The Philippine Journal of Orthopaedics

ORIGINAL ARTICLE

Survival Analysis of Pathologic Fractures in Metastatic Bone Disease: A Retrospective Study on the Prognostic Role of Primary Tumor Site and Hematologic Markers in a Single Philippine Tertiary Center

Katrina Ysabel R. Naraval, MD,[1] Daniela Kristina D. Carolino, MD, FPOA,[1,3] Edwin Joseph R. Guerzon, MD, FPOA[1,2]

[1]*Institute of Orthopaedics and Sports Medicine, St. Luke's Medical Center, Quezon City, Philippines*
[2]*Institute of Orthopaedics and Sports Medicine, St. Luke's Medical Center Global City, Philippines*
[3]*Musculoskeletal Tumor Unit, Philippine Orthopedic Center*

ABSTRACT

Background. Metastatic bone disease (MBD) poses a risk for skeletal-related events, including pathologic fractures and spinal cord compression, subsequently leading to higher mortality after definitive surgery. Estimation of survival is crucial in the treatment of metastatic pathologic fractures to help set realistic expectations for patients, their families, and physicians.

Objective. To determine the predictors of mortality in patients diagnosed with pathologic fracture secondary to metastatic bone disease in terms of hematologic and serologic markers such as preoperative hemoglobin, absolute lymphocyte count, and preoperative albumin.

Methodology. This retrospective cohort study involved 128 patients: 109 who were treated surgically and 19 who were treated non-surgically, from January 2010 to December 2020. Risk factors studied were age, preoperative serum albumin, absolute lymphocyte count (ALC), and hemoglobin, primary tumor site, whether surgery was done, presence of visceral metastases, presence of other bony lesions, and chemotherapy/radiotherapy use. Cox proportional-hazards regression was employed to determine the accuracy of each risk factor as a predictor of mortality.

Result. The patients' mean age was 60.05 years (SD = 11.10), and 56.25% were female. The most common site of primary tumor was the breast (32.02%), then the lung (25.00%). Among patients with low hemoglobin, 11.27% expired within the first six months from the time MBD was established, while 17.54% survived up to one year; however, this difference was not statistically significant (p = 0.310). Similarly, no significant difference in survival was observed among patients with low albumin, with 95.77% expiring within six months and 98.25% surviving up to one year (p = 0.511). In contrast, a statistically significant difference was found among those with low ALC, with 16.90% expiring within six months compared to 10.53% surviving up to one year (p = 0.002). Surgical treatment was performed on 85.16% of the study population. The proportion of surgical patients who survived within six months (82.46%) did not differ significantly from those who expired (87.32%, χ^2 = 0.59, p = 0.441).

Conclusion. The primary tumor site was an independent prognostic factor for survival in patients diagnosed with pathologic fractures from MBD, with primary lung malignancy having the poorest chance of survival. While preoperative serum albumin, hemoglobin, and ALC were not statistically significant predictors, they remain clinically useful as indicators of nutritional and physiologic status when assessing surgical risk. These findings are particularly relevant in local settings where access to timely diagnostic scans may be limited. In such contexts, readily available laboratory tests can play a valuable role in guiding risk stratification and shared decision-making in the management of MBD.

Keywords. bone neoplasms, pathological fractures, secondary, prognosis, retrospective studies, survival analysis

ISSN 0118-3362 (Print)
eISSN 2012-3264 (Online)
Printed in the Philippines.

Received: July 15, 2025.
Accepted: September 19, 2025.
Published Online: October 25, 2025.
https://doi.org/10.69472/poai.2025.23

Corresponding author: Katrina Ysabel R. Naraval, MD
Institute of Orthopedics and Sports Medicine,
St. Luke's Medical Center, 2nd floor,
279 E. Rodriguez Sr. Ave.,
Quezon City, 1112 Metro Manila, Philippines
Tel. No.: (+632) 8723-0101 local 4155
E-mail: khayanaraval@gmail.com
ORCiD: https://orcid.org/0009-0006-6789-4610

INTRODUCTION

Metastatic bone disease (MBD) is the most common cause of malignancy in the bone, typically affecting patients in the terminal stage of their illness. This condition carries a high risk for skeletal-related events, including pathologic fractures and spinal cord compression in 10% of cases.[1–3] Pathologic fractures significantly increase mortality rates, with reports showing 60–83% mortality at one year and 70–94% at two years post-surgery.[4–6]

Surgical stabilization procedures, though invasive, are often necessary for palliation, pain relief, early mobilization, and reduced morbidity, especially since many patients are in the late stages of cancer.[6–9] However, surgery carries inherent risks that may worsen outcomes for critically ill patients. For those unfit for surgery, nonoperative management such as immobilization, non-weight bearing, and bracing can offer symptom relief.[10] Radiotherapy and chemotherapy have also demonstrated palliative benefits for patients with severe comorbidities or poor prognosis.[11] Overall, management should be tailored individually.

Estimating survival in patients with metastatic pathologic fractures is essential for setting realistic expectations for patients, families, and physicians.[3,12–14] Yet, prognostic assessments can be subjective. Several studies have developed scoring systems incorporating factors from spinal and extremity metastases to guide prognosis.[15–17] However, many omit hematologic or serologic parameters that may better reflect physiologic status.[14] Readily available serologic markers (e.g., serum albumin, hemoglobin, absolute lymphocyte count) correlate with nutrition, physiologic reserve, and survival, yet are underrepresented or inconsistently weighted in current tools, particularly for extremity disease.[14,18–22] In addition, some prognostic scores require detailed imaging that is not always available for extremity pathologic fractures, especially in resource-constrained settings, underscoring the value of simple laboratory-based indicators.[10,18] Known risk factors for mortality include the site of the primary tumor and preoperative functional status. Lung-origin tumors have the highest mortality (80%) when compared to breast (48%), kidney (79%), and prostate (40%) origins.[13,23] Functional status is commonly measured using the Eastern Cooperative Oncology Group (ECOG) Performance Status. Lower ECOG scores (0–1) correlate with reduced mortality, while higher scores (2–5) indicate poorer outcomes, although specific percentages are lacking in studies.[12,13,23,24]

Among hematologic and serologic parameters, hemoglobin, absolute lymphocyte count (ALC), and serum albumin have shown prognostic value.[12,13,18] Hemoglobin, assessed via complete blood count (CBC), is widely used in clinical settings. Preoperative anemia (<80–100 g/L) is a strong negative prognostic factor.[12,13,25] ALC, also obtained from the CBC, reflects immune function and wound healing but is not considered an independent predictor of survival in MBD.[12,13,19] Serum albumin is a marker of nutritional and visceral protein status; low levels are linked to poor surgical recovery and are significant in cancer survival prognosis.[13,14,19,20] These readily available laboratory values can assess physiological status and may help predict cancer survival outcomes.[18,21] Because CBC and serum albumin are inexpensive, routine, and easily extracted from clinical records, isolating them has practical value for risk stratification when advanced imaging is not immediately available.[10,20]

As of writing, local studies have not yet evaluated the prognostic significance of preoperative hemoglobin, ALC, and serum albumin levels in patients presenting with pathologic fractures secondary to metastatic bone disease. This study, therefore, aimed to identify key prognostic factors associated with diminished survival and to assess the validity of these factors in predicting outcomes among patients who underwent surgery for pathologic fractures secondary to metastatic bone disease of the axial or appendicular skeleton.

METHODOLOGY

Study design

This was a retrospective cohort, single-center study involving patients diagnosed with pathologic fractures of the axial or appendicular skeleton treated surgically and non-surgically from January 2010 to December 2020.

Study population

Adult patients aged more than 20 years with histologic proof of metastases and with available mortality data at six months and one year were included. Patients without information relating to the presence or absence of bone or visceral metastases, histopathology reports dated before the year 2010, patients diagnosed with carcinoma in situ, primary bone or soft tissue sarcoma, or hematologic malignancy were excluded from the study.

Data collection

Purposive data gathering was done by the primary author by scanning the daily patient census using the keywords "metastatic bone disease," "pathologic fracture," and related terms such as "metastatic" and "pathologic." Patients who appeared in the search were collected and filtered according to the inclusion and exclusion criteria. Patients' data and clinical information were then retrieved from electronic patient records (MDportal, HCQC, Digichart). Data included age at diagnosis, site of primary tumor, site of pathologic fracture, presence of visceral or other bony metastases, laboratory data including preoperative serum albumin, hemoglobin, and ALC values, surgical procedure performed (if any), course in the wards, and follow-up dates.

Preoperative hemoglobin (g/L) was taken at the time of admission or before any blood transfusion, and values less than 100.0 g/L were categorized as low, and those 100.0 g/L

and above were categorized as normal. ALC (cells/mcL) was computed from the complete blood count as WBC count x 1000 x percent lymphocyte (expressed as a decimal). ALC levels less than 500 cells/mcL were categorized as low, and those with greater than or equal to 500 cells/mcL were categorized as normal. Preoperative serum albumin (g/L) was also obtained at the time of admission or before any albumin correction, with values less than 35.0 g/L categorized as low and those 35.0 g/L and above categorized as normal.[13]

Oncologic diagnosis was classified into six groups: breast, lung, prostate, renal, thyroid (representing the top five primary carcinomas in our population), and other sites. The presence of visceral metastases was determined preoperatively based on imaging such as computed tomography (CT) scan of the chest and abdomen, and magnetic resonance imaging (MRI) of the brain. If the visceral metastases were discovered after surgery, this information was not utilized in the study because the authors aimed to determine survival rates with the information and parameters available during the time of decision-making, and this lowers the risk of overestimating the number of patients with visceral metastasis at the time of management. The same approach was used regarding the number of bone metastases, which was determined by nuclear bone scan imaging. The official results of all scans were reviewed by a consultant radiologist and the primary author.

Data analysis

Data were analyzed using STATA Statistical Software, Version 13. College Station, TX: StataCorp LP. A p-value of 0.05 was considered statistically significant. Descriptive statistics for continuous variables were summarized as means and standard deviations, while categorical variables were reported as frequencies and percentages. Comparative analyses of nominal variables (including primary tumor site, surgical status, chemotherapy and/or radiotherapy exposure, organ-specific visceral metastases, axial or appendicular involvement, and hematologic laboratory markers) according to mortality status (expired versus alive) was done using the Chi-Square Test of Homogeneity or Fisher's Exact Test, if the assumption of at least five expected frequencies per cell was not met. The Mann-Whitney U Test was used for ordinal or non-normally distributed continuous data, while the independent t-test was used for normally distributed continuous data.

We used survival analysis approaches in our inferential analyses to allow for differences in the time to mortality. Particularly, Kaplan-Meier survival curve analysis was utilized to determine the median time of mortality, with curves stratified by preoperative hemoglobin, ALC, and serum albumin (low vs normal) and by surgical status. Cox proportional-hazards regression with adjusted models for specific confounders was also employed to determine the hematologic and serologic predictors of mortality in patients who underwent surgery and in patients who did not.

Addressing bias

We limited our inclusion and exclusion criteria to information available at the time of presentation to reduce selection bias and confounding by indication. The index date was set at admission or the first confirmatory imaging of the fracture. Information bias was minimized by using official preoperative imaging reports, standardized laboratory definitions, and dual review of imaging classifications. Adjustments for key prognostic factors in multivariable Cox models were made during analysis. Residual confounding and selection bias inherent to retrospective designs may remain and are acknowledged.

Ethical clearance

This study was conducted in adherence to the ethical principles outlined in the Declaration of Helsinki (2013) and by the Guidelines of the International Conference on Harmonization - Good Clinical Practice (ICH-GCP), E6 (R2), and other applicable provisions of ICH-GCP 6 (as amended). Approval for the conduct of the study was obtained from the Institutional Review Board (IRB) and Institutional Ethics Review Committee (IERC) of St. Luke's Medical Center (Protocol Code: SL-21002).

RESULTS

One hundred and twenty-eight patients met the inclusion criteria, 109 of whom underwent surgical stabilization for pathologic or impending pathologic fracture and 19 of whom did not. All 128 were followed up for survival (Table 1).

Most participants were female (56.25%). The mean age of the respondents was 60.05 years (SD = 11.10). In particular, the age of those who survived up to one year was 56.26 years (SD = 10.52), while those who expired within six months had a mean age of 63.10 years (SD = 10.67). The mean age of the respondents who expired was significantly older (t = −3.62, p = 0.001).

The most common primary tumor site was the breast (32.02%), followed by the lung (25.00%), and the kidney (7.81%). Histological diagnosis of skeletal metastasis was obtained on the same day as surgical stabilization in the surgical group. Among those with primary lung cancer, the proportion of those who expired (32.39%) was significantly higher (χ^2 = 4.65, p = 0.031) compared to the other primary malignancies. Pathologic fractures were more common in the spine (64.06%) than in the appendicular skeleton (35.94%).

The mean preoperative hemoglobin, ALC, and serum albumin were 118.6 g/L (SD=1.79), 1,214.25 cells/mcL (SD = 736.97), and 25.0 g/L (SD=0.44), respectively (Table 1). We found that 14.06% of the participants had low hemoglobin, 14.06% had low ALC count, and 96.88% had low serum albumin. Of those with low hemoglobin, 11.27% expired within the first six months from the index date, while 17.54% survived up to one year; this difference shows no statistical significance

Table 1. Demographic and clinical profiles of the respondents according to mortality status (N = 128)

Characteristics	Mortality status			Test statistic	*p*-value (Two-tailed)
	Alive >6 mos to 1 year (n = 57)	Expired Within 6 mos (n = 71)	Total (N = 128)		
Age (Years; x̄, SD)	56.26 (10.52)	63.10 (10.67)	60.05 (11.10)	-3.62	0.001†
Sex (f, %)				0.01	0.982
Male	25 (43.86%)	31 (43.66%)	56 (43.75%)		
Female	32 (56.14%)	40 (56.34%)	72 (56.25%)		
Location of primary malignancy (f, %)					
Breast	20 (35.09%)	21 (29.58%)	41 (32.02%)	0.44	0.507
Lung	9 (15.79%)	23 (32.39%)	32 (25.00%)	4.65	0.031*
Thyroid	5 (8.77%)	3 (4.23%)	8 (6.25%)	1.12	0.465
Prostate	5 (8.77%)	5 (7.04%)	10 (7.81%)	0.13	0.751
Renal	7 (12.28%)	6 (8.45%)	13 (10.16%)	0.51	0.476
Others					
Colorectal	3 (5.26%)	2 (2.82%)	5 (3.91%)	0.71	0.479
Endometrial	0 (0.00%)	1 (1.41%)	1 (0.78%)	-0.90	0.368
Hepatocellular	1 (1.75%)	3 (4.23%)	4 (3.13%)	-0.80	0.423
Nasopharyngeal/Pharyngeal	1 (1.75%)	1 (1.41%)	2 (1.56%)	0.15	0.877
Neuroendocrine	0 (0.00%)	1 (1.41%)	1 (0.78%)	-0.90	0.368
Pancreatic	0 (0.00%)	2 (2.82%)	2 (1.56%)	-1.28	0.201
Parotid	1 (1.75%)	1 (1.41%)	2 (1.56%)	0.15	0.877
Round Cell	1 (1.75%)	0 (0.00%)	1 (0.78%)	1.12	0.263
Unknown	0 (0.00%)	1 (1.41%)	1 (0.78%)	-0.90	0.368
Urothelial	0 (0.00%)	1 (1.41%)	1 (0.78%)	-0.90	0.368
Vulvar	2 (3.51%)	0 (0.00%)	2 (1.56%)	1.59	0.112
Site of pathologic fracture (f, %)				1.67	0.197
Spine	40 (70.18%)	42 (59.15%)	82 (64.06%)		
Appendicular	17 (29.82%)	29 (40.85%)	46 (35.94%)		
Laboratory Findings					
Preoperative hemoglobin (x̄, SD)	11.75 (1.86)	11.95 (1.75)	11.86 (1.79)		
Low preoperative hemoglobin (<100.0g/L)	10 (17.54%)	8 (11.27%)	18 (14.06%)	-0.62	0.535
Normal preoperative hemoglobin (≥100.0g/L)	47 (82.46%)	63 (88.73%)	110 (85.94%)	1.03	0.310
Absolute lymphocyte count (x̄, SD)	1,440.21 (795.81)	1,032.84 (635.43)	1,214.25 (736.97)		
Low absolute lymphocyte count (<500 Cells/mcL)	6 (10.53%)	12 (16.90%)	18 (14.06%)	3.22	0.002†
Normal absolute lymphocyte count (≥500 Cells/mcL)	51 (89.47%)	59 (83.10%)	110 (85.94%)	1.06	0.302
Serum albumin (x̄, SD)	2.52 (0.41)	2.47 (0.46)	2.50 (0.44)		
Low serum albumin (<35.0/L)	56 (98.25%)	68 (95.77%)	124 (96.88%)	0.66	0.511
Normal serum albumin (≥35.0g/L)	1 (1.75%)	3 (4.23%)	4 (3.13%)	0.64	0.628
Chemotherapy or Radiation Therapy (f, %)					
For primary malignancy	27 (47.37%)	35 (49.30%)	62 (48.44%)	0.05	0.828
For metastasis	15 (26.32%)	13 (18.31%)	28 (21.88%)	1.19	0.276
Visceral metastasis (f, %)					
Brain	8 (14.04%)	13 (18.31%)	21 (16.41%)	0.42	0.516
Lung	10 (17.54%)	15 (21.13%)	25 (19.53%)	0.26	0.611
Liver	3 (5.26%)	10 (14.08%)	13 (10.16%)	2.70	0.101
Others: Adrenal	1 (1.75%)	1 (1.41%)	2 (1.56%)	0.02	1.000
Bony metastasis (f, %)				0.01	0.951
Axial	31 (54.39%)	39 (54.93%)	70 (54.69%)		
Appendicular	26 (45.61%)	32 (45.07%)	58 (45.31%)		
Surgery status				0.59	0.441
With surgery	47 (82.46%)	62 (87.32%)	109 (85.16%)		
Without surgery	10 (17.54%)	9 (12.68%)	19 (14.84%)		

Note: Comparative analyses were conducted using the Chi-Square Test of Homogeneity or Fisher's Exact Test (if expected frequencies were less than 5.00) and an independent t-test.

*Significant at 0.05; †Significant at 0.01

(p = 0.310). Similarly, no significant difference was observed in survival between patients with low albumin, with 95.77% expiring within six months and 98.25% surviving up to one year (p = 0.511). In contrast, a statistically significant difference was found in those with low ALC, with 16.90% of patients expiring within six months compared to 10.53% still alive up to one year (p = 0.002).

For patients with normal hemoglobin, normal ALC, and normal albumin, no statistically significant differences in values were observed between those alive up to one year and those who expired within the first six months. Only 1.75% of those who survived up to one year had normal albumin levels. This is because the study population's albumin levels were generally lower than normal. These findings suggest that despite low albumin levels, survival rates did not differ significantly.

Most (85.16%) respondents had surgery, and the proportion of these patients who survived up to six months (82.46%) was not significantly different (χ^2 = 0.59, p = 0.441) from those who expired (87.32%).

Almost half (48.44%) had received chemotherapy or radiation therapy for their primary malignancy, while 21.88% had these treatments for their metastases. The mortality rate in patients who underwent adjuvant chemotherapy or radiotherapy for the primary malignancy was 49.30% and was not a significant risk factor for mortality (p = 0.828). Similarly, those who received adjuvant chemotherapy or radiotherapy for metastasis had a mortality rate of 18.31% but this was also not significant (p = 0.276).

In terms of visceral metastases, 19.53% had lung metastasis (p = 0.611), 16.41% had brain metastasis (p = 0.516), and 10.16% had liver metastasis (p = 0.101). The most common sites of bony metastases were axial bones (54.69%, p = 0.951).

Table 2 shows that 40.63% of the respondents expired within six months, while 14.84% expired within six to 12 months. Results also showed that the median mortality time for patients with low preoperative hemoglobin, low ALC, and low serum albumin was within six months (95% CI = 6 to 6).

Table 3 depicts the Cox proportional hazards regression analyses of the predictors of mortality among the respondents according to the surgical status. Hazard ratios were adjusted for significant confounders, including age, primary lung malignancy, and primary renal malignancy. The adjusted hazard ratio of mortality among those without surgery was 25% higher than those with low preoperative hemoglobin (aHR = 1.26, p = 0.842) and low ALC (aHR = 1.26, p = 0.842) than those with normal hemoglobin and absolute lymphocyte count. In addition, low serum albumin was not associated with the hazard of mortality among those without surgery (aHR = 1.00, p = 1.000). On the other hand, the adjusted hazards for mortality among those with surgery with low preoperative hemoglobin (aHR = 1.26, p = 0.842), low absolute lymphocyte count (aHR = 1.20, p = 0.612), and low serum albumin (aHR = 1.45, p = 0.609) were 31%, 20%, and 45% higher, respectively, than those with normal serologic results. These results were not statistically significant ($p > 0.05$).

Figure 1 illustrates the Kaplan-Meier survival estimates according to the level of preoperative hemoglobin, level of absolute lymphocyte count, and level of serum albumin. The time interval from the index date to mortality was shorter among those with low preoperative hemoglobin, low ALC, low serum albumin, and without surgery, compared to those with high or normal preoperative hemoglobin, ALC, normal serum albumin, and with surgery.

Table 2. Frequency distribution of mortality according to the time of mortality among the respondents (N = 128)

Outcome	Time of mortality			
	6 months		12 months	
	Frequency (f)	Percentage (%)	Frequency (f)	Percentage (%)
Mortality status (Expired)	52	40.63%	19	14.84%

Table 3. Univariate Cox proportional hazards regression analysis of the predictors of mortality among the respondents according to the surgical status (N=128)

Predictors	Mortality status (Expired)											
	Without surgery						With surgery					
	cHR	p-values (Two-tailed)	95% CI	aHR	p-values (Two-tailed)	95% CI	cHR	p-values (Two-tailed)	95% CI	aHR	p-values (Two-tailed)	95% CI
Low Pre-operative Hemoglobin (<100.0g/L)	1.14	0.901	0.14–9.29	1.25	0.842	0.14–11.18	1.20	0.656	0.54–2.64	1.31	0.507	0.59–2.92
Low absolute lymphocyte Count (<500 Cells/mcL)	1.14	0.901	0.14–9.29	1.25	0.842	0.14–11.18	1.02	0.948	0.53–1.96	1.20	0.612	0.60–2.39
Low serum albumin (<35.0g/L)	0.88	0.901	0.11–7.11	1.00	1.000	0.09–11.03	1.22	0.783	0.30–5.00	1.45	0.609	0.35–6.05

Note: cHR = Crude Hazard Ratio; aHR = Adjusted Hazard Ratio; Hazard ratios were adjusted for significant confounders: age, primary malignancy of lungs, primary malignancy of renal

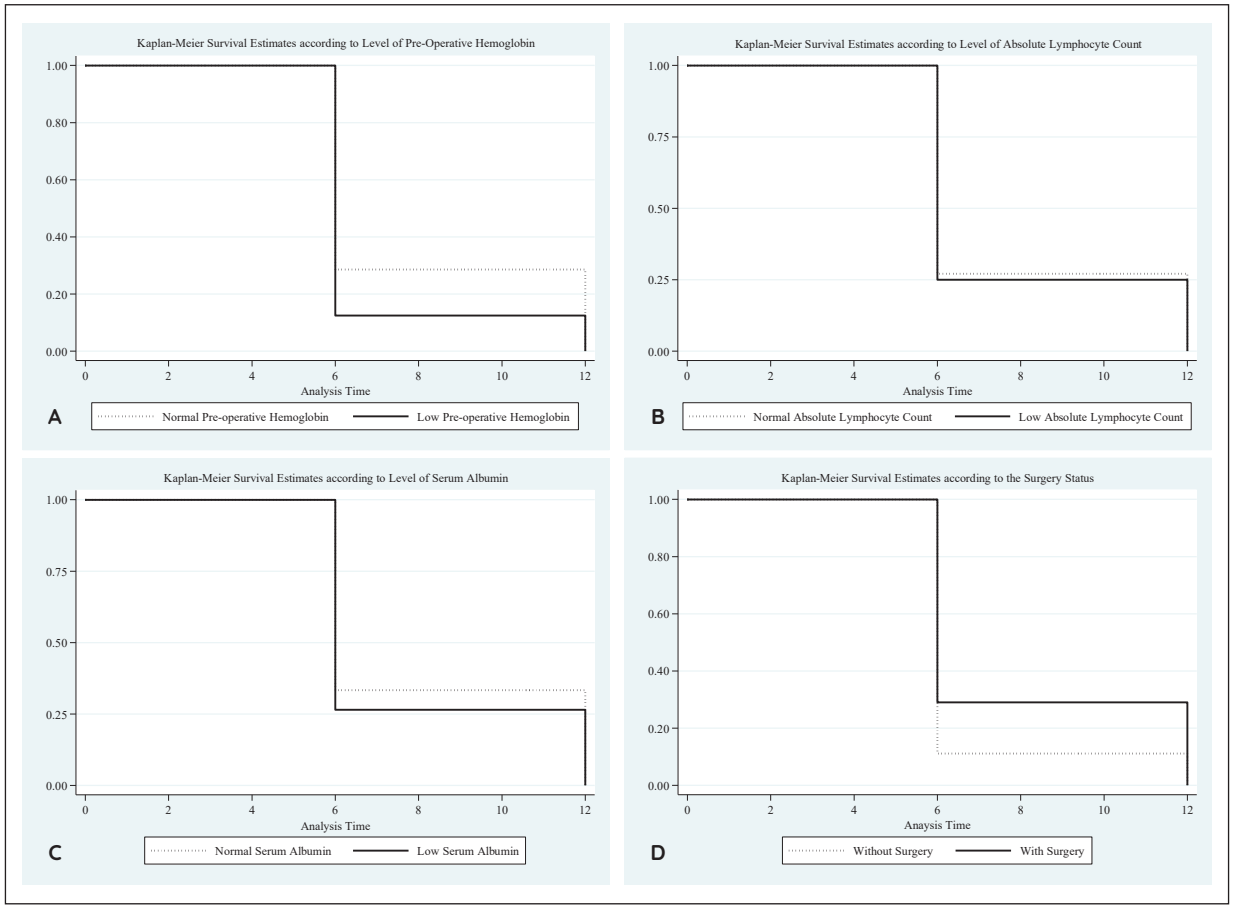

Figure 1. Kaplan-Meier survival estimates according to the level of preoperative hemoglobin **(A)**, level of absolute lymphocyte count **(B)**, level of serum albumin **(C)**, and surgery status **(D)**.

DISCUSSION

Pathologic fractures due to skeletal metastases from cancers of the breast, prostate, thyroid, lung, and kidney contribute significantly to patient morbidity and mortality.[3,13,18,23] We report a six-month mortality of 40.63% which is similar to previous reports (49.6%).[14] One-year mortality was 14.84%, lower than previously reported mortality rates of 60–83%.[6,12,13,18,23,25] The primary tumor site was an independent prognostic factor of survival in patients diagnosed with pathologic fracture from MBD, with primary lung malignancy having the poorest chance of survival. Preoperative serum albumin, hemoglobin, and ALC were not found to be significant in predicting survival in these patients.

The relationship between the primary site of malignancy and long-term survival in patients with pathologic fracture secondary to MBD has been well-established.[6,12,14,23,25] The most common primary malignancy was the breast, with lung coming in second, similar to our study's results (32.02% and 25.00%, respectively). Although more common overall, the prognoses of patients with MBD from breast cancer were significantly better than those with lung cancer.[3,12–14]

The spine was the most common location of MBD.[3,8,12,14] Pathological metastatic fractures of the spine and extremities may debilitate patients due to severe pain, prolonged recumbency, and possible weakness. We found that most pathological fractures were detected at the same time as the bony metastases. This suggests that both axial and appendicular metastasis may be primarily asymptomatic or tolerable in pain, therefore, difficult to detect during the early stage without regular surveillance.[8,18,25] The estimated life expectancy should guide management. Surgeons rely on careful assessment of various preoperative factors and scoring systems such as those by Bauer,[15] Tomita,[16] and Tokuhashi[17] to prognosticate and deduce which patients may benefit from surgical intervention. In our literature review, we found no prognostic scoring systems that used laboratory parameters to reflect the physiologic status of patients with MBD.

Multiple serologic parameters have been examined in studies in attempts to predict survival in patients diagnosed with MBD.[12,13,18,23,26] Serum albumin is readily available, evaluates nutritional status,[19] and prognosticates cancer survival.[12,27] Our study showed that patients who died within six months of being diagnosed with MBD more often had low preoperative serum albumin, ALC, and hemoglobin levels, whereas those who survived beyond one year were likely to have normal preoperative hemoglobin and ALC; however, these differences were not found to be statistically significant. Other reports have shown these three parameters

to have significant risks for mortality among patients with MBD in the spine, pelvis, or extremities.[12,13,18,25] Preoperative hemoglobin level was reported to be the only independent predictor of survival in early survival analyses.[12,25] Preoperative serum albumin has been reported in retrospective studies and a systematic review as an independent prognostic factor of survival in MBD from various malignancies[12,14,21,22] while ALC has been shown as an independent predictor for survival in MBD in the femur.[12] Further, low albumin levels were noted to be a general characteristic of the study population in our studies. All these findings may be because most of the patients diagnosed with MBD with concomitant pathologic fracture already represent the terminal stage of the disease.[12–14,18,23] These markers can be used for prognostication, but existing data should be corroborated by further research.

Our nonsurgical patients were either not medically fit to undergo any extensive procedure or were amenable only to systemic therapy. These conditions may have contributed to a higher mortality rate.[12,14] The surgical patients, on the other hand, were likely better candidates for surgery.[9,13,23] Despite these baseline differences, mortality did not differ between these two groups in our study. Again, these findings represent patients diagnosed with MBD as those already in the terminal stage of the disease, highlighting low survivability.

Several limitations are present in this study. The study population was selected based on search terms "metastatic bone disease," "pathologic fracture," and related keywords such as "metastatic" and "pathologic", which may have led to some cases being excluded in the process. There were also missing census files from the institute registry: six months from the year 2019, six months from the year 2018, 12 months from the year 2017, six months from the year 2016, and one month from the year 2015. Attempts made to retrieve these data were unsuccessful. These missing records contributed to the reduced sample size, which may have introduced residual confounding factors that can obscure modest but real effects. This study did not compare the mortality rates of patients with pathologic fractures to those with impending pathologic fractures. The presence of a pathologic fracture has been reported to be a negative predictor of survival.[18,25] Stratified analyses by anatomic distribution (isolated axial or appendicular involvement versus multiple skeletal disease) were not performed, which represents another limitation. This is also seen in other studies and may influence outcomes.[7,18,22] Aside from skeletal involvement, the pattern of metastatic spread influences prognosis. Visceral metastasis reaching the lungs is most common (59%), followed by the liver (15%).[4] A higher mortality rate is seen in these patients.[23] Brain metastasis is common in primary malignancies in the upper half of the body and carries a poor prognosis.[2] While bone and solid organ metastases often go hand-in-hand and indicate a poor prognosis, bone-only metastases reportedly have better outcomes.[2,4]

Other prognostic factors, such as hospital characteristics, patient comorbidities, specific surgical intervention, and surgical or medical complications, were not studied since this information was not available in our population. Patients may have had preexisting metastatic lesions identified by bone scan, without histologic confirmation. Most patients were confirmed to have MBD via biopsy on the day of surgical intervention. This occurs in up to 30% of patients with skeletal metastases.[28] Patients with an unknown primary tumor may have poorer outcomes due to delays in staging and treatment. Comorbidities, in addition to nutritional status, also contribute to the patient's surgical tolerance or postoperative complications.[28]

Treatment decisions were likely influenced by patients' overall picture as determined by the multi-disciplinary approach rather than immediate surgical indications. Patients in critical states were either not cleared up for surgery or chose to have palliative management instead. This selection bias is nearly unavoidable when comparing the mortality rates of surgical and non-surgical patients. In our center, numerous patients were worked up for MBD but did not undergo biopsy, further contributing to the low patient numbers in the non-operative group.

Peri-operative functional outcomes of patients were not considered in this study, but have been previously found to be significant risk factors for survival.[12,18,23] Furthermore, we grouped each cancer by primary location, without accounting for tumor stage, grade, and histologic subtype, all of which can influence prognosis.[12,13]

Studies involving a more homogenous population may improve the generalizability of findings. Expanding the case identification strategy, strengthening data management systems, and including patients with impending fractures may improve the representation of the sample and provide richer analysis. Collecting more detailed information on metastatic spread, tumor characteristics, comorbid conditions, complications, and perioperative functional outcomes could also allow for a more refined understanding of patient prognosis. Additionally, there may be value in exploring whether nutritional support could benefit patients with low preoperative albumin.

Conducting multicenter studies may help overcome limitations related to small sample size and single-institution bias and would allow for greater applicability of the findings across varied clinical settings. Taking these steps could lead to more accurate survival models and better support individualized care for patients with metastatic bone disease.

CONCLUSION

We found that the primary tumor site was an independent prognostic factor for survival in patients diagnosed with pathologic fractures from MBD, with primary lung malignancy having the poorest chance of survival. While preoperative serum albumin, hemoglobin, and ALC were not statistically significant predictors, they remain clinically useful as indicators

of nutritional and physiologic status when assessing surgical risk. These findings are particularly relevant in local settings where access to timely diagnostic scans may be limited. In such contexts, readily available laboratory tests can play a valuable role in guiding risk stratification and shared decision-making in the management of MBD.

A more standardized and comprehensive study design that addresses the current study's limitations may provide clearer guidance for future survival analyses in patients with pathologic fractures secondary to MBD. Conducting multicenter studies can help overcome limitations related to small sample size and single-institution bias, thereby improving the generalizability of the findings across varied clinical settings. Additional research is also needed to assess the potential benefits of nutritional supplementation in patients with low preoperative albumin levels.

ACKNOWLEDGMENTS

The authors would like to acknowledge all the members of the Institute of Orthopedics and Sports Medicine, St. Luke's Medical Center, especially our institute directors, training officer, research head, and the research committee, for their unwavering support.

STATEMENT OF AUTHORSHIP

All authors certified fulfillment of ICMJE authorship criteria.

CREDIT AUTHOR STATEMENT

KYRN: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **DKDC:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **EJRG:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition.

DATA AVAILABILITY STATEMENT

Datasets generated and analyzed are included in the published article.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

FUNDING SOURCE

None.

REFERENCES

1. Adamsbaum C, Mascard E, Guinebretière JM, Kalifa G, Dubousset J. Intralesional Ethibloc injections in primary aneurysmal bone cysts: an efficient and safe treatment. Skeletal Radiol. 2003;32(10):559–66. PMID: 12856159 DOI: 10.1007/s00256-003-0653-x
2. Huang JF, Shen J, Li X, et al. Incidence of patients with bone metastases at diagnosis of solid tumors in adults: a large population-based study. Ann Transl Med. 2020;8(7):482. PMID: 32395526 PMCID: PMC7210217 DOI: 10.21037/atm.2020.03.55
3. Behnke NK, Baker DK, Xu S, et al. Risk factors for same-admission mortality after pathologic fracture secondary to metastatic cancer. Support Care Cancer. 2017;25(2):513–21. PMID: 27704262 DOI: 10.1007/s00520-016-3431-8
4. Narazaki DK, De Neto Alverga CC, Baptista AM, Caiero MT, de Camargo OP. Prognostic factors in pathologic fractures secondary to metastatic tumors. Clinics. 2006;61(4):313–20. PMID: 16924322 DOI: 10.1590/s1807-59322006000400007
5. Vincenzi B, Frezza AM, Schiavon G, et al. Bone metastases in soft tissue sarcoma: a survey of natural history, prognostic value and treatment options. Clin Sarcoma Res. 2013;3(1):6. PMID: 23594799 PMCID: PMC3637638 DOI: 10.1186/2045-3329-3-6
6. Forsberg JA, Wedin R, Boland PJ, Healey JH. Can we estimate short- and intermediate-term survival in patients undergoing surgery for metastatic bone disease? Clin Orthop Relat Res. 2017;475(4):1252–61.
7. Guzik G. Oncological and functional results after surgical treatment of bone metastases at the proximal femur. BMC Surg. 2018;18(1):5. PMID: 29370790 PMCID: PMC5784608 DOI: 10.1186/s12893-018-0336-0
8. Cho JH, Ha JK, Hwang CJ, Lee DH, Lee SL. Patterns of treatment for metastatic pathological fractures of the spine: The efficacy of each treatment modality. Clin Orthop Surg. 2015;7(4):476–82. PMID: 26640631 PMCID: PMC4667116 DOI: 10.4055/cios.2015.7.4.476
9. Willeumier JJ, Linden YM, van de Sande MAJ, Dijkstra PDS. Treatment of pathological fractures of the long bones. EFORT Open Rev. 2016;1(5):136–45. PMID: 28461940 PMCID: PMC5367617 DOI: 10.1302/2058-5241.1.000008
10. Damron TA, Mann KA. Fracture risk assessment and clinical decision making for patients with metastatic bone disease. J Orthop Res. 2020;38(6):1175–90. PMID: 32162711 PMCID: PMC7225068 DOI: 10.1002/jor.24660
11. Chow E, Zeng L, Salvo N, et al. Update on the systematic review of palliative radiotherapy trials for bone metastases. Clin Oncol (R Coll Radiol). 2012;24(2):112–24. PMID: 22130630 DOI: 10.1016/j.clon.2011.11.004
12. Nathan SS, Healey JH, Mellano D, et al. Survival in patients operated on for pathologic fracture: Implications for end-of-life orthopedic care. J Clin Oncol. 2005;23(25):6072–82. PMID: 16135474 DOI: 10.1200/JCO.2005.08.104
13. Nathan SS, Chan L, Tan WL, et al. The need for a system of prognostication in skeletal metastasis to decide best end-of-life care - A call to arms. Ann Acad Med Singapore. 2010;39(6):476–81. PMID: 20625625
14. Sim DS, Zainul-Abidin S, Sim EY, et al. Serum albumin level predicts survival after surgical treatment of metastatic femur fractures: A retrospective study. J Orthop Surg Res. 2020;15(1):128. PMID: 32245389 PMCID: PMC7118955 DOI: 10.1186/s13018-020-01632-7
15. Bauer HCF, Wedin R. Survival after surgery for spinal and extremity metastases: Prognostication in 241 patients. Acta Orthop. 1995;66(2):143–6. PMID: 7740944 DOI: 10.3109/17453679508995508
16. 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. PMID: 11224867 DOI: 10.1097/00007632-200102010-00016
17. 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. PMID: 16205345 DOI: 10.1097/01.brs.0000180401.06919.a5
18. Sørensen MS, Gerds TA, Hindsø K, et al. Prediction of survival after surgery due to skeletal metastases in the extremities. Bone Joint J. 2016;98-B(2):271–7. PMID: 26850435 DOI: 10.1302/0301-620X.98B2.36107
19. Rocha NP, Fortes RC. Total lymphocyte count and serum albumin as predictors of nutritional risk in surgical patients. Arq Bras Cir Dig. 2015;28(3):193–6. PMID: 26537145 PMCID: PMC4737361 DOI: 10.1590/S0102-67202015000300012

20. Cross MB, Yi PH, Thomas CF, Garcia J, Della Valle CJ. Evaluation of malnutrition in orthopaedic surgery. J Am Acad Orthop Surg. 2014;22(3):193–9. PMID: 24603829 DOI: 10.5435/JAAOS-22-03-193
21. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J. 2010;9:69. PMID: 21176210 PMCID: PMC3019132 DOI: 10.1186/1475-2891-9-69
22. Kotian RN, Puvanesarajah V, Rao S, El Abiad JM, MOrris CD, Levin AS. Predictors of survival after intramedullary nail fixation of completed or impending pathologic femur fractures from metastatic disease. Surg Oncol. 2018;27(3):462–7. PMID: 30217303 DOI: 10.1016/j.suronc.2018.05.028
23. Hill T, D'Alessandro P, Murray K, Yates P. Prognostic factors following pathological fractures. ANZ J Surg. 2015;85(3):159–63. PMID: 25182567 DOI: 10.1111/ans.12830
24. Katagiri H, Takahashi M, Wakai K, Sugiura H, Kataoka T, Nakanishi K. Prognostic factors and a scoring system for patients with skeletal metastasis. J Bone Joint Surg Br. 2005;87(5):698–703. PMID: 15855375 DOI: 10.1302/0301-620X.87B5.15185
25. Hansen BH, Keller J, Laitinen M, et al. The Scandinavian Sarcoma Group skeletal metastasis register: Survival after surgery for bone metastases in the pelvis and extremities. Acta Orthop Scand Suppl. 2004;75(311):11–5. PMID: 15188660 DOI: 10.1080/00016470410001708270
26. Katagiri H, Okada R, Takagi T, et al. New prognostic factors and scoring system for patients with skeletal metastasis. Cancer Med. 2014;3(5):1359–67. PMID: 25044999 PMCID: PMC4302686 DOI: 10.1002/cam4.292
27. Karhade A V., Thio QCBS, Kuverji M, Ogink PT, Ferrone ML, Schwab JH. Prognostic value of serum alkaline phosphatase in spinal metastatic disease. Br J Cancer. 2019;120(6):640–6. PMID: 30792532 PMCID: PMC6461951 DOI: 10.1038/s41416-019-0407-8
28. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr. Prognostic importance of comorbidity in a hospital-based cancer registry. J Am Med Assoc. 2004;291(20):2441–7. PMID: 15161894 DOI: 10.1001/jama.291.20.2441