

Recurrence and Risk Factors of Giant Cell Tumors in Hand Bones: A Systematic Review

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Background: Giant cell tumor of bone (GCTB) is a locally aggressive tumor that may affect the bones of the hand and rarely causes pulmonary metastasis. It exhibits a variable recurrence rate after surgical interventions, which presents challenges in its management. This systematic review aims to delineate recurrence rates and identify risk factors for GCTB in the hand.

Methods: We conducted a systematic literature search in April 2024, following PRISMA guidelines, on PubMed and TDNet for studies reporting postsurgical recurrence of GCTB in the hand. Cohort and case-control studies provided recurrence rates, whereas case reports and series were utilized to identify risk factors, compensating for the sparse data in the primary studies. We used descriptive statistics, χ^2 tests, and logistic regression to analyze demographics, lesion characteristics, treatments, and outcomes.

Results: We reviewed 13 cohort and case-control studies involving 244 patients, finding an overall recurrence rate of 19.57%. Curettage was associated with higher recurrence rates compared with other surgical methods. After additional review of case reports, a limited range of motion in patients emerged as a significant protective factor against recurrence, suggesting potential benefits in surgical management and outcome prediction.

Conclusions: The significant recurrence rate associated with curettage highlights the need for alternative surgical strategies in GCTB management of the hand. The protective role of limited ROM underscores the importance of thorough preoperative assessments to optimize surgical approaches and enhance patient outcomes. (*Plast Reconstr Surg Glob Open* 2024; 12:e6253; doi: 10.1097/GOX.0000000000006253; Published online 16 October 2024.)

INTRODUCTION

Giant cell tumor of bone (GCTB) is an intermediate, locally aggressive tumor that rarely metastasizes, accounting for 5% of primary bone tumors and 20% of benign bone tumors. It typically occurs between the ages of 30 and 50 years, with a slight predominance in female patients.¹ Although seldom fatal, benign bone tumors can significantly disrupt local bone architecture, especially in peri-articular locations.² Approximately 5% of cases occur

in the small bones of the hands or feet, with less than 5% developing pulmonary metastasis.¹

The primary challenge in managing GCTB is the wide range of local recurrence rates after surgical treatment, which varies depending on the treatment modality.^{1,3} There is no widely accepted consensus on the ideal treatment method. Local recurrence rates have been reported to range from 7% to 50%, with modern techniques showing improvement in these rates.^{2,4} However, some techniques with lower recurrence rates may lead to severe morbidity and worse functional outcomes.³ Thus, a better understanding of the precise recurrence rate and its risk factors can aid in patient selection and treatment decision-making.

This article aims to systematically review available data in the literature and provide insights for healthcare providers evaluating patients with GCTB of the hand. It seeks

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to accurately define the postoperative recurrence rate of these tumors and identify associated risk factors. Our objective is to improve clinical recognition, diagnosis, and treatment for patients with GCTB who are at higher risk of recurrent disease.

METHODS

In April 2024, we conducted a systematic literature search on PubMed and TDNet, which aggregates articles from OVID, Clinical Key, and Unpaywall. We used the keywords “hand,” “giant cell tumor,” and “recurrence,” without restricting the publication year or language, in accordance with PRISMA guidelines. This systematic review did not require approval from the institutional review board. We included publications that presented original research on GCTB in the hand, excluding review articles and studies on other etiologies or locations of GCTB. To deepen our understanding of the risk factors associated with GCTB and compensate for the sparse data in primary studies, we formed a separate cohort of articles from the case reports and series collected during the screening process. Two authors independently reviewed all articles using predefined criteria, resolving any disagreements through discussion until a consensus was reached. Reports were assessed for eligibility by the authors using their titles and, when necessary, their abstracts. Exclusions were categorized by reasons such as studies not related to the hand, review or a description of a technique, missing sources, absence of surgical treatment, lack of recurrence outcomes, and presence of other hand diseases (Fig. 1).

Data collected included study design, patient demographics, lesion characteristics, clinical findings, imaging results, preoperative grading, treatment modalities, follow-up, and outcomes. Data were divided into subgroups of patients with and without recurrence. If Campanacci grades (Table 1) were not stated, they were assessed using information from the imaging studies performed.

Descriptive statistics outlined the demographic, clinical, and pathological features. Continuous variables such as age and durations were presented as means with SDs, and categorical variables were expressed as proportions. Statistical analyses, including *t* test, χ^2 test, and Fisher exact test, were conducted using Microsoft Excel 2021 and R software version 4.3.2 to compare characteristics between “no recurrence” and “recurrence” groups, with a significance level set at a *P* value of less than 0.05. We used logistic regression to identify potential predictors of recurrence from variables showing significant differences between groups. Analyses were conducted using R software, to refine the model and retain only significant predictors.

RESULTS

Among the 227 studies identified, 83 publications were selected based on our inclusion criteria (Fig. 1). This selection comprised 12 retrospective cohort studies and one case-control study, in addition to 58 case reports and 10 case series. (See table, Supplemental Digital Content 1, which displays the included studies. <http://links.lww.com/PRSGO/D575>.)

Takeaways

Question: What are the recurrence rates and risk factors for giant cell tumors of the hand bones after surgical treatment?

Findings: This systematic review of 13 cohort and case-control studies involving 244 patients found an overall recurrence rate of 19.57% for giant cell tumors in the hand. Curettage was associated with higher recurrence rates compared with other surgical methods. Limited range of motion was found to be a significant protective factor in case reports.

Meaning: Surgical technique significantly impacts recurrence rates of giant cell tumors in the hand. Limited range of motion may serve as a protective factor.

The analysis of cohort and case-control studies included 244 patients, of whom 40.98% were women, 47.54% were men, and 11.48% were not specified.⁵⁻⁷ These individuals had a mean age of 32.80 years, with ages ranging from 15 to 79 years.⁸⁻¹⁶ Of the lesions analyzed, 55.41% occurred on the right side and 44.59% on the left.^{8,15,16} Most tumors were in the distal radius, accounting for 87.70% of cases (Table 2).

The studies reviewed reported on the preoperative Campanacci grading: 22.88% of the tumors were classified as grade 2 and 77.12% as grade 3.^{8,9,12-15} Unfortunately, details on clinical symptoms and their duration were often omitted. The average follow-up period was 89.25 months, and the recurrence rate across all studies was 19.57%, with a mean time to recurrence of 14.96 months. Pulmonary metastasis was reported in 2.87% of the patients at presentation or during follow-up.^{8,10,15,17}

No significant association was found between recurrence likelihood and factors such as Campanacci grade,⁸ pathological fractures,^{6,8,12} age,^{6,12} or sex.^{6,12} However, the technique of curettage was associated with the highest recurrence rate.^{6,9} Less than 2 months of symptom duration or marked soft tissue swelling was related to a higher recurrence rate in one study.¹² In contrast, factors such as cortical penetration and tumor location did not consistently predict recurrence across the studies.^{6,8,12}

To enhance our understanding of tumor characteristics and risk factors for recurrence, we divided the patients into two groups based on whether they experienced recurrence. Among the 87 patients analyzed, 38 experienced recurrences, whereas 49 did not. (See table, Supplemental Digital Content 2, which displays recurrence and no recurrence factors and their significance. <http://links.lww.com/PRSGO/D576>.) In the group without recurrence, clinical symptoms such as pain, swelling, and limited range of motion (ROM), as well as surgical interventions such as en bloc resection and amputation, were statistically more significant compared with the group with recurrence. Logistic regression confirmed that limited ROM was a significant predictor of nonrecurrence ($P=0.02573$) (Fig. 2). Further logistic regression analysis showed that longer durations of symptoms were significantly associated with a reduced likelihood of recurrence ($P=0.047$). Additionally, the presence of a lesion and treatment via

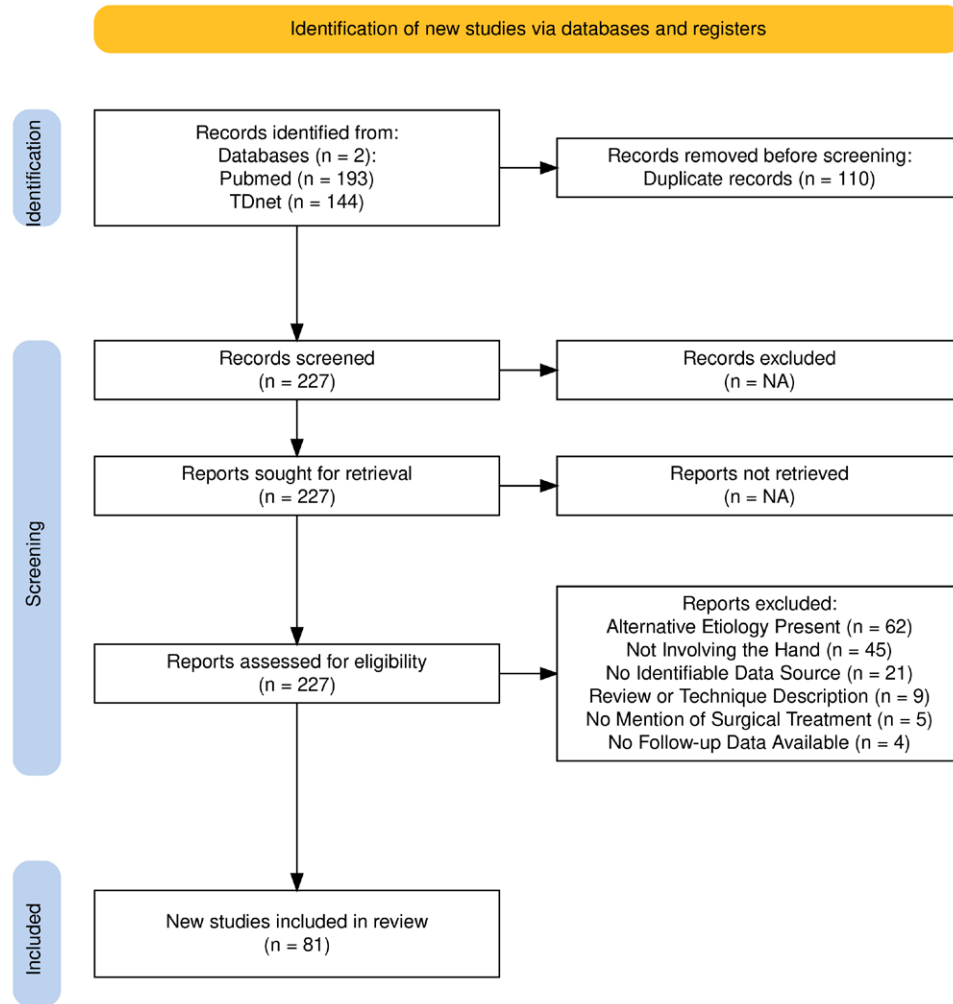


Fig. 1. Flow chart of the review process.

Table 1. Campanacci Radiographic Classification

Grade	Description	Clinical Significance
1	No cortical disruption with a well-defined sclerotic medullary margin	Typically asymptomatic or mild symptoms. Low risk of recurrence
2	Bone insufflation with cortex thinning and a well-defined nonsclerotic medullary margin	May cause pain. Moderate risk of recurrence. May require surgical intervention or other treatments
3	Unclear margins with cortical disruption and soft tissue extension	Often symptomatic. High risk of recurrence. Requires aggressive treatment including surgery and adjuvant therapies

Table 2. Anatomical Location of Tumor

Tumor Location	No. Patients (%)
Distal radius	214 (87.7)
Metacarpal	16 (6.56)
Phalanx	2 (0.82)
Scaphoid	2 (0.82)
Humerus	10 (4.1)
Total	244 (100)

curettage were more common in patients with recurrence ($P < 0.005$).

Further analysis using logistic regression to investigate confounding factors showed that the limited ROM

independently acts as a protective factor against recurrence, regardless of the surgical procedure performed, with an odds ratio of 0.28. This protective effect of limited ROM was confirmed through mediation analysis, demonstrating its significance independent of Campanacci grade ($P = 0.004$) and duration of symptoms (pseudo- R^2 value of 0.085).

Further logistic regression analyses were conducted to assess the clinical implications of lesions and potential confounders such as Campanacci grade and surgical treatments. The regression exploring the relationship between lesions, Campanacci grade, and recurrence did not reach statistical significance ($P = 0.087$) (Fig. 2). However, the logistic regression examining the association between lesions, type of operation, and recurrence identified a significant

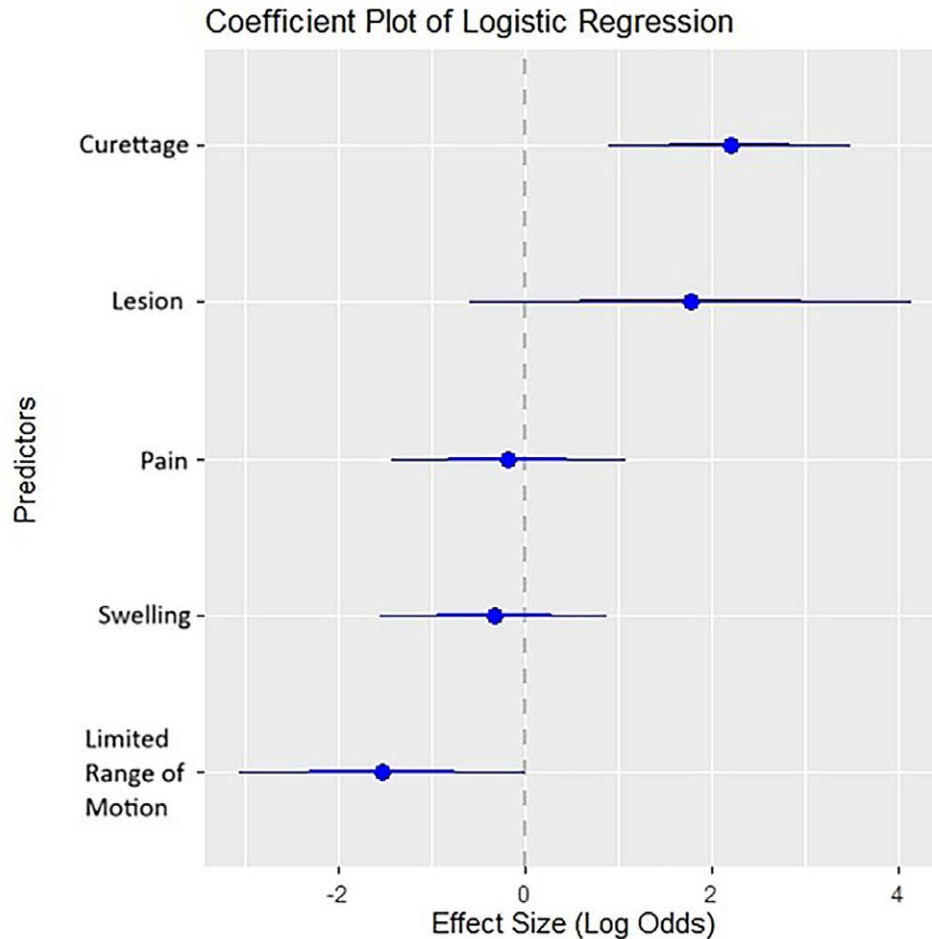


Fig. 2. Effect sizes of predictors on giant cell tumor recurrence—estimated effects of predictors on giant cell tumor of bone recurrence with confidence intervals.

negative association for major operations, such as resection, en bloc resection, or amputation, indicating that these procedures are likely to reduce the risk of recurrence ($P < 0.003$). Another logistic regression analysis did not find a significant association between the duration of symptoms, presence of lesions, and recurrence, with a pseudo- R^2 value of 0.1028. Additionally, lesions alone did not significantly impact the likelihood of recurrence ($P = 0.144$).

DISCUSSION

GCTB in the hand exhibits variable recurrence rates across the literature, reflecting the challenge of achieving complete tumor removal while preserving function.^{2,4} Our systematic review found a recurrence rate of 19.57%, consistent with previously reported rates,^{2,4} with a median recurrence interval of 16 months, shorter than previously documented.^{4,18} Notably, curettage emerged as the technique associated with the highest recurrence rate, corroborating existing literature.^{2,9,11}

In line with our systematic case review, several studies did not find significant associations between recurrence and factors such as Campanacci grade, pathological fractures, cortical penetration, or tumor location.^{6,8} However,

another study¹² reported findings that differ, suggesting that factors such as symptom duration of less than 2 months, significant soft tissue swelling, cortical penetration, and tumor location are linked to a higher recurrence rate. It should be noted that this study¹² does not exclusively focus on GCTB of the hand, which may limit the generalizability of its findings.

Further investigation of relevant preoperative and operative risk factors (**Supplemental Digital Content 2**, <http://links.lww.com/PRSGO/D576>) identified limited ROM as a significant protective factor, independent of symptom duration, Campanacci grade, or the type of procedural treatment applied. Although the biological basis of this finding is not fully understood, we propose that limited ROM may indicate lesser involvement of the tumor with surrounding tissues, potentially facilitating complete removal and reducing recurrence risks. However, this hypothesis needs to be validated through further research. Additionally, a longer symptom duration was found to be a significant protective factor, which may suggest a more benign nature of the disease process.

Risk factors for recurrence were identified as the clinical presence of a lesion and curettage treatment at first. Curettage is a well-established risk factor for recurrence,

consistent with previous findings.^{2,9,11} However, the influence of lesions on recurrence was not found to be independently significant on further logistic regression analysis and may be moderated by Campanacci grade and surgical technique.

Despite the valuable insights gained from this systematic review, several limitations should be acknowledged. The reliance on data from case reports and series may limit the generalizability of findings due to selection and publication biases. To ensure data reliability from case reports and series, we conducted a comprehensive qualitative analysis. Additionally, heterogeneity in reporting standards across studies introduces variability that complicates data interpretation. The limited number of studies meeting inclusion criteria, especially those detailing specific risk factors like Campanacci grade, might have reduced the statistical power necessary to detect significant associations. Moreover, retrospective study designs introduce potential recall and selection biases. Finally, inconsistencies in defining and measuring clinical outcomes such as recurrence rates could affect the reliability of the results. For a more robust evolution of findings, we transparently outlined our inclusion criteria and search strategy and framed discussions within the context of case reports' descriptive and exploratory nature.

In conclusion, this systematic review refines our understanding of recurrence rates for GCTB in the hand, providing valuable insights for clinical decision-making. The identification of limited ROM as an independent protective factor against recurrence underscores the importance of personalized treatment approaches. Future research should aim to address the limitations of this study and validate the findings in larger, more diverse patient populations.

CONCLUSIONS

This systematic review reveals a recurrence rate of 19.57% for GCTB in the hand. Notably, curettage, identified as having the highest recurrence rate, significantly influences outcomes, emphasizing the critical role of surgical technique in managing these tumors. Despite extensive analysis, no significant correlations were found between recurrence and factors such as Campanacci grade, pathological fractures, or cortical penetration. Furthermore, from the analysis of case reports and series, limited ROM emerged as a protective factor against recurrence. We hypothesize that this finding suggests less tumor involvement with surrounding tissues, potentially facilitating complete removal and reducing recurrence risks. However, further research is needed to validate this hypothesis and elucidate the underlying mechanisms. These insights underscore the necessity for precise surgical strategies and comprehensive preoperative assessments to optimize treatment efficacy for patients with GCTB in the hand. Considering the high recurrence rate associated with curettage, future practice should explore alternative surgical approaches to mitigate recurrence risks and improve patient outcomes.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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