revealed that age (p=0.028), chemotherapy (p=0.003), location of metastasis (p=0.021), surgical treatment for bone lesions (p=0.038), and quality of life assessed by ECOG questionnaire at three, six, and twelve months after surgery (p=0.001) were significant prognostic factors affecting survival of patients with metastatic bone disease.

Conclusions: Surgical intervention is a significant prognostic factor affecting survival in patients with metastatic bone disease. Patients with shorter life expectancies may require less invasive surgery, whereas those with longer survival estimates may require more extensive and durable reconstructive surgery. Other factors, such as age, location of lesions, number of bone lesions, and chemotherapy, also influence survival. The study further revealed that the ECOG performance status (0-2 and 3-5) of patients at three, six, and twelve months post-surgery is a statistically significant factor affecting survival.

Overall, the study underscores the importance of considering various prognostic factors when managing patients with metastatic bone disease. These findings may help guide clinical decision-making and improve the overall prognosis and quality of life of patients with this condition.

Keywords: Metastatic; Bone; Cancer; Chemotherapy; Surgery; Survival period

Address for correspondence:

Mahmoud Abumarzouq
Department of Orthopedic, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia
E-mail: mahmoudabumarzouq@hotmail.com

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INTRODUCTION

In recent years, the National Cancer Registry unit of Malaysia has reported a significant increase in cancer incidence. In 2007, a total of 18,219 new cancer cases were registered, with 57.6% of cases already at advanced stages at the time of diagnosis [1]. Breast cancer was found to be the most common cancer in females, while colorectal cancer was the second most common cancer overall, and lung cancer was the most common cancer in males and the third most common cancer in the general population [2].
Metastasis to the bone from carcinomas is a major medical and social issue. Approximately 50% of primary cancers tend to disseminate to the bone, which is the third most frequent site of metastatic spread after the lung and liver [3]. Prostate, breast, and kidney cancers have the highest predilection to disseminate to the bone, followed by the lung and thyroid. The most common sites of involvement are the spine, pelvis, ribs, skull, and proximal long bones [4-5]. While six-month survival rates have been reported for patients with primary solid tumours such as prostate cancer (98%), breast cancer (89%), lung cancer (50%), and kidney cancer (51%), management of metastatic bone disease remains challenging [6]. Treatment options for metastatic bone disease include medical treatment, radiation therapy, chemotherapy, and surgical intervention. Among these options, surgical intervention for metastatic bone lesions has shown promising outcomes. Bone pain is frequently the first sign of metastatic disease, and approximately 80% of all breast cancer patients will have one episode of bone pain that requires treatment. Pathologic fractures are a major cause of prolonged disability [7]. Skeletal-related events (SREs) significantly impact morbidity, performance status, quality of life (QOL), functional capacity, and survival. Despite numerous studies and scoring systems that have been developed to identify prognostic factors in metastatic bone disease, none have been able to provide definitive conclusions on the exact factors contributing to the severity and survival of the disease [8-9]. It should be noted that not all cases of metastatic bone disease require surgical intervention. The present study was conducted at the orthopaedic oncology and reconstructive surgery centre of University Sains Malaysia (USM) in Kelantan, the only tertiary centre for this specialty in the region. USM covers the entire east coast of Malaysia and receives referrals from other states, thus providing a comprehensive source of information on patients with metastatic bone disease.

The study examined recorded patient folders from 2008 to 2016 to identify prognostic factors affecting the survival of patients with bone metastatic disease who were treated surgically.

METHODS

This retrospective study aimed to analyse the survival prognostic factors and quality of life outcomes in patients who underwent surgical intervention for metastatic bone disease. The study population was identified by reviewing the records of 250 patients with metastatic bone disease who were treated between 2008 and 2015 at the orthopaedic oncology unit of Hospital Universiti Sains Malaysia [10].

Inclusion criteria for the study were patients who underwent surgical intervention related to metastatic bone disease, had a history of solid tumour, presented with bone lesions, had metastatic lesions at any site (limbs, spine, and pelvic), and were followed up at our clinic for at least 18 months post-operation. Exclusion criteria included patients who died intra-operatively, patients with multiple myeloma and lymphoma, patients treated conservatively, and patients who underwent surgery solely for spine metastasis [11].

After applying the inclusion and exclusion criteria, a total of 40 patients were included in the study. The data collected from the patient records included age at presentation, type of primary tumour, date of diagnosis for primary tumour, treatment modes of the primary tumour (chemotherapy, radiotherapy, type of surgery), presence of visceral or cerebral metastases, solitary or multiple skeletal metastases, presence of solitary or multiple lesions of the spine, presentation of the patient (pain, pathological fracture, neurological problems), date of diagnosis for bone metastasis, type of surgery, date of the surgery, date of death taken from Malaysian registry centre, and survival time calculated from the date of the surgery to the date of death [12].

The performance status of the survived patients was assessed using the Eastern Cooperative Oncology Group (ECOG) questionnaire to evaluate their quality of life at three, six, and twelve months after the surgery. The survival analysis was performed using the Kaplan-Meier method [13].

Descriptive statistics, including means, standard deviations, and frequency distributions, were calculated for continuous and categorical variables, respectively. The correlation between survival time and various prognostic factors was analysed using Cox regression analysis.

Tab.1. Summary of results that show the association between survival and prognostic factors and median survival of patients post operation.

Variables	n. patients	Survival Status n (%)		Median	p-values*
		Survive	Died	Survival until 1-9-2015	
Age					
Below 60	26	14(%46.15)	12	53	0.028
Above 60	11	9(18.2%)	2	14	
Types of tumor					
Rapid growth	18	12(33.3%)	6	46	0.674
Slow growth	19	11(42.1%)	8	16	
Chemotherapy					
Yes	20	14(30.0%)	8	15	0.003
No	17	9(47%)	6	58	
Radiotherapy					
Yes	27	18(33.3%)	9	53	0.304
No	10	5(50%)	5	36	
Metastatic lesion					
Solitary	24	14(41.7%)	10	16	0.38
multiple	13	9(30.8%)	4	58	
Location					
Appendicular	8	8(0%)	0	12	0.021
Axial bone	23	10(56.5%)	13	58	
Combine both	6	5(16.7%)	1	14	
Organ metastasis					
Yes	19	13(31.6%)	6	46	0.212
No	18	10(44.4%)	8	36	
Surgery					
Harrington	5	5(0%)	0	36	0.038
Nailing	1	1(0%)	0	16	
Endoprosthesis	23	0(56.5%)	13	58	
Allograft	5	5(0%)	0	10	
curettage& bone cement	3	2(33.3%)	1	15	
ECOG post op.					
3 month (0-2)	25	11(65%)	14	58	0.001
3 month (3-5)	12	12(0%)	0	10	
6 month (0-2)	25	11(56.0%)	14	58	0.001
6 month (3-5)	12	12(0%)	0	9	
1 year (0-2)	19	5(73.7%)	14	75	0.001
1 year (3 - 5)	18	8(0%)	0	12	

*Pearson Chi-square applied

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The level of significance was set at $p < 0.05$.

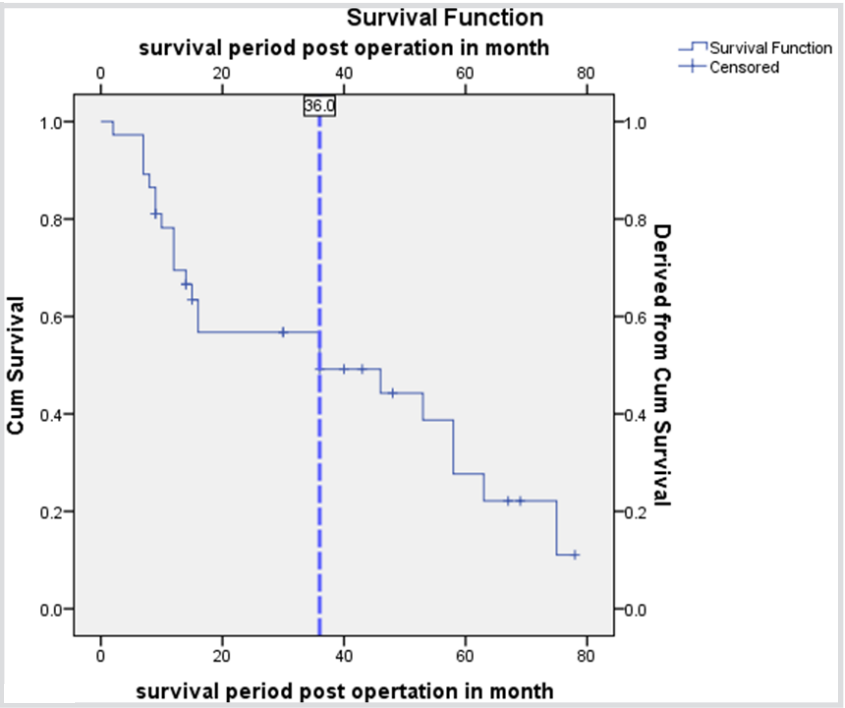
RESULTS

A total of 40 patients (29 female and 11 male) were included in this study, with a mean age of 54.43 years at presentation. Age was equally distributed, with 30% of patients (12/40) above 60 years and 70% below 60 years (28/40). The largest ethnic group was Malay (90%, n=36), followed by Chinese (10%, n=4) (Tab. 1.).

The most common primary tumour was breast cancer (42.5%, n=17), followed by thyroid cancer (17.5%, n=7), renal cancer (15.0%, n=6), unknown primary tumour (7.5%, n=3), lung cancer (5%, n=2), and other primary tumours (prostate cancer, testicular cancer, nasopharyngeal cancer, and ovarian cancer, each n=1, 2.5%).

Prognostic factors evaluated included pathological fracture (76.92%, n=30), neurological deficit (5.13%, n=2), and major surgeries such as resection and endoprosthesis placement surgery (58.97%, n=24). The second most common surgery performed was Harrington procedure for pelvic involvement (17.95%, n=7), followed by minor surgeries such as allograft and osteosynthesis (12.36%, n=5), curettage and bone cementing (6.82%, n=3), and intramedullary nailing for pathological fracture (2.27%, n=1). Quality of life was evaluated using the ECOG questionnaire at 3 and 12 months after surgery. Patients were divided into two groups based on ECOG scores: ECOG 0-2 (good quality of life) and ECOG 3-5 (poor quality of life). At 3 months, 33.33% of patients (n=13) had an ECOG score of 0-2, while 66.67% (n=27) had an ECOG score of 3-5. At 12 months, 48.72% of patients (n=19) had an ECOG score of 0-2, while 51.28% (n=20)

Fig.1.2. Survival period post operation in month.



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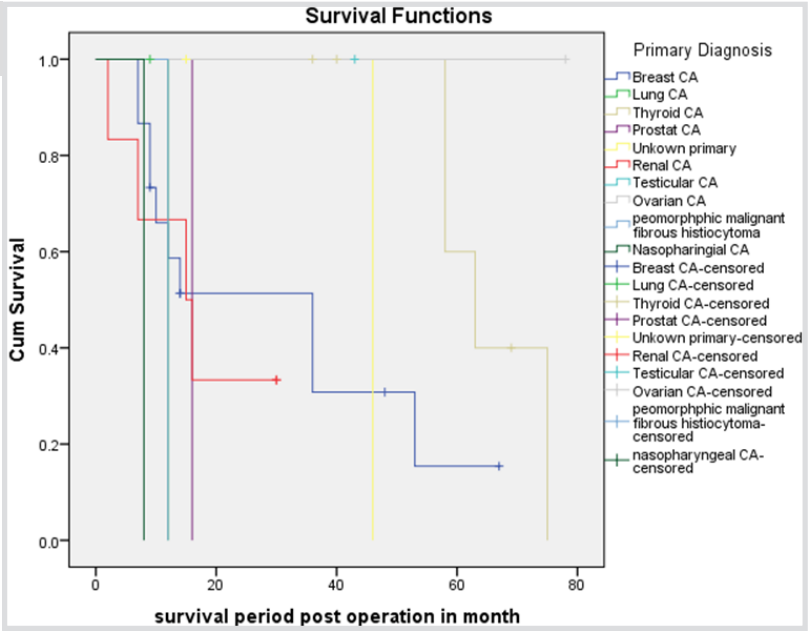

had an ECOG score of 3-5. Survival was analysed using the Kaplan-Meier method. After 18 months of follow-up, 14 patients (37.8%) survived, while 23 (62.16%) died. The global median survival for all patients was 36 months (Fig.1.1). Survival was significantly different between age groups, with 46.2% of patients under 60 years surviving compared to 18.2% of patients over 60 years (p=0.028). Histopathological investigation showed that 18 patients had a rapid-growing tumour, of whom 12 died and 6 survived (33.3%). For the slow-growing tumour, 19 patients were identified, of who 11 died and 8 survived (42.1%). The difference was not statistically significant (p=0.674) (Fig.1.2). Regarding metastasis, 24 patients had solitary metastasis, of whom 14 died and 10 survived (41.7%), with a median survival of 58 months. Multiple metastases were found in 13 patients, of whom 9 died and 4 survived (30.8%), with a median survival of 16 months. The difference was not statistically significant (p=0.38).
The location of metastasis was significantly associated with survival (p=0.021). Eight patients had appendicular bone.

DISCUSSION

The present review examined the clinical characteristics, treatment approaches, and prognostic factors of surgically treated patients with bone metastases (Fig.2.1). The study sample consisted of individuals with a mean age of 54.43 years, with a male-to-female ratio of 1:3. Our findings showed a slightly lower mean age at presentation compared to other studies, while gender distribution was consistent with the literature [14].

Breast cancer was found to be the most common primary solid tumour, followed by thyroid, renal, and lung cancer. This contrasts with previous studies that reported varying tumour types as the most common. In terms of bone involvement, the proximal femur was the most frequently affected site, followed by the pelvic, lower limb, and spine metastasis. However, other studies have reported the axial bones to be more commonly involved than the appendicular skeleton [15].
Treatment approaches varied based on the extent and location of the lesions. Internal fixation was the most common treatment for long bone lytic lesions, while intramedullary nailing was only performed in a few cases. Delayed presentation of patients was associated with increased bone damage and the need for replacement surgery [16] The Harrington procedure, allograft, and osteosynthesis were used for pelvic involvement, see the figure (Fig.3.1). Resection and endoprosthesis placement were frequently performed for proximal humerus and proximal femur, distal femur, and proximal tibia lesions (Fig.3.2).
The quality of life of the patients was evaluated using the ECOG questionnaire, which was administered three, six, and twelve months after surgery. The ECOG results significantly correlated with survival, with patients with a performance status of 3 or 4 having a 50% higher risk of dying than those with better performance status. Pathological fracture was a negative prognostic factor, although it was not found to significantly influence survival. Previous chemotherapy was a significant prognostic factor, likely due to patients with advanced disease at the initial treatment of the primary lesion being more likely to

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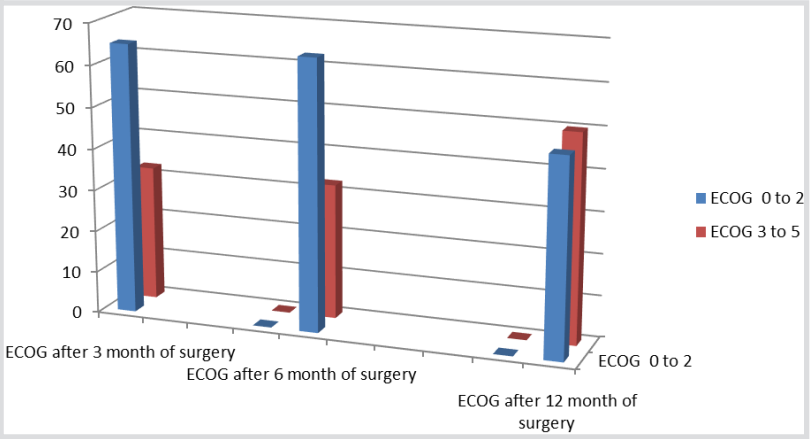
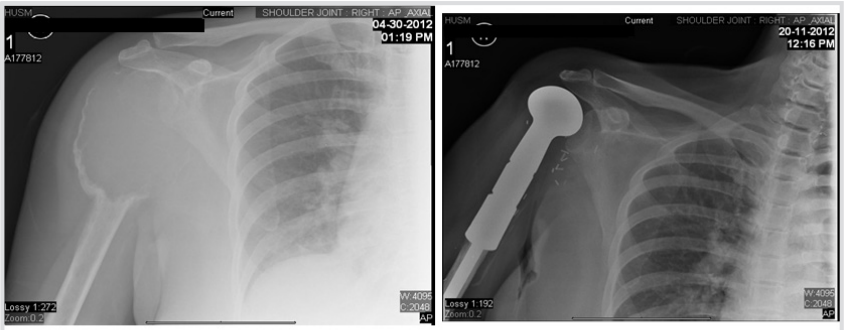


Fig.3.1. The Harrington procedure was performed for lytic and destruction of hip joint.

This is x-ray any 3d reconstructed ct of patient , 39 femal diagnosed with thyroid cancer and Harrington procedure was performed for lytic and destruction of hip joint the patient Survive 63 moth

ECOG 0-2

Fig.3.2. Resection and endoprosthesis placement were frequently performed in this x-ray.



This is x-ray of 51years old female diagnosed with thyroid cancer and resection and endoprosthesis performed for lytic and destruction proximal humerus the patient Survive 36 moth

receive chemotherapy. The type of surgery was found to significantly affect survival, while the site of the primary tumour, radiotherapy, and pathological fracture were not significantly associated with survival. The performance status was affected by age and the type of surgery, but not by spine metastasis or the site of the primary tumour [17].

CONCLUSION

The present study provides important insights into the clinical characteristics, treatment approaches, and prognostic factors of surgically treated patients with bone metastases. These findings highlight the need for tailored treatment approaches based on the location and extent of bone involvement, as well as the importance of considering prognostic factors when making treatment decisions. Further research is needed to better understand the optimal treatment strategies for this patient population [18].

In conclusion, the study found that surgery was a significant prognostic factor affecting survival in patients with metastatic bone disease. Patients with short life expectancies may require less invasive surgery, while those with longer survival estimates may require more durable reconstructive and extensive surgery to improve their quality of life and survival. Age, location, number of bone lesions, and chemotherapy were also significant prognostic factors affecting survival. The study also identified the performance status ECOG (0-2 and 3-5) after surgery as a statistically significant factor affecting the survival range of patients. However, some limitations of the study were identified, including incomplete clinical records and a relatively small number of patients. As a recommendation, national-level collaboration is needed to evaluate the prognostic factors of patients with metastatic bone disease with other centers in Malaysia and possibly in South East Asia to obtain larger data and patient numbers for more robust analysis.

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