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# SURVIVAL PREDICTORS IN CANCER PATIENTS WITH BONE METASTASIS: RETROSPECTIVE COHORT SINGLE-CENTER STUDY

**Background**. Bone metastasis, a frequent complication in cancer patients, is associated with a significant decline in quality of life and reduced survival. Overall survival prognosis is critical for selecting the optimal treatment strategy, particularly for planning orthopedic surgery in patients with bone metastasis. The **aim** of the study was to delineate prognostic factors for overall survival in patients with bone metastasis following orthopedic surgery. **Materials and Methods**. 136 patients with bone metastasis treated at the National Cancer Institute (Ukraine) between 2006 and 2025 were included in a retrospective, single-center cohort study. The effects of the primary tumor type, number of metastases, presence of a pathologic fracture, prior treatment, and type of surgery on overall survival were assessed. Survival was analyzed using the Kaplan—Meier method, and the log-rank test was used for group comparisons. Multivariate Cox regression was used to identify independent prognostic factors. **Results**. The median overall survival was 32.8 months. Patients with solitary metastases had significantly better survival than those with multiple metastases (median 44.8 vs 18.4 months; $p = 0.021$). Pathologic fractures were associated with worse survival (median 25.4 vs 64.6 months; $p = 0.014$). In multivariate analysis, multiple metastases (HR 1.95; 95% CI 1.18—3.22; $p = 0.009$) and pathologic fractures (HR 1.82; 95% CI 1.05—3.17; $p = 0.034$) were identified as independent adverse factors. Combined treatment was associated with a lower risk of death (HR 0.48; 95% CI 0.26—0.91; $p = 0.023$). The type of surgery was not an independent factor affecting survival. **Conclusion**. The number of metastases and the presence of a pathologic fracture are key prognostic factors affecting survival in patients with bone metastasis. The results delineating prognostic factors in patients with bone metastasis may be useful for risk stratification and personalized treatment.

**Keywords:** bone metastasis, survival, prognosis, Kaplan—Meier method, Cox regression, pathologic fracture, oncoorthopedics.

5.1% of all cancer patients have bone metastasis (BM) at diagnosis. They occur frequently in breast cancer (65%—70%), prostate cancer (65%—90%), lung cancer (17%—64%), renal cell cancer (20%—25%), and thyroid cancer (65%) [1]. The number of patients with BM increases as advanced medical management and radical surgery improve the overall survival (OS) of cancer patients. BM may be a cause of skeletal-related events like pain syndrome in bones (60%—84%), pathologic fractures (9%—29%), spinal cord compression with neurological disorders (15%—20%), and hypercalcemia (20%),

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which adversely affect the quality of life and worsen the prognosis. The estimated one-year survival following orthopedic surgery is 36% [2]. In Ukraine, late diagnosis and the lack of unified treatment algorithms adversely affect treatment outcomes for patients with BM. The differential diagnosis of BM requires a thorough examination to exclude synchronous or metachronous primary bone neoplasms [3]. The use of prognostic tools to assess the general conditions and survival of patients, as well as the selection of the appropriate treatment method, is considered an indispensable component of the complex approach for the treatment of patients with BM. The prognosis for survival in such patients is of great importance in selecting an optimal treatment strategy to improve the patient's quality of life and decrease the risk of postoperative complications [4]. As a method of choice for improving the quality of life, in certain situations, orthopedic interventions may even be unfavorable from a prognostic view [5]. Opposed to surgical methods, a broad armamentarium of non-surgical treatment approaches is available depending on the localization, size, and number of BM. The aim of the study was to assess the associations between the type of primary tumor, the number of BM, the type of surgery, the presence of a pathologic fracture, and the survival of cancer patients with BM.

## Materials and Methods

The retrospective single-center cohort study included patients treated at the National Cancer Institute (Kyiv, Ukraine). The patients' files covering January 2006 to December 2025 were selected from the National Cancer Registry. Adult patients (≥18 years) with metastatic bone lesions and the following orthopedic interventions were included in the study. The inclusion criteria were: age ≥18 years, confirmed BM, orthopedic interventions due to metastatic bone lesions, and availability of follow-up data. The exclusion criteria were: age <18 years, primary bone tumor without metastatic lesions, incompleteness of clinical data, and surgeries unrelated to BM treatment.

The clinical data were retrieved from the cancer registry and the patients' records. The following data were taken into account: the demographic characteristics of the patients, type of primary tumor, the number of metastases (solitary or multiple), localization of metastases, presence of a pathological fracture or impending fracture, type of surgery, prior cancer treatment, postoperative complications, and dates of surgery and last follow-up or date of death. The surgery was attributed to one of the two major types — endoprosthetics and osteosynthesis. In the survival analysis of the present study, cases of plate fixation and interlocking intramedullary nailing were combined into a single osteosynthesis group. The follow-up period was calculated from the surgery date to the date of the last visit or the date of death. The patients alive at the end of the present study were considered censored in the survival analysis. The primary endpoint for the analysis was the OS. The postoperative complications, such as implant failure, local tumor progression, metal-associated infection, or endoprosthesis dislocation, were considered secondary endpoints.

The data were loaded and analyzed in Microsoft Excel. For statistical processing, Python (3.x version) was used with *pandas*, *numpy*, *lifelines,* and *matplotlib libraries.* Survival was assessed by the Kaplan–Meier method, with survival curves compared by the log-rank test. The effects of prognostic factors were evaluated by the Cox proportional hazards model. The multivariate analysis included the following independent OS predictors: the type of primary tumor, number of metastases (solitary or multiple), presence of a pathological fracture or impending fracture, type of surgery, and prior cancer treatment. The results were presented as a hazard ratio (HR) with a 95% confidence interval (CI). The assumption of hazard proportionality was checked graphically. The difference was considered significant at $p < 0.05$.

## Results

Of the 187 patients with orthopedic surgery due to metastatic bone lesions, 136 patients were included in this study. The most frequent primary tumor in our study was renal cancer (39.7%), followed by breast cancer (23.5%), bone cancer/sarcoma (8.1%), and lung cancer (3.7%). Other cancers (prostate, uterine, colorectal, thyroid cancers, and CNS tumors, etc.) accounted for the rest of 25% of the cases. In 82 patients (60.3%), BMs were solitary, and in 52 (38.2%) — multiple. In two cases, the BM number was not recorded in the files. 93 patients

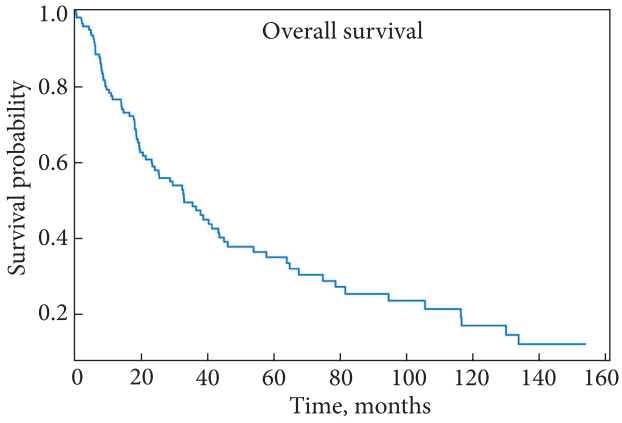


***Fig. 1.*** The Kaplan—Meier analysis of OS in patients who underwent orthopedic surgery due to metastatic bone lesions

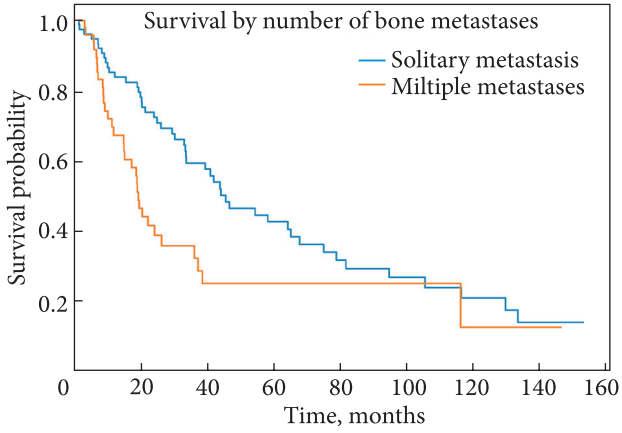


***Fig. 2.*** The Kaplan—Meier curves for comparison of OS for patients with solitary and multiple metastases ($p = 0.021$)

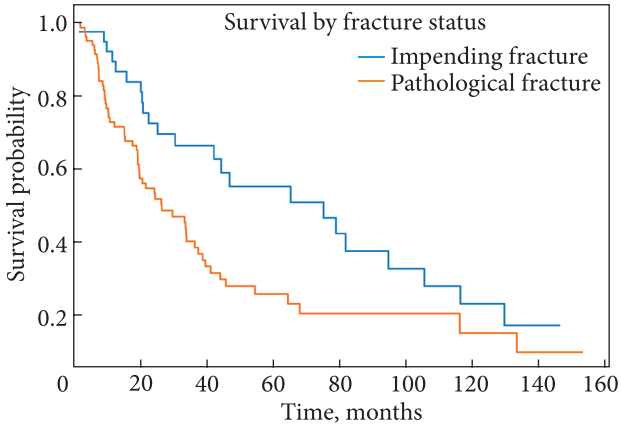


***Fig. 3.*** The Kaplan—Meier curves demonstrating OS depending on fracture status (pathological fracture vs impending fracture). $p = 0.014$

(68.4%) were hospitalized due to pathological fractures, while 43 patients (31.6%) were treated because of the risk of pathological fractures. The following types of surgery were performed to treat metastatic bone lesions: plate fixation (50.7%), endoprosthetics (35.5%), and interlocking intramedullary nailing (5.9%). In 8.1% of cases, other techniques were utilized. 64.7% of surgical interventions were radical and 34.3% palliative.

The OS median in patients who underwent orthopedic surgery for metastatic bone lesions was 32.8 months (Fig. 1). Patients with solitary metastases had significantly better OS than those with multiple metastases (median 44.8 vs 18.4 months, $p = 0.021$) (Fig. 2).

The presence of a pathologic fracture was associated with a significant decrease in OS. The OS median in patients with pathologic fractures was significantly less compared to patients with impending fractures (25.4 months vs 64.6 months, $p = 0.014$) (Fig. 3).

OS varied significantly in patients with different types of primary tumors, with the longest median (41.2 months) in breast cancer and the shortest median (18.1 months) in lung cancer (Fig. 4). Among the studied patients, in 40 cases (29.4%), surgery was the only modality of the previous treatment of the underlying disease, while in 96 patients (70.6%), a combined treatment was employed. Although there was no significant difference in OS depending on the previous treatment (single modality vs combined modality, $p = 0.505$) (Fig. 5), in the multivariate analysis, combined treatment was identified as an independent factor associated with a decreased risk of death. This discrepancy may be explained by the non-homogeneous distribution of prognostically unfavorable factors among the groups.

Osteosynthesis (plate fixation and interlocking intramedullary nailing) was performed in 77 patients, while endoprosthetics — in 48 patients. In the osteosynthesis group, the OS median was 32.3 months, and in the endoprosthetics group — 41.2 months. Nevertheless, despite the trend of better survival in the endoprosthetics group, the difference was not significant ($p = 0.386$) (Fig. 6).

Multivariate logistic regression was used to find out independent unfavorable predictors (Table). The following factors were identified as the most significant independent unfavorable predictors: multiple metastases (HR 2.13; 95% CI 1.30—3.50; $p = 0.003$) and the presence of a pathological fracture (HR 1.81; 95% CI 1.04—3.14; $p = 0.036$). The combined previous treatment (surgery + other modalities) was significantly associated with a de-

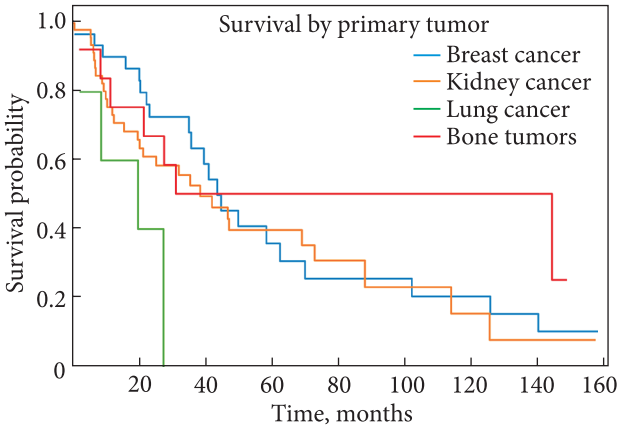


***Fig. 4.*** The Kaplan—Meier curves demonstrating OS depending on the tumor type

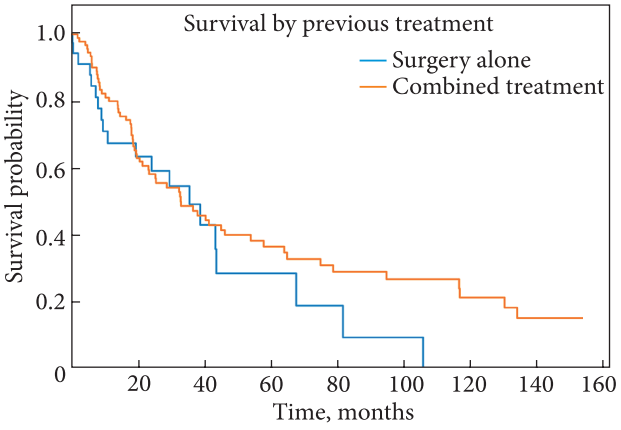


***Fig. 5.*** The Kaplan—Meier curves demonstrating OS depending on the modality of the previous treatment for primary tumor (surgery alone vs combined treatment). The OS difference is not significant ($p = 0.505$)

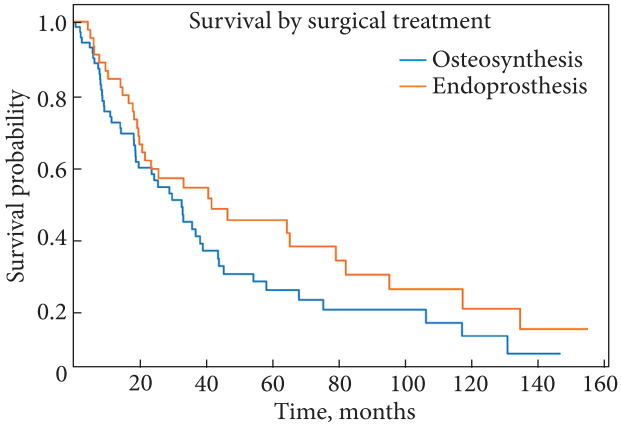


***Fig. 6.*** The Kaplan—Meier curves demonstrating OS of patients with BM in groups of osteosynthesis and endoprosthetics ($p = 0.386$)

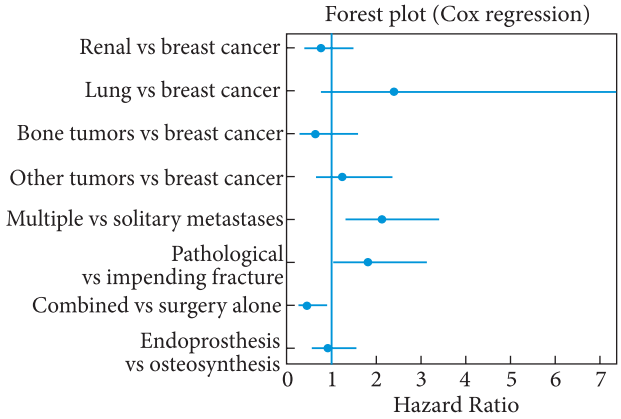


***Fig. 7.*** The forest plot of multivariate logistic Cox regression analysis of OS

crease in the risk of death compared to surgery only (HR 0.47; 95% CI 0.25—0.90; $p = 0.023$). Neither the type of cancer nor the type of surgery was an independent OS predictor (Table, Fig. 7).

Complications were registered in 18 patients of 136 (13.2%). The most frequent type of complications was the fracture of the metal plate (9 cases). In 5 cases, local tumor progression at the resection site occurred. There were three cases of metal-associated infection and one case of dislocation of the endoprosthesis head.

## Discussion

We have analyzed factors affecting the survival of patients with BM after orthopedic surgery. The number of metastases, the presence of a pathological fracture, and the type of previous treatment were identified as the most significant predictors

**Risk factors associated with OS (multivariate logistic regression analysis)**

| Variables | HR | 95% CI | *p* |
|---|---|---|---|
| Renal cancer vs breast cancer | 0.77 | 0.40—1.48 | 0.429 |
| Lung cancer vs breast cancer | 2.39 | 0.78—7.34 | 0.127 |
| Bone cancer vs breast cancer | 0.64 | 0.27—1.54 | 0.320 |
| Other cancers vs breast cancer | 1.25 | 0.65—2.37 | 0.506 |
| Multiple metastases vs solitary metastases | **2.13** | **1.30—3.50** | **0.003** |
| Pathological fracture vs impending fracture | **1.81** | **1.04—3.14** | **0.036** |
| Combined treatment vs surgery only | **0.47** | **0.25—0.90** | **0.023** |
| Endoprosthetics vs osteosynthesis | 0.94 | 0.57—1.56 | 0.812 |

of OS. In our study, OS was slightly higher than in several international clinical studies [1, 6—10]. This may be explained by the peculiarities of patient selection, particularly the inclusion of patients with a more favorable prognosis and predominantly solitary metastases. Our results confirmed that the number of metastatic lesions is a key prognostic factor. This aligns with the literature, which reports worse survival in patients with multiple metastases [7, 9]. The pathological fracture identified as an independent unfavorable prognostic factor in our study is consistent with the data from Raschka et al. [10] and the conclusions of the current meta-analysis [11]. Unadjusted Cox proportional hazards regression analysis did not reveal a significant difference by the modality of the previous treatment for the primary tumor (surgery alone vs combined treatment). Nevertheless, the multivariate analysis demonstrated a significant decrease in the risk of death in patients who received combined treatment. This may be explained by the effect of confounding factors [1, 6]. The OS varied depending on the type of primary tumor, as shown earlier in several studies [5, 7]. It should be noted that the distribution by the types of cancer in our cohort, in general, is consistent with that in other studies. Nevertheless, in our study, the proportion of cases of prostate and thyroid cancer was relatively low, although these cancer types are frequently associated with BM [1, 5]. The OS rates for different cancer types were generally compatible with those in other studies, namely, a better prognosis was for breast cancer and renal cancer, while the worst one was for lung cancer [9, 12]. The absence of a significant difference among the surgery types agrees with the data by Raschka et al. [10]. The rate of postoperative complications (13.2%) was within the range of this parameter in other studies (10% — 20%) [10, 13, 14]. Our results highlight the importance of a multidisciplinary approach in the treatment of patients with BM [1, 13, 15].

Although there are some limitations in our study, in particular, its retrospective design and single-center pattern, our findings may serve as the basis for the development of clinically oriented prognostic models.

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ПРЕДИКТОРИ ВИЖИВАНОСТІ ПАЦІЄНТІВ
ІЗ КІСТКОВИМИ МЕТАСТАЗАМИ ЗЛОЯКІСНИХ
НОВОУТВОРЕНЬ: РЕТРОСПЕКТИВНЕ КОГОРТНЕ
МОНОЦЕНТРОВЕ ДОСЛІДЖЕННЯ

**Стан питання.** Метастатичне ураження кісток є частим ускладненням злоякісних новоутворень, асоційованим зі значним зниженням якості життя й виживаності пацієнтів. Прогнозування виживаності пацієнтів є ключовим для вибору оптимальної тактики лікування, зокрема ортопедичних втручань. **Метою дослідження** було визначити прогностичні фактори загальної виживаності в пацієнтів із метастазами в кістки, яким виконано ортопедичні хірургічні втручання. **Матеріали та методи.** Проведено ретроспективне когортне моноцентрове дослідження 136 пацієнтів із кістковими метастазами, прооперованих у Національному інституті раку (Київ, Україна) в період від 2006 до 2025 року. Аналізували вплив типу первинної пухлини, кількості метастазів, наявності патологічного перелому, виду попереднього лікування та типу оперативного втручання на загальну виживаність. Виживаність оцінювали методом Каплана—Мейєра, порівняння груп — за допомогою логрангового критерію. Для визначення незалежних прогностичних факторів використовували багатофакторну регресію Кокса. **Результати.** Медіана загальної виживаності становила 32,8 місяця. Пацієнти із солітарними метастазами мали достовірно кращу виживаність порівняно з пацієнтами з множинними метастазами (медіана 44,8 проти 18,4 місяця; $p = 0{,}021$). Наявність патологічного перелому асоціювалася зі зниженням виживаності (25,4 проти 64,6 місяця; $p = 0{,}014$). У багатофакторному аналізі незалежними несприятливими факторами були множинні метастази (HR 1,95; 95% ДІ 1,18—3,22; $p = 0{,}009$) та патологічний перелом (HR 1,82; 95% ДІ 1,05—3,17; $p = 0{,}034$). Комбіноване лікування асоціювалося зі зниженням ризику смерті (HR 0,48; 95% ДІ 0,26—0,91; $p = 0{,}023$). **Висновки**. Отримані результати можуть бути використані для стратифікації ризику та персоналізації лікування у пацієнтів із метастазами в кістки, яким виконано ортопедичні хірургічні втручання.

**Ключові слова:** кісткові метастази, виживаність, метод Каплана—Мейєра, регресія Кокса, патологічний перелом, онкоортопедія.