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Red cell distribution width-to-albumin ratio as a prognostic indicator for giant cell tumor of bone

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Abstract

Giant cell tumor of bone (GCTB) is a locally aggressive, benign neoplasm with the risk of recurrence and metastasis. Cheap and reliable prognostic markers remain limited. This study aimed to evaluate the prognostic significance of routine hematologic and biochemical parameters, particularly the red cell distribution width (RDW)-to-albumin ratio and the systemic immune-inflammation index (SII), in patients with GCTB. Patients treated surgically for histologically confirmed GCTB between 2010 and 2024 were retrospectively analyzed. Preoperative laboratory data, including RDW, serum albumin, and derived indices, were reviewed. Logistic regression and receiver operating characteristic (ROC) analyses were performed to assess predictors of recurrence and metastasis. A total of 72 patients (36 women, 36 men; mean age 30.4 years) were included. During follow-up, 23.6% experienced recurrence and 20.8% developed metastasis. Patients with recurrence had significantly lower albumin (3.85 vs. 4.12 g/dL, p=0.002) and higher RDW-to-albumin ratios (3.48 vs. 3.22, p=0.005). Logistic regression identified albumin as a protective factor (OR=0.136, p=0.004) and RDW-to-albumin as an independent risk factor (OR=3.13, p=0.020). ROC analysis demonstrated moderate predictive ability for both markers (AUC 0.761 for albumin; 0.733 for RDW-to-albumin). For metastasis, RDW-to-albumin above 4.4 was associated with a twofold higher probability (AUC=0.671). Campanacci grade, tumor volume, and SII were not significantly related to outcomes. In conclusion, the RDW-to-albumin ratio showed moderate prognostic performance, comparable to other inflammation-based indices, and may serve as a simple, inexpensive adjunct for risk stratification pending external validation.

Keywords: Giant cell tumor of bone, recurrence, metastasis, red cell distribution width, albumin, systemic inflammation

Introduction

Giant cell tumor of bone (GCTB) is a locally aggressive neoplasm that typically arises in the epimetaphyseal region of long bones in young adults [1,2]. Although classified as a benign tumor, GCTB is characterized by a high propensity for local recurrence and, in a subset of patients, pulmonary metastasis [3–5]. These clinical features pose a significant challenge in long-term management, highlighting the need for reliable prognostic markers. Campanacci grade, tumor size, and resection type have been associated with recurrence in previous studies [6–8]. Building on this evidence, we investigated whether routine hematologic indices could provide additional prognostic value in GCTB.

In recent years, increasing attention has been directed toward systemic markers of inflammation and nutrition, which are readily available from routine laboratory tests. Indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have been linked to prognosis in various malignancies [9,10]. Similarly, the red cell distribution width (RDW), which reflects variability in erythrocyte size, has been associated with systemic inflammation and adverse outcomes in both hematologic and solid tumors [11–14].

More recently, composite parameters such as the RDW-to-albumin ratio have been proposed to capture both nutritional and inflammatory components simultaneously, offering a potentially

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stronger prognostic signal than individual markers. However, the role of these indices in GCTB remains poorly defined.

The present study was designed to evaluate the prognostic significance of preoperative hematologic and biochemical markers in patients with GCTB. Although giant cell tumour of bone is benign on histology, its stromal cells create a RANKL- and IL-6-rich milieu that drives osteoclast activity and bone loss. The clinical effectiveness of denosumab in this setting supports the central role of the RANKL pathway [15–17]. Inflammation disrupts erythropoiesis, increasing RDW, while serum albumin—as a negative acute-phase reactant—declines [18]. Our hypothesis was that RDW-to-albumin ratio and SII might provide additional preoperative prognostic information for recurrence and metastasis. By focusing on accessible, inexpensive laboratory parameters, this work seeks to provide practical tools that may aid risk stratification and follow-up planning in clinical practice.

Material and Methods

Study Design and Patient Selection

This study was conducted as a retrospective, single-center analysis. Patients who underwent surgical treatment for histologically confirmed giant cell tumor of bone (GCTB) between 2010 and 2024 were considered eligible. Only cases with complete preoperative clinical data and laboratory results were included. Patients with missing data, active infections, or systemic inflammatory diseases that could affect hematologic values were excluded. We used preoperative laboratory values obtained at a clinically stable visit and excluded patients who had an acute intercurrent infection or a diagnosed systemic inflammatory disease at the time of blood sampling.

Clinical and Demographic Variables

Demographic characteristics such as age and sex, as well as tumor-related variables including anatomical location, Campanacci grade, tumor volume, malignant transformation, recurrence, metastasis, and survival status, were obtained from patient charts and electronic hospital records. Campanacci grades and imaging measurements were assigned independently by two experienced surgeons blinded to recurrence/metastasis outcomes. Disagreements were resolved by consensus in a joint review.

Laboratory Parameters

Preoperative routine blood tests were reviewed for hemoglobin, total leukocyte count, neutrophils, lymphocytes, monocytes, platelets, red cell distribution width (RDW), and serum albumin. From these baseline measurements, additional inflammatory indices were calculated: the neutrophil-to-platelet ratio (NPR), the systemic immune-inflammation index (SII, defined as neutrophil×platelet/lymphocyte), and the RDW-to-albumin ratio. These variables were selected to provide a comprehensive view of the patients' systemic inflammatory and nutritional status.

Statistical Analysis

All analyses were performed using JAMOVI (version 2.7.9) statistical software. Continuous variables were summarized as the mean ± standard deviation or the median with range, depending on the distribution, while categorical variables were expressed as frequencies and percentages. Group comparisons were performed using the Mann–Whitney U test. Logistic regression models were applied to evaluate predictors of recurrence, with serum albumin and RDW-to-albumin ratio entered as independent variables. Model discrimination was assessed using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated, along with the optimal cut-off values. Statistical significance was defined as a two-tailed p-value<0.05.

Ethical Considerations

The study was designed and conducted in accordance with the principles of the Declaration of Helsinki. All patient data were anonymized prior to analysis, and approval was obtained from the institutional ethics committee.

Results

Demographic and Clinical Characteristics

A total of 72 patients were included, with a mean age of 30.4 years (range, 8–66). The cohort consisted of 36 women and 36 men, and tumor laterality was nearly balanced (48.6% right, 51.4% left). Campanacci grades were distributed as 5.6% Grade 1, 68.1% Grade 2, and 26.4% Grade 3. Tumor volume was ≤50 cm^3 in 45.8%, 50–100 cm^3 in 23.6%, and >100 cm^3 in 30.6% of cases. Malignant transformation occurred in 5.7%. At follow-up, recurrence was observed in 23.6%, metastasis in 20.8%, and a mortality rate of 2.8% (Table 1).

Recurrence Analysis

Patients with recurrence had significantly lower serum albumin and higher RDW-to-albumin ratios compared with those without recurrence (Table 2). Median albumin was 3.85 g/dL in the recurrence group versus 4.12 g/dL in the non-recurrence group (p=0.002), while RDW-to-albumin ratio was 3.48 versus 3.22 (p=0.005). Other parameters, such as hemoglobin, leukocyte count, platelet count, and derived ratios, showed no meaningful differences between groups. Logistic regression indicated that albumin was an independent protective factor (OR 0.136; 95% CI 0.034–0.537; p=0.004), whereas RDW-to-albumin was an independent predictor of recurrence (OR 3.13; 95% CI 1.19–8.21; p=0.020). ROC analysis showed that both albumin (AUC 0.761; cut-off ~4.0 g/dL) and RDW-to-albumin (AUC 0.733; cut-off ~4.37) were able to distinguish recurrent from non-recurrent cases with moderate accuracy (Figure 1) (Table 3).

Metastasis Analysis

Patients who developed metastasis had lower albumin (median 3.74 vs. 4.10 g/dL; p=0.032) and higher RDW-to-albumin ratios (median 3.45 vs. 3.23; p=0.046). The Neutrophil-to-platelet ratio (p=0.040) and monocyte-to-lymphocyte ratio (p=0.036)

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were also higher in patients with metastasis, whereas SII did not differ significantly. Neither Campanacci grade nor tumor volume showed an association with recurrence or metastasis. Malignant transformation was rare and not related to any of the hematological or biochemical markers examined.

Logistic regression suggested that the RDW-to-albumin ratio increased the likelihood of metastasis, though the result did not reach statistical significance (OR 1.85;95% CI 0.92–3.69; p=0.083). ROC curve analysis indicated only moderate discriminative performance (AUC 0.671) (Figure 2). A ratio above approximately 4.4 was associated with a clear increase in metastatic probability, rising from 13.5% at lower values to over 32% at higher values. At this threshold, sensitivity was 53% and specificity 65%, with an overall accuracy of 62.7%. Although the predictive power was limited, the trend suggests a potential role of RDW-to-albumin as a marker of metastatic risk.

Table 1. Baseline demographics

Characteristic	Value
N (patients)	72
Age, years	Mean (SD) 30.4 (13.4); range 8–66
Sex	Female 36 (50.0%); Male 36 (50.0%)
Side	Right 35 (48.6%); Left 37 (51.4%)
Campanacci grade	Grade 1: 4 (5.6%); Grade 2: 49 (68.1%); Grade 3: 19 (26.4%)
Tumor volume (cm³)	0–50: 33 (45.8%); 50–100: 17 (23.6%); >100: 22 (30.6%)
Malignant transformation	4 (5.7%)
Local recurrence	17 (23.6%)
Metastasis	15 (20.8%)

Values are n (%) unless otherwise specified. Age reported as mean (SD) and range

Table 2. Comparison of hematological and biochemical parameters according to recurrence and metastasis status

Parameter	Recurrence (+) Median	Recurrence (–) Median	p value	Metastasis (+) Median	Metastasis (–) Median	p value
Albumin (g/dL)	3.85	4.12	0.002	3.74	4.10	0.032
RDW/Albumin ratio	3.48	3.22	0.005	3.45	3.23	0.046
Neutrophil-to-platelet ratio (NPR)	0.018	0.016	0.282	0.020	0.016	0.040
Monocyte-to-lymphocyte ratio (MLR)	0.190	0.220	0.599	0.280	0.200	0.036
Systemic immune-inflammation index (SII)	753	700	0.346	812	700	0.188

ns: not significant, ↑: elevated compared to reference group

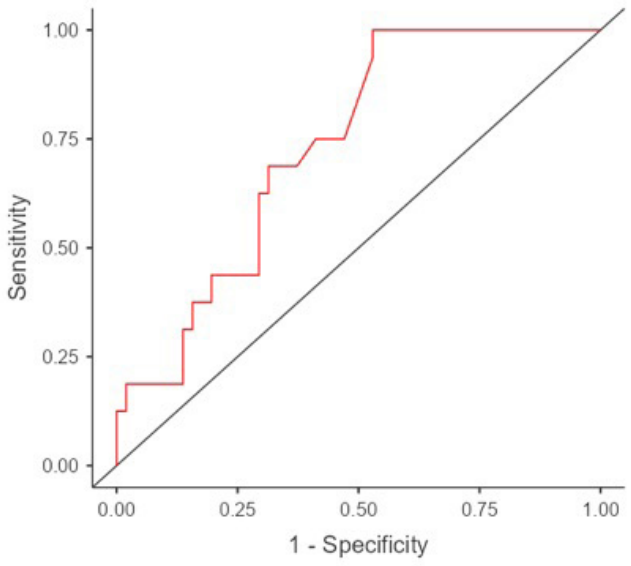

Figure 1. ROC curve for RDW-to-albumin ratio in predicting recurrence

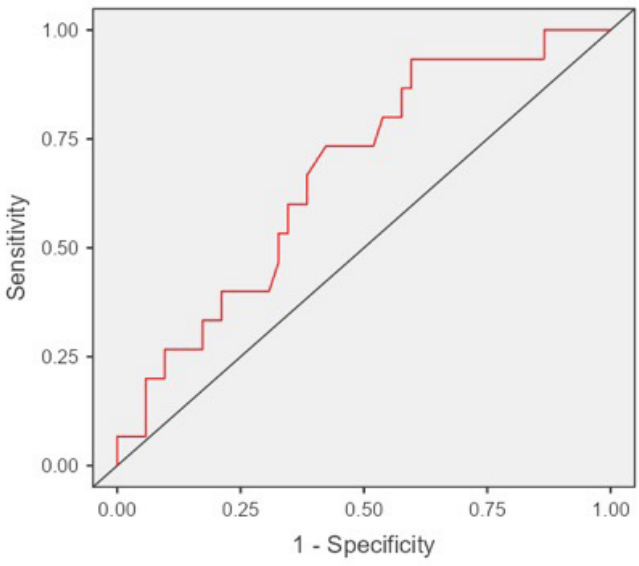

Figure 2. ROC curve for RDW-to-albumin ratio in predicting metastasis

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Table 3. ROC analysis for RDW-to-albumin ratio in predicting recurrence and metastasis

Biomarker	Outcome	AUC	Cut-off value	Sensitivity (%)	Specificity (%)
RDW/Albumin ratio	Recurrence	0.733	~4.37	68	66
RDW/Albumin ratio	Metastasis	0.671	~4.4	53	65

Discussion

Although giant cell tumor of bone (GCTB) is histologically benign, its clinical course is often unpredictable, and recurrence remains a major concern even after adequate surgery [19]. In the present series, we observed that both serum albumin and the RDW-to-albumin ratio were significantly associated with local recurrence, while higher RDW-to-albumin values also tended to accompany metastatic disease. Patients with elevated RDW-to-albumin ratios had nearly a twofold increase in metastatic probability, particularly when the ratio exceeded 4.4. In contrast, tumor volume, and SII showed no significant associations with recurrence or metastasis. These findings suggest that routine biochemical and hematologic parameters, particularly RDW-to-albumin, may provide simple yet valuable insight into disease behavior in GCTB.

Inflammation-based indices have gained increasing attention as surrogate markers of tumor behavior. The neutrophil-to-lymphocyte ratio (NLR) has been linked to recurrence [20,21] and metastasis in several malignancies and was reported to triple the risk of relapse in GCTB when exceeding a threshold of 2.25 [22]. However, other inflammation-related indices such as the RDW-to-albumin ratio and the systemic immune-inflammation index (SII) have also been investigated, as they may better reflect the combined systemic inflammatory and nutritional status influencing tumor progression.

RDW reflects anisocytosis and underlying disturbances in erythropoiesis, which may occur in the setting of chronic inflammation and oxidative stress[12,23]. Elevated RDW has been independently linked to poor outcomes in various cancers, including osteosarcoma and colorectal carcinoma, and has been suggested as a marker of a tumor-promoting inflammatory environment [11,12]. Serum albumin, conversely, reflects both nutritional reserve and systemic inflammatory burden. Reduced albumin levels are associated with impaired immune competence and increased tumor aggressiveness [24]. Combining these two parameters into the RDW-to-albumin ratio may therefore provide a broader representation of the host–tumor interaction. Our findings align with this concept, demonstrating that patients with higher RDW-to-albumin ratios experienced both higher recurrence and a trend toward metastasis.

GCTB develops within an inflammatory, osteoclast-driven milieu. Stromal tumor cells up-regulate RANKL and recruit osteoclast-type giant cells, while cytokines such as IL-6 intensify bone resorption[15–17]. These local signals have systemic echoes: RDW tends to rise when inflammation disrupts erythropoiesis, and serum albumin—as a negative acute-phase reactant—falls. The RDW/albumin ratio brings these two responses into a single, low-cost measure and can reflect a background that favors local aggressiveness and earlier recurrence, even in a tumor with benign histology. Our results are in line with prior GCTB reports linking inflammation-based indices (e.g., NLR, F-NLR, PNI) to recurrence and extend this concept to RDW/albumin as a preoperative marker[8,11,13,20,21].

RDW has gained increasing recognition as a marker of adverse outcomes in solid tumors. A comprehensive meta-analysis demonstrated that elevated RDW was consistently linked to worse overall and disease-free survival across multiple cancer types[13]. Similarly, in osteosarcoma, higher RDW was associated with metastasis and poor chemotherapy response, confirming its value as an independent prognostic factor [12]. Our findings extend this evidence to GCTB, indicating that even in a tumor considered benign but locally aggressive, RDW-based markers may provide clinically meaningful risk stratification.

Serum albumin is another well-established prognostic marker reflecting nutritional reserve and systemic inflammatory status. Hypoalbuminemia has been shown to predict poor outcomes in colorectal and other cancers [25–27]. In our study, decreased albumin was independently associated with recurrence, while its combination with RDW in the RDW-to-albumin ratio provided stronger predictive capacity. This supports the idea that composite indices integrating nutritional and inflammatory components may outperform single markers.

An interesting observation was the lack of prognostic significance for the systemic immune-inflammation index (SII). Although SII has been validated in several solid malignancies, it failed to show significance in our cohort[10,28,29]. This may reflect differences in tumor biology: unlike carcinomas, GCTB is characterized mainly by local aggressiveness rather than systemic immune dysregulation. Furthermore, albumin and RDW may more directly capture nutritional and hematopoietic alterations, providing a stronger signal in this context.

Taken together, these results indicate that routinely obtained laboratory parameters, particularly the RDW-to-albumin ratio, may assist in identifying patients at higher risk for recurrence or metastasis following surgery for GCTB. While the predictive power of these indices was moderate, their accessibility and low cost make them attractive adjuncts in postoperative surveillance. Larger, multicenter studies are needed to validate these findings and to integrate hematologic, radiologic, and molecular markers into a unified prognostic framework for GCTB.

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Conclusion

This study is one of the few to examine the prognostic role of RDW-to-albumin ratio and related hematologic indices in GCTB. The use of histologically confirmed cases and uniform surgical management strengthens the reliability of the data. However, its retrospective, single-center design and limited sample size may restrict the generalizability of the findings. This single-center retrospective study is subject to selection bias and residual confounding. Non-tumour influences on RDW and albumin cannot be ruled out entirely; results should be interpreted as hypothesis-generating. In conclusion, the RDW-to-albumin ratio demonstrated moderate prognostic performance, comparable to other inflammation-based indices, and may serve as a simple, inexpensive adjunct to identify patients at higher risk of recurrence; external validation is required.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
The study received ethical approval from the Dr. Abdurrahman Yurtaslan, Ankara Oncology SUAM Non-Interventional Clinical Research Ethics Committee (Date: 18.09.2025; Decision No: 2025-09/142).

References

1. Futamura N, Urakawa H, Tsukushi S, et al. Giant cell tumor of bone arising in long bones possibly originates from the metaphyseal region. Oncol Lett. 2016;11:2629–34.
2. Schütte HE, Taconis WK. Giant cell tumor in children and adolescents. Skeletal Radiol. 1993;22:173–6.
3. Chan CM, Adler Z, Reith JD, Gibbs Jr CP. Risk factors for pulmonary metastases from giant cell tumor of bone. JBJS. 2015;97:420–8.
4. Becker RG, Galia CR, Pestilho JFCS, et al. Giant cell tumor of bone: A multicenter epidemiological study in brazil. Acta Ortopédica Bras. 2024;32:e273066.
5. Chen C-C, Liau C-T, Chang C-H, et al. Giant cell tumors of the bone with pulmonary metastasis. Orthopedics. 2016;39:e68–73.
6. Muheremu A, Niu X. Pulmonary metastasis of giant cell tumor of bones. World J Surg Oncol. 2014;12:261.
7. He Y, Zhang J, Ding X. Prognosis of local recurrence in giant cell tumour of bone: What can we do? Radiol Med. 2017;122:505–19.
8. Yapar A, Atalay İB, Ulucaköy C, et al. The relationship between recurrence and lung metastasis in giant cell tumor of bone. Turkish J Clin Lab. 2020;11:23–8.
9. Bal O, Acikgoz Y, Yildiz B, et al. Simple and easily accessible prognostic markers in ewing sarcoma; neutrophil-lymphocyte ratio, neutrophil-platelet score and systemic-inflammation index. J Cancer Res Ther. 2023;19:1241-7.
10. Wang X, Wu Z, Zhang Z, Jiang Z. Prognostic and clinicopathological value of systemic immune-inflammation index in patients with osteosarcoma: a meta-analysis. Front Immunol. 2024;15:1416068.
11. Li X, Mohammadi MR. Combined diagnostic efficacy of red blood cell distribution width (RDW), prealbumin (PA), platelet-to-lymphocyte ratio (PLR), and carcinoembryonic antigen (CEA) as biomarkers in the diagnosis of colorectal cancer. Mol Biomed. 2023;3:98–106.
12. Zheng J, Yuan X, Guo W. Relationship between red cell distribution width and prognosis of patients with osteosarcoma. Biosci Rep. 2019;39:BSR20192590.
13. Hu L, Li M, Ding Y, et al. Prognostic value of RDW in cancers: a systematic review and meta-analysis. Oncotarget. 2016;8:16027.
14. Ai L, Mu S, Hu Y. Prognostic role of RDW in hematological malignancies: a systematic review and meta-analysis. Cancer Cell Int. 2018;18:61.
15. Xu SF, Adams B, Yu XC, Xu M. Denosumab and giant cell tumour of bone—a review and future management considerations. Curr Oncol. 2013;20:e442.
16. Kim Y, Nizami S, Goto H, Lee FY. Modern interpretation of giant cell tumor of bone: predominantly osteoclastogenic stromal tumor. Clin Orthop Surg. 2012;4:107–16.
17. Li H, Gao J, Gao Y, et al. Denosumab in Giant Cell Tumor of Bone: Current Status and Pitfalls. Front Oncol. 2020;10:580605.
18. Gruys E, Toussaint MJM, Niewold TA, Koopmans SJ. Acute phase reaction and acute phase proteins. J Zhejiang Univ Sci B. 2005;6:1045–56.
19. Balke M, Schremper L, Gebert C, et al. Giant cell tumor of bone: treatment and outcome of 214 cases. J Cancer Res Clin Oncol. 2008;134:969–78.
20. Liang S, Li Y, Liu H, Wang B. Pre-operative prognostic nutritional index was associated with recurrence after surgery in giant cell tumor of bone patients. J Bone Oncol. 2020;25:100324.
21. Liang S, Wang B, Liu H, et al. Combined fibrinogen and neutrophil-lymphocyte ratio as a biomarker in predicting recurrence of giant cell tumor of bone. Future Oncol. 2022;18:3191–7.
22. Yapar A, Atalay BI, Tokgoz AM, et al. Prognostic significance of the preoperative neutrophil-to-lymphocyte ratio patients with giant cell tumor of bone. Afr Health Sci. 2021;21:1250–8.
23. He Y, Liu C, Zeng Z, et al. Red blood cell distribution width: a potential laboratory parameter for monitoring inflammation in rheumatoid arthritis. Clin Rheumatol. 2018;37:161–7.
24. Guven DC, Sahin TK, Erul E, et al. The association between albumin levels and survival in patients treated with immune checkpoint inhibitors: A systematic review and meta-analysis. Front Mol Biosci. 2022;9:1039121.
25. Liao C-K, Yu Y-L, Lin Y-C, et al. Prognostic value of the C-reactive protein to albumin ratio in colorectal cancer: an updated systematic review and meta-analysis. World J Surg Oncol. 2021;19:139.
26. Biswas B, Rastogi S, Khan SA, et al. Hypoalbuminaemia is an independent predictor of poor outcome in metastatic Ewing's sarcoma family of tumours: a single institutional experience of 150 cases treated with uniform chemotherapy protocol. Clin Oncol. 2014;26:722–9.
27. Basoli S, Cosentino M, Traversari M, et al. The prognostic value of serum biomarkers for survival of children with osteosarcoma of the extremities. Curr Oncol. 2023;30:7043–54.
28. Huang X, Hu H, Zhang W, Shao Z. Prognostic value of prognostic nutritional index and systemic immune□inflammation index in patients with osteosarcoma. J Cell Physiol. 2019;234:18408–14.
29. Ouyang H, Wang Z. Predictive value of the systemic immune-inflammation index for cancer-specific survival of osteosarcoma in children. Front Public Heal. 2022;10:879523.