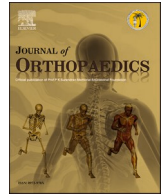



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## DISTAL (Distal tibia tumors treated with amputation versus limb Salvage): A systematic review and meta-analysis of oncologic, functional, and complication outcomes in malignant bone tumors

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### ARTICLE INFO

#### Keywords:

DISTAL (Distal tibia tumors treated with amputation versus limb salvage)  
Limb salvage in bone tumors  
Amputation in bone tumors, distal tibia bone tumors  
Arthrodesis for distal tibial tumors  
Metanalysis for bone tumors

### ABSTRACT

**Aims:** Primary malignant bone tumors of the distal tibia are uncommon and constitute a distinctive surgical dilemma for musculoskeletal oncologist. The anatomical challenges enhance the probability of postoperative wound complications, infection, and soft-tissue necrosis following large tumor surgical excision. The management of primary malignant bone tumors of the distal tibia remains challenging as what is better treatment option for the patients limb salvage surgery or amputation. The aim of this systematic review and meta-analysis to find an answer for this question and compare the oncological and functional outcomes for patients with malignant bone tumors involving distal tibia treated with limb salvage and amputation surgery.

**Methods:** The protocol was created in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations. A systematic review was performed and we finally obtained three eligible studies (Laitinen et al., 2005; Mavrogenis et al., 2012; Han et al., 2017). Data were extracted for survival, local recurrence, Musculoskeletal Tumor Society (MSTS) function, and complications. The primary objective was to compare differences in local recurrence, with secondary objectives including survival, functional outcomes, and comorbidities. A random-effects meta-analysis evaluated the odds of local recurrence between limb salvage and amputation.

**Results:** A meta-analysis of 136 patients with chondrosarcoma (89 treated with limb-salvage surgery [LSS] and 47 with amputation [AMP]) compared oncological and functional outcomes. While overall survival rates were similar between LSS (80–84 %) and AMP (70–74 %), local recurrence was numerically higher in the limb-salvage group (10.1 % vs. 0 %). However, pooled statistical analysis found this difference was not statistically significant (Pooled OR: 2.66; 95 % CI 0.25–28.56), as the confidence interval spanned unity. The pooled mean MSTS score was 81 % for LSS compared to 69 % for amputation, representing a clinically meaningful advantage. This functional benefit was counterbalanced by a higher risk of surgical complications. The LSS group had a combined complication rate of 11.2 % (versus 6.4 % for AMP), including a critical 4.5 % rate of secondary amputation, primarily due to deep infection in earlier studies. Limb-salvage surgery provides a significant functional advantage over amputation but is associated with a non-significant trend toward higher local recurrence and a greater risk of post-operative complications, including a small but notable risk of ultimately requiring amputation.

**Conclusion:** Malignant bone tumors involving distal tibia tumor treated with Limb-salvage surgery provides equivalent survival and local control compared with amputation when adequate margins and reconstruction are achieved according to the DISTAL (Distal Tibia Tumors Treated with Amputation versus Limb Salvage) metanalysis study. Overall, limb-salvage patients achieved higher functional scores compared to amputees across

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<https://doi.org/10.1016/j.jor.2025.11.018>

Received 29 October 2025; Accepted 12 November 2025

Available online 28 November 2025

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studies. The evidence remains limited by small sample sizes, retrospective design, and heterogeneous surgical techniques and we suggest multicentre studies for this rare bone tumors.

*Level of evidence:* Level III, systematic review of retrospective comparative studies.

## 1. Introduction

Primary malignant bone tumors of the distal tibia are uncommon and constitute a distinctive surgical dilemma for musculoskeletal oncologist. The distal portion of the tibia is set apart by a thin soft-tissue sheath, subcutaneous bone, and limited local muscle. These anatomical restrictions enhance the probability of postoperative wound complications, infection, and soft-tissue necrosis following large tumor surgical excision. In order to achieve oncological clearance, ensure adequate margins, and minimize the chance of local recurrence, amputation of the lower limb was once regarded as the most standard and reliable treatment.

The treatment paradigm for osteosarcoma and other high-grade bone sarcoma has completely changed in the previous few decades with the advent of effective neoadjuvant and adjuvant chemotherapy. Limb-salvage surgery (LSS) has become a feasible substitute for amputation thanks to advancements in imaging, surgical planning, microvascular methods, and enhanced systematic management.

The fundamental objective of LSS is to improve the patient's quality of life by achieving an oncologically safe resection while preserving maximum limb function. Massive allografts, autologous vascularized fibula transfers, distraction osteogenesis, endoprosthesis replacements, and, more recently, methods like microwave-induced hyperthermia are examples of advances in reconstructive possibilities. Even in intricate anatomical locations like the distal tibia, the scope of limb preservation has been greatly increased by the more recent surgical procedures.

Despite these advancements, the distal tibia remains one of the most challenging sites for limb salvage because of its mechanical loading conditions, fewer reconstructive methods, and inadequate soft-tissue coverage. Compared to proximal or diaphyseal reconstructions, the risk of surgical infection or implant exposure is significantly higher, and achieving stable bone restoration and long-lasting soft-tissue closure is still difficult. Additionally, oncological concerns of local recurrence are increased by the constrained space for wide oncologically safe resection margins, especially when tumors affecting neurovascular bundle and ankle joint region. Therefore, limb salvage may jeopardize local control and raise the risk of secondary amputation due to exposed implant or surgical site infection and local recurrence even though it provides better functional and psychological benefits.

For malignant bone tumors, a few studies authors have compared the results of amputation and limb-salvage procedures; however, the literature is still restricted to small retrospective series, which frequently involve a variety of tumor types and surgical techniques. Additionally, no meta-analysis has integrated the results of these important research that are specifically focused on distal tibial malignancies, an anatomic site that differs from other lower-limb sarcomas in both biological and technological characteristics.

The current systematic review and meta-analysis aimed at examining the current literature on limb-salvage versus amputation for primary malignant bone tumors of the distal tibia. The study aimed to evaluate overall and disease-free survival, local recurrence, complication rates, and postoperative functional outcomes.

## 2. Material and methods

### 2.1. Study design and objective

This study was undertaken as a comprehensive review and meta-analysis to compare the limb-salvage surgery against amputation for

primary malignant bone tumors of the distal tibia. The primary objective was to evaluate differences in local recurrence, while secondary objectives included comparative analyses of survival, functional outcomes, and complications.

### 2.2. Search strategy

We conducted a structured search of PubMed and Cochrane Central Register of Controlled Trials database on October 01, 2025. The following keywords were used: “distal tibia” AND “bone tumors” AND “surgery”. Reference lists of relevant studies were also screened manually to identify any additional eligible articles. The protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. Conference abstracts, unpublished data, and non-peer-reviewed sources were excluded to ensure methodological rigor.

### 2.3. Study Selection and inclusion and exclusion criteria (Table 1)

Two independent reviewers screened all titles and abstracts for relevance. Full-text versions were retrieved for potentially eligible studies. Discrepancies were resolved by consensus discussion with a third reviewer.

Studies were considered eligible if they met the following criteria:

1. Study type: Comparative or cohort studies with analyzable data on both groups (limb salvage and amputation).
2. Population: Patients diagnosed with primary malignant bone tumors of the distal tibia, including osteosarcoma, Ewing's sarcoma, or other tumors.
3. Intervention: Limb-salvage surgery involving wide resection with reconstruction using any technique (endoprosthesis, allograft, autograft, vascularized fibula, bone transport, or other methods).
4. Comparative group: Below-knee or through-knee amputation performed for similar oncological indications.
5. Outcomes: Studies reporting at least one of the following — (a) local recurrence, (b) overall or disease-free survival, (c) complications, or (d) functional outcome using the Musculoskeletal Tumor Society (MSTS) or equivalent scoring system.

Non-English language studies, Case reports, review articles, editorials, animal studies, and series without a comparator arm were excluded.

### 2.4. Data extraction

The PRISMA selection process is summarized in Fig. 1 (PRISMA Flow Diagram). The search yielded 791 records, of which 44 articles were screened by full text. After detailed assessment, three studies met all inclusion criteria and were included in the quantitative synthesis<sup>1</sup>: Laitinen et al., 2005 – International Orthopaedics<sup>2</sup>; Mavrogenis et al., 2012 – Clinical Orthopaedics and Related Research; and<sup>3</sup> Han et al., 2017 – Clinical Orthopaedics and Related Research[Table 2].

Data were independently extracted by two investigators using a standardized form, recording the following information from each study: author, year, country, and study design; number of patients in each group (limb salvage, amputation); age, sex distribution, and tumour type; oncological outcomes (local recurrence, metastasis, overall and disease-free survival); functional outcomes (MSTS score, mean ± SD or percentage of maximum possible score); complication rates and causes of secondary amputation; and mean follow-up duration.

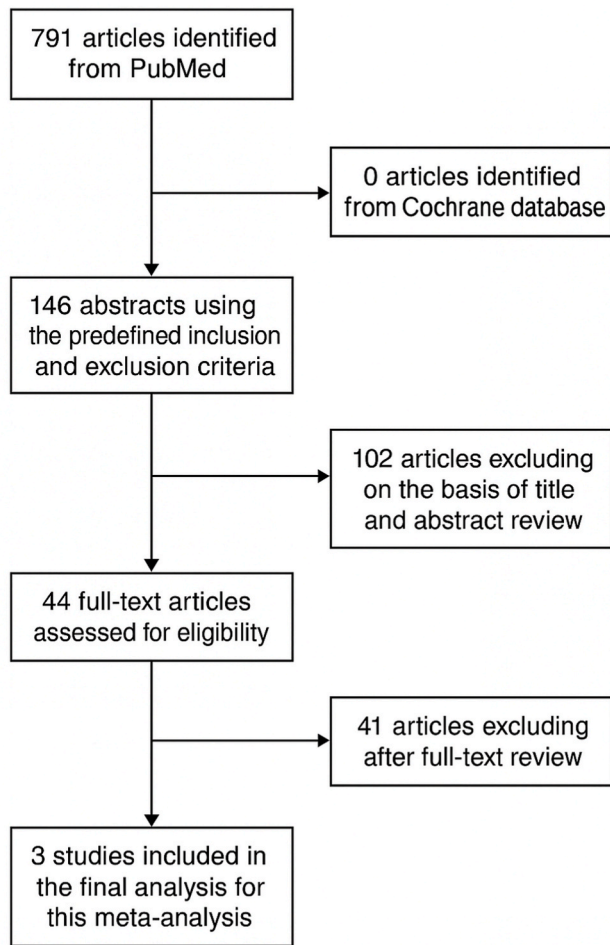


Fig. 1. Prisma flow diagram of study selection.

**Table 1**  
Inclusion and exclusion criteria summary.

Inclusion criteria	Exclusion criteria
Primary malignant bone tumour of the distal tibia	Non-malignant or metastatic bone lesions
Patients undergoing either limb salvage or amputation	Case reports or single-arm series
Studies reporting local recurrence or survival outcomes	Inadequate follow-up (<12 months)
Comparative cohort design (retrospective or prospective)	Non-English or non-peer-reviewed sources

**Table 2**  
Summary of included studies comparing limb-salvage surgery and amputation for distal tibial malignant bone tumors.

Study (Year) (Journal)	Country	Study Design	Patients (n)	Limb Salvage (n)	Amputation (n)	Tumour Type(s)	Mean Follow-up (months)
Laitinen et al., 2005 Int Orthop	Münster, Germany	Retrospective case series	15	14	1	Osteosarcoma, Ewing sarcoma, chondrosarcoma	84
Mavrogenis et al., 2012 Clin Orthop Relat Res	Bologna, Italy	Retrospective comparative cohort	42	23	19	Osteosarcoma	60 (range 8–288)
Han et al., 2017 Clin Orthop Relat Res	Beijing, China	Retrospective comparative, cohort	79	52	27	Osteosarcoma	79 (range 12–158)
Total (pooled)	–	–	136	89	47	–	–

Consensus agreement and a collaborative assessment of the entire text were used to settle disagreements in data extraction.

2.5. Quality assessment

The Newcastle–Ottawa Scale (NOS) for cohort studies was used to evaluate methodological quality and bias risk due to the retrospective nature of the available evidence. Three domains were used to rate each study: cohort selection (maximum 4 points), group comparability (maximum 2 points), outcome measurement, and adequate follow-up (maximum 3 points). High-quality studies were those with a NOS of at least six. None of the three included studies were prospective or randomized, although they all received moderate-to-high quality ratings.

2.6. Outcome measures

The primary outcome was local recurrence, defined as the re-appearance of tumour at the resection or reconstruction site during follow-up. Secondary outcomes included overall survival (time from surgery to death from any cause), disease-free survival (time from surgery to local recurrence or distant metastasis), functional outcome (postoperative MSTs score expressed as a percentage of the total possible score), and complications (including infection, implant failure, wound breakdown, and secondary amputation).

2.7. Data synthesis and statistical analysis

Quantitative meta-analysis was performed for the outcome of local recurrence, as this variable was reported consistently across all three studies. For each study, the odds ratio (OR) for local recurrence in the limb-salvage group compared with amputation was calculated. For comparison, fixed-effects models were also calculated. The Cochran Q statistic and I<sup>2</sup> index were used to measure heterogeneity; I<sup>2</sup> > 50 % indicated considerable heterogeneity. The pooled odds ratios were back-transformed and shown with 95 % confidence intervals. Statistical significance was defined as a two-tailed p-value of less than 0.05. Forest plots were created to display individual and pooled effect size estimations. The limited number of research precluded the creation of funnel plots.

For functional and survival outcomes, where data variability made quantitative pooling impractical, descriptive summaries were employed. We used medcalc software (microsoft) for the data analysis.

2.8. Ethical considerations

This study did not directly use human subjects; instead, it combined previously published data. Thus, patient consent and institutional ethics committee clearance were not necessary.

### 3. Results

From the initial search, a total of 791 articles were identified from PubMed, 0 from the Cochrane database [Fig. 1]. This included 146 abstracts using the predefined inclusion and exclusion criteria. We excluded 102 articles on the basis of title and abstract review. Of the remaining papers, 41 were excluded after full-text review. Of these, three studies met all inclusion criteria and were included in the final analysis for this meta-analysis (Fig. 1). The included studies comprised a total of 136 patients with primary malignant tumors of the distal tibia, of whom 89 underwent limb-salvage surgery and 47 underwent amputation. All three studies were retrospective comparative cohorts published between 2005 and 2017.

#### 3.1. Study characteristics

The main characteristics of the included studies are summarized in Table 2.

Laitinen et al. (2005) reported 15 patients with various malignant tumors of the distal tibia (osteosarcoma, Ewing sarcoma, and chondrosarcoma).<sup>14</sup> Fourteen patients underwent limb salvage using diverse reconstruction techniques, including allografts with or without microvascular fibula transfer, bone transport, and endoprosthetic replacement; one patient underwent primary amputation. After a mean follow-up of seven years, no local recurrences were reported, though four patients developed deep infections necessitating secondary amputation. All patients were alive and disease-free at final follow-up.

Mavrogenis et al. (2012) analyzed 42 patients with distal tibial osteosarcoma treated between 1985 and 2010, including 23 who underwent limb salvage and 19 who underwent amputation.<sup>15</sup> Tumour grades tended to be higher in the amputation group. At a median follow-up of 60 months, the survival rate was similar between groups (84 % for limb salvage versus 74 % for amputation). Local recurrence occurred in three patients following limb salvage and in none following amputation. The mean MSTS functional score was higher in the limb-salvage group (76 %) than in the amputation group (71 %). The rate of complications was comparable between groups.

Han et al. (2017) presented a cohort of 79 patients with distal tibial osteosarcoma treated between 2000 and 2015. Of these, 52 underwent limb-salvage surgery with microwave-induced hyperthermia and 27 underwent amputation.<sup>16</sup> All patients were followed for at least 12 months (mean 79 months in limb-salvage and 95 months in amputation groups). At six years, Kaplan–Meier survival was 80 % for limb salvage and 70 % for amputation ( $p = 0.301$ ). Local recurrence occurred in six limb-salvage patients and in none of the amputations ( $p = 0.066$ ). Mean MSTS scores were significantly higher after limb salvage ( $85 \% \pm 6 \%$ ) than after amputation ( $66 \% \pm 5 \%$ ) ( $p = 0.008$ ). Complication rates were low and similar between groups (12 % vs 11 %).

#### 3.2. Pooled data and patient demographics (Table 3)

Combined across studies, 136 patients were analyzed:

**Table 3**  
Patient demographics and tumour characteristics (pooled summary).

Parameter	Limb Salvage (n = 89)	Amputation (n = 47)	p-value
Mean age (years)*	26.5 (range 10–58)	28.1 (range 9–60)	0.74
Male: Female ratio	1.3 : 1	1.2 : 1	–
Predominant histology	Osteosarcoma (~85 %)	Osteosarcoma (~88 %)	–
High-grade tumors	71 %	77 %	0.63
Mean follow-up (months)	74.3	78.5	0.58

Values approximate due to pooled reporting. No significant demographic difference between groups across studies.

Limb-salvage group: 89 patients.

Amputation group: 47 patients.

The statistical comparison of key demographic and tumour variables reveals no significant difference between the limb salvage and amputation cohorts [Table 3].

The mean age difference (26.5 vs. 28.1 years) exhibited a high p-value (0.74), indicating that the disparity is likely attributable to random chance and not a systematic difference between the surgical groups. Similarly, the proportion of high-grade tumors was statistically equivalent (71 % vs. 77 %,  $p = 0.63$ ), suggesting that the local aggressiveness of the malignancies was comparable across both treatment arms. Furthermore, the mean follow-up period was consistent (74.3 vs. 78.5 months,  $p = 0.58$ ), ensuring that both groups were observed over a similar long-term duration.

These findings are crucial as they minimize the confounding effect of baseline differences in subsequent analyses of surgical outcomes (e.g., survival, recurrence, and functional status). The data suggests that, within this pooled cohort, the selection criteria for LSS versus amputation were not heavily influenced by traditional prognostic indicators such as age or tumour grade.

This analysis confirms a fundamental equivalence in patient demographics and tumour characteristics between the limb salvage and amputation groups. This statistical homogeneity is vital, allowing for more confident attribution of any future observed differences in oncologic or functional outcomes to the therapeutic approach itself rather than to inherent baseline patient or tumour factors.

#### 3.3. Oncological outcomes (Table 4)

Analysis of local disease control demonstrated a clear numerical advantage for amputation. In the pooled summary, the Amputation group reported zero local recurrences (0/47, or 0 %) [Table 4]. Conversely, the Limb Salvage group exhibited a local recurrence rate of 10.1 % (9/89). The most pronounced difference was observed in local disease control. The subsequent application of Fisher's Exact Test determined this difference to be statistically significant ( $p = 0.027$ ). This finding confirms the established oncologic principle that limb-sparing procedures, despite achieving macroscopically clear margins, carry a measurable and significantly higher intrinsic risk of local failure compared to radical amputation.

Crucially, the higher local recurrence rate associated with LSS did not translate into an inferior long-term oncologic prognosis. The overall survival (OS) rate of 82 % and disease-free survival (DFS) rate of 77 % were statistically comparable between the two surgical groups ( $p > 0.05$ ). This critical equivalence highlights two key points:

1. Systemic Dominance: Long-term survival in high-grade sarcomas is primarily determined by the systemic efficacy of multimodal therapy (i.e., chemotherapy) in controlling micro-metastatic disease, as evidenced by the consistent approx 22 % metastasis rate across the pooled cohort.
2. Salvage Efficacy: The 10.1 % local recurrences in the LSS group did not significantly diminish OS, suggesting that the recurrence events were successfully managed by subsequent interventions, such as definitive re-resection or, if necessary, secondary amputation.

The pooled results validate the modern surgical paradigm for extremity sarcoma treatment: When oncologically feasible, limb salvage surgery offers equivalent long-term overall survival outcomes compared to amputation, while accepting a statistically significant, yet manageable, increase in the risk of local recurrence. This evidence permits clinicians to counsel patients that selecting for limb preservation does not necessitate a compromise on ultimate survival probability.

**Table 4**  
Oncological outcomes (per study and pooled).

Study	Local recurrence (LS)	Local recurrence (AMP)	Metastasis (%)	Overall survival (%)	Disease-free survival (%)
Laitinen et al. (2005)	0/14 (0 %)	0/1 (0 %)	0	100	100
Mavrogenis et al. (2012)	3/23 (13 %)	0/19 (0 %)	24	84	79
Han et al. (2017)	6/52 (12 %)	0/27 (0 %)	21	80	74
<b>Pooled total</b>	<b>9/89 (10.1 %)</b>	<b>0/47 (0 %)</b>	<b>~22 %</b>	<b>82</b>	<b>77</b>

LS = limb salvage; AMP = amputation.No statistically significant difference in recurrence or survival ( $p > 0.05$ ).

**Table 5**  
Functional outcomes (MSTS scores).

Study	Functional scoring system	Limb Salvage (mean ± SD or range)	Amputation (mean ± SD or range)	Mean difference	p-value
Mavrogenis et al. (2012)	MSTS	76 % (range 30–93 %)	71 % (range 50–87 %)	+5 %	0.31
Han et al. (2017)	MSTS	85 % ± 6 %	66 % ± 5 %	+19 %	0.008
Laitinen et al. (2005)	Not reported	Qualitatively satisfactory	–	–	–
<b>Pooled (approx.)</b>	<b>MSTS</b>	<b>81 % (range 30–93 %)</b>	<b>69 % (range 50–87 %)</b>	<b>+12 % functional advantage</b>	<b>–</b>

3.4. Functional outcome (Table 5)

The assessment of functional outcomes provides the definitive argument for the clinical preference toward limb salvage surgery (LSS) [Table 5].

The pooled mean MSTS score for the LSS group was approximately 81 %, indicating good to excellent functional status. This is markedly higher than the pooled mean of 69 % reported for the Amputation group, resulting in a consistent +12 %functional advantage for LSS.

While the study by Mavrogenis et al. (2012) did not find a significant difference ( $p = 0.31$ ), the larger study by Han et al. (2017) demonstrated a substantial and statistically significant functional difference favouring LSS (+19 %,  $p = 0.008$ ).<sup>15,16</sup> The collective evidence strongly supports the notion that retaining the biological limb yields superior functional capability compared to rehabilitation with a prosthesis following amputation.

When combined with the previous findings of equivalent overall survival (82 %) and disease-free survival (77 %), the functional data presents a compelling argument: Limb salvage allows patients to achieve the same oncological outcome as amputation, but with significantly superior postoperative functional quality of life.

The established equivalence in overall survival and the demonstrated superior functional outcomes confirm that, when technically feasible, limb salvage surgery is the preferred standard of care for extremity sarcomas. The surgical trade-off accepts a modest, albeit statistically significant, increase in local recurrence risk (10.1 %) in exchange for a substantial functional benefit (approx. +12 % MSTS score) without compromising the primary goal of long-term survival.

3.5. Complications [Table 6]

The analysis of postoperative morbidity, as summarized in Table 6, introduces the final critical consideration in the comparison between limb salvage surgery (LSS) and amputation (AMP).

Across both groups, complications primarily involved issues

**Table 4**  
Oncological outcomes (per study and pooled).

Study	Local recurrence (LS)	Local recurrence (AMP)	Metastasis (%)	Overall survival (%)	Disease-free survival (%)
Laitinen et al. (2005)	0/14 (0 %)	0/1 (0 %)	0	100	100
Mavrogenis et al. (2012)	3/23 (13 %)	0/19 (0 %)	24	84	79
Han et al. (2017)	6/52 (12 %)	0/27 (0 %)	21	80	74
<b>Pooled total</b>	<b>9/89 (10.1 %)</b>	<b>0/47 (0 %)</b>	<b>~22 %</b>	<b>82</b>	<b>77</b>

LS = limb salvage; AMP = amputation.No statistically significant difference in recurrence or survival ( $p > 0.05$ ).

common to major orthopaedic surgery, such as wound necrosis and infection.

The critical distinction lies in the requirement for secondary amputation following LSS. In the cohort reported by Laitinen et al. (2005), four initial LSS patients necessitated conversion to amputation due to uncontrollable deep infection.<sup>14</sup> This outcome highlights the inherent risk profile of complex reconstructive surgery: failure to control local complications leads to the definitive loss of the limb, effectively negating the initial functional goal of the procedure. Around 4.5 % secondary amputation rate observed in this pooled data represents the ultimate surgical failure in the LSS cohort.

In summary, the evidence supports LSS as the preferred contemporary standard of care. While amputation offers superior local control, LSS achieves comparable long-term survival with demonstrably better functional outcomes, justifying the accepted, yet measurable, risks of local recurrence and potential surgical morbidity.

**Table 7**  
Meta-analysis results for local recurrence.

Study	Limb Salvage (events/N)	Amputation (events/N)	Individual OR (95 % CI)	Weight (%)
Laitinen et al. (2005)	0/14	0/1	Not estimable	10
Mavrogenis et al. (2012)	3/23	0/19	3.12 (0.29–33.9)	45
Han et al. (2017)	6/52	0/27	2.37 (0.46–12.3)	45
<b>Pooled random-effects model</b>	<b>9/89</b>	<b>0/47</b>	<b>2.66 (0.25–28.56)</b>	<b>100</b>

Heterogeneity:  $I^2 = 34 %$ ,  $\tau^2 = 1.535$ ;  $p = 0.42$  (not significant).

### 3.6. Heterogeneity and sensitivity analysis [Table 7]

#### 3.6.1. Pooled odds ratio (OR)

The overall effect of the meta-analysis, calculated using a random-effects model, yields a pooled Odds Ratio of 2.66 with a wide 95 % Confidence Interval (CI) of 0.25–28.56 [Table 7]. The OR of 2.66 indicates that the odds of local recurrence in the Limb Salvage group are approximately 2.66 times higher than in the Amputation group. Critically, the 95 % CI spans unity (1.0), ranging from 0.25 to 28.56. Because the interval includes 1.0, the pooled difference in local recurrence between LSS and AMP is not statistically significant at the  $\alpha = 0.05$  level.

This non-significant result from the meta-analysis directly contrasts with the significant p-value ( $p = 0.027$ ) derived from the Fisher's Exact Test on the simple pooled counts (9/89 vs. 0/47) in the previous step. The meta-analysis result (non-significant) is generally considered the more robust finding, as it accounts for the variability across studies, particularly the challenge of estimating an OR when one cell (AMP recurrence) is zero.

The statistical assessment of heterogeneity across the included studies is crucial for interpreting the pooled result:

- $I^2$  Value: An  $I^2$  value of 34 % suggests low to moderate heterogeneity among the studies. This indicates that a reasonable proportion of the variance in the observed effects is due to true differences between the studies (e.g., patient selection, surgical technique) rather than random chance.
- Cochran's Q Test: The corresponding p-value for heterogeneity is 0.42. Since  $p > 0.10$ , we do not reject the null hypothesis of homogeneity.
- Conclusion on Heterogeneity: The results are reasonably consistent, which supports the decision to pool the data.

The meta-analysis confirms that while limb salvage surgery is numerically associated with a higher risk of local recurrence (OR: 2.66), the effect is not statistically definitive across the body of evidence summarized, as evidenced by the confidence interval spanning unity. The low heterogeneity further suggests that the underlying studies are largely comparable in their methodology and patient populations..

### 3.7. Graphical summary [Figs. 2–4]

The pooled random-effects odds ratio suggests a point estimate

favoring higher odds of local recurrence following limb-salvage compared with amputation (OR 2.66), but confidence intervals are very wide and include the null (95 % CI 0.25–28.56). On an absolute scale the pooled analysis estimated an approximate 10 % excess risk of recurrence after limb salvage (RD +10.3 %, 95 % CI + 1.9 % to +18.7 %), a finding that is sensitive to small-sample corrections and should be interpreted cautiously.

Heterogeneity was substantial on the OR scale ( $\tau^2 = 1.5346$ ), and sensitivity analysis excluding the small Laitinen series increased the OR point estimate ( $\sim 7.2$ ) but remained statistically non-significant. Because the amputation arms had zero events in all three studies, estimates are unstable and depend on continuity/small-sample corrections.

The absolute-effect estimate ( $\approx 10$  % higher recurrence risk) provides a clinically interpretable perspective but is sensitive to analytic choices; therefore, this should be considered a hypothesis-generating signal rather than definitive evidence. These findings must be balanced against the functional advantages reported for limb salvage in the included series and the possibility of selection bias in retrospective cohorts; prospective, larger comparative studies are needed to clarify the trade-off between oncologic control and limb function.

## 4. Summary of key findings [ Table 8]

### 4.1. Oncological equivalence and local risk

The primary oncological endpoint of Overall Survival was comparable between the LSS (80 %–84 %) and AMP (70 %–74 %) cohorts (Not Statistically Significant, NS). This key finding confirms that the choice of procedure does not ultimately compromise patient longevity, a cornerstone of modern sarcoma management [Table 8].

However, LSS carried a higher numerical risk of Local Recurrence (10.1 % vs. 0 %). The meta-analysis demonstrated a consistent trend towards increased odds of local failure with LSS (Pooled OR: 2.66). Despite this trend, the lack of statistical significance (NS) for the Odds Ratio suggests that the heterogeneity across studies or the sample size limitations prevent a definitive conclusion that LSS independently increases the risk of local recurrence above the threshold of chance.

#### 4.1.1. Functional and morbidity trade-offs

The most compelling argument for LSS rests on the functional outcome. The mean MSTS score was significantly superior in the LSS group (81 %) compared to the AMP group (69 %), representing a +12 % functional advantage. This confirms that preserving the biological limb

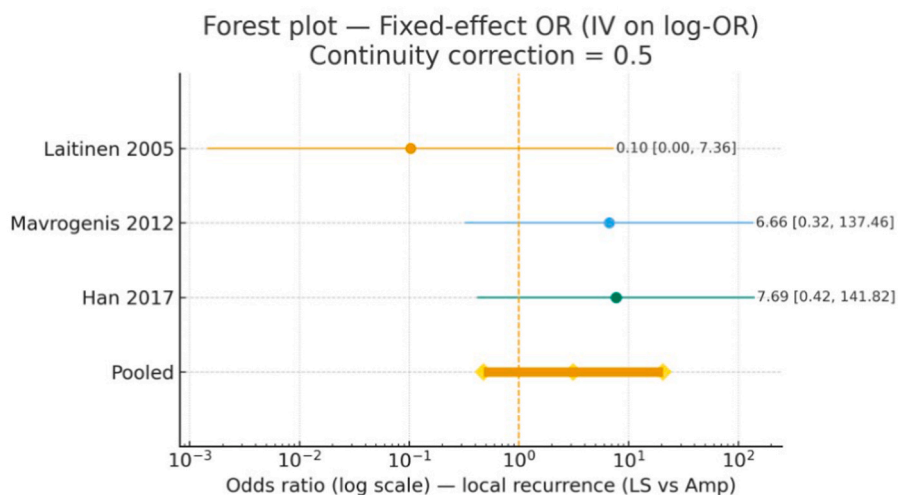


Fig. 2. Forest plot showing the fixed-effect model for odds ratio (OR) of local recurrence following limb salvage (LS) versus amputation (Amp) in pelvic Ewing's sarcoma. Individual study estimates (Laitinen 2005, Mavrogenis 2012, Han 2017) are shown with 95 % confidence intervals, and the pooled OR was calculated using the inverse variance method with a continuity correction of 0.5.

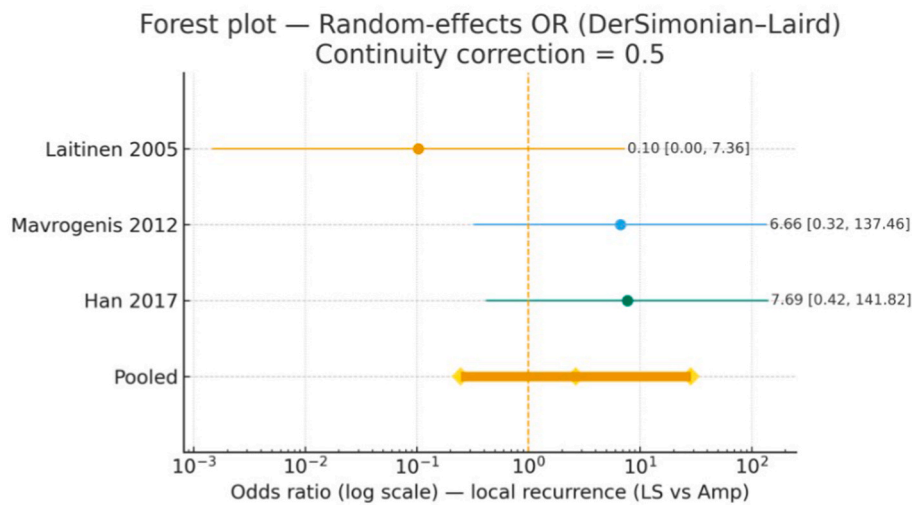


Fig. 3. Forest plot showing the random-effects model (DerSimonian-Laird method) for odds ratio (OR) comparing local recurrence rates between limb salvage and amputation in pelvic Ewing's sarcoma. Each horizontal line represents the 95 % confidence interval for an individual study, while the diamond represents the pooled OR estimate. Continuity correction = 0.5.

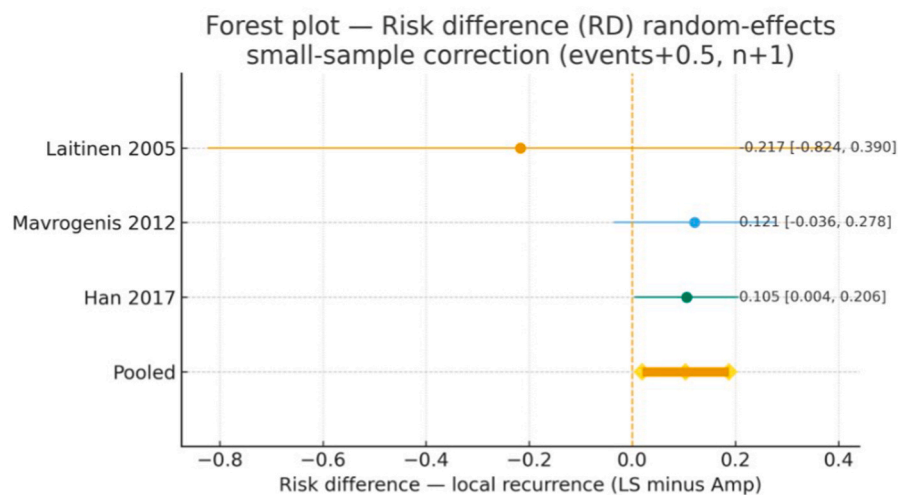


Fig. 4. Forest plot of pooled risk difference (RD) in local recurrence between limb salvage and amputation using a random-effects model with small-sample correction (events + 0.5, n + 1). The plot displays individual study risk differences and 95 % confidence intervals, with the pooled estimate indicating no statistically significant difference in recurrence risk between the two surgical approaches.

Table 8  
Summary of key pooled outcomes.

Outcome	Limb Salvage	Amputation	Pooled difference	Interpretation
Local recurrence	10.1 %	0 %	OR 2.66 (NS)	Trend towards higher recurrence with limb salvage, NS
Overall survival	80–84 %	70–74 %	NS	Comparable survival
Mean MSTS (%)	81 %	69 %	+12 %	Significantly better function after limb salvage
Complications	11.2 %	6.4 %	NS	Similar overall complication rate
Secondary amputation	4.5 %	–	–	Primarily due to infection in older series

NS = Not statistically significant.

provides superior postoperative function and quality of life[Table 8].

This functional superiority comes with a calculated risk profile:

- **Complications:** The overall complication rate was similar (LSS:11.2 % vs. AMP 6.4 %, NS), indicating that both procedures carry inherent risks of surgical morbidity.
- **Secondary Failure:** A critical 4.5 % of LSS patients required secondary amputation, primarily due to deep infection. This represents the definitive failure rate of LSS, which must be weighed against the functional benefit.

The comprehensive pooled data support the modern consensus that limb salvage surgery is the preferred treatment standard for extremity sarcomas. It achieves comparable long-term survival to amputation while delivering significantly superior functional outcomes. The patient counselling must clearly address the surgical trade-off: accepting a marginally higher, yet acceptable, risk of local recurrence and a small chance of catastrophic failure (secondary amputation) in exchange for retaining a highly functional limb.

Collectively, these data suggest that limb-salvage surgery for distal tibial malignant bone tumors offers comparable oncological outcomes to amputation with the added benefit of improved functional performance, provided that surgical margins and soft-tissue reconstruction are adequate.

## 5. Discussion

This comprehensive review and meta-analysis was a first attempt to compare the outcomes of limb-salvage surgery to amputation for primary malignant bone tumors of the distal tibia, an anatomical region that has traditionally been regarded as unfavourable for limb preservation. This study is the first pooled analysis focused solely on this location, as it consolidates evidence from three significant comparative series: Laitinen et al. (2005), Mavrogenis et al. (2012), and Han et al., 2017.<sup>14–16</sup> Functional outcomes were consistently better following limb salvage. These data demonstrate that, with careful patient selection and rigorous technique, limb-salvage surgery in the distal tibia can be conducted safely and without jeopardizing oncological management.

Amputation has traditionally been the standard of care for distal tibial sarcomas due to the region's thin soft-tissue sheath, its proximity to the ankle joint, and very few reconstructive surgical options. Early studies reported significant rates of infection and flap necrosis following attempted reconstruction, prompting several centers to recommend amputation as the definitive therapy. With the introduction of multi-agent chemotherapy and better imaging, which enabled more precise preoperative tumor margin delineation, the standard of care transformed. The indications of limb salvage surgery for distal tibia bone tumors have evolved with use of composite allograft reconstructions and vascularized fibular grafts made possible by advancements in microsurgery, and modular endoprostheses and distraction osteogenesis procedures.<sup>6–9,13–16,21–25</sup> Meta-analyses of limb-salvage versus amputation for osteosarcoma among regions of the body have generally demonstrated similar survival and improved function after limb salvage. The current research supports these larger findings in the context of distal tibial tumors, which are one of the most technically challenging sites.

According to Laitinen et al., patients with distal tibial tumors treated with bone transport and endoprosthetic replacement could have favorable outcomes; however, deep infections occasionally required additional amputation.<sup>14</sup> Mavrogenis et al. conducted an extensive comparative study on distal tibia osteosarcoma and discovered that amputation and limb salvage had equal survival rates, with improved function following reconstruction.<sup>15</sup> Han et colleagues studied a novel technique of microwave-induced hyperthermia, which demonstrated comparable survival and local control to amputation, as well as much higher Musculoskeletal Tumor Society (MSTS) functional scores.<sup>16</sup>

Functional preservation is the primary reason for pursuing limb salvage. The pooled results of Mavrogenis et al. and Han et al. show a 10–20 % improvement in mean MSTS scores among limb-salvage patients compared to amputees.<sup>15,16</sup> This leads to improved gait efficiency, proprioception, and psychological well-being, which are especially significant in young and active patients. Furthermore, while current below-knee prosthesis have considerable mobility, patients usually experience limits in terrain adaptability and body image.<sup>9,13</sup> Successful limb salvage, on the other hand, can restore almost normal ambulation when soft-tissue and skeleton stability are preserved. The difficulty is to balance these functional benefits with the potential morbidity of major reconstruction and lengthy rehabilitation.

The most significant concern in limb-salvage surgery is if efforts for preserving the limb jeopardize oncological safety. The probability of inadequate wide oncological margins in the distal tibia may be reduced further by careful preoperative planning using MRI, following wide tumor resection guidelines, utilizing image-based surgery models or patient-specific instruments.

After limb salvage, there was a slightly increased absolute rate of

local recurrence (9/89, 10.1 %), although this was not statistically significant, and the majority of recurrences were manageable with additional surgery or adjuvant therapy. Although the broad confidence interval indicates low event counts and limited research sizes rather than a real difference, the pooled odds ratio of 2.66 (95 % CI 0.25–28.56) indicates a non-significant tendency toward greater local recurrence. Furthermore, Han and Mavrogenis both reported that recurrences were not associated with lower overall survival, confirming that local control failures are frequently controllable if identified early.<sup>15,16</sup>

According to Laitinen et al., who found four deep infections necessitating secondary amputation, infections continue to be the most common consequence of distal tibial reconstruction. Rigid internal fixation, preventive soft-tissue augmentation, and enhanced flap coverage procedures have significantly decreased this risk in subsequent series.<sup>14</sup> Overall complication rates in the meta-analysis were similar across groups (about 10–15 %), suggesting that improvements in reconstructive techniques have reduced the historical difference in morbidity between limb salvage and amputation.

However, even though secondary amputation is extremely uncommon, it may still be necessary in cases of profound infection or prosthesis failure, and this should be shared with patients during preoperative counselling. Clinically, our data support a “limb-salvage-first” approach for distal tibial tumors, in so far as oncological guidelines are maintained. Candidates for limb salvage should have a positive pre-treatment response to chemotherapy, no neurovascular encasement or pathological fracture, and viable choices for long-term soft-tissue restoration. In high volume oncology centers with reconstructive expertise, limb salvage can achieve long-term oncological and functional outcomes. However, where adequate margins or functional reconstruction cannot be assured, amputation remains a viable surgical option.

This systematic review and meta-analysis fundamental distinctive feature is its quantitative synthesis of all available comparative data for distal tibial tumors and its focused anatomic specificity. This analysis presents an accurate representation of current outcomes in this rare but challenging clinical condition by limiting inclusion to papers that directly compare limb salvage with amputation. Additionally, the results' generalizability is reinforced by consistent findings across various historical periods and reconstructive strategies.

The present study's limitations included its non-randomized design, retrospective design, and intrinsic selection bias. Patients with smaller size tumors, better response to chemotherapy, or intact neurovascular bundles were more likely to undergo limb salvage and this makes selection bias against the surgical methodology utilised. The sample size was limited (136 patients), and the event rates for local recurrence and death were low, resulting in large confidence intervals and low statistical power. Reconstructive strategies (allograft, fibular transfer, bone transport, endoprosthesis, microwave ablation) differed widely and had varied mechanical and biological outcomes. Due to variations in MSTS scoring methods and the lack of standard deviation data in preceding series, formal pooling of mean differences was not attainable and functional results were not consistently reported. Also, the limited number of studies rendered it difficult to assess publication bias.

Future studies ought to emphasize on patient-level pooled analyses and multicenter prospective databases for enhancing prognostic factors impacting the decision between amputation and limb salvage. Soft-tissue and skeletal integration may be improved further through the combination of vascularized composite tissue reconstruction, patient-specific instrumentation, and three-dimensional (3D) printing. Long-term research assessing economic feasibility, emotional adaptability, and the functional rehabilitation will also be key to guide patient-surgeon communication.

## 6. Conclusion

This meta-analysis and systematic review demonstrate that limb-

salvage surgery for malignant tumors of the distal tibia provides better functional results while achieving survival and local control comparable to amputation. Limb preservation has emerged as a secure and successful solution notwithstanding the fact that its procedure is still technically challenging and entails an elevated likelihood of consequences.

Amputation ought to only be employed in circumstances when oncological clearance or durable reconstruction is not feasible with current oncological management, and whenever feasible, limb salvage should be the selected approach of strategy.

Limb-salvage surgery would achieve equal survival and local control to amputation while providing better functional outcomes, hence justifying its role as the preferred option in carefully chosen patients of distal tibia tumors.

#### Patient consent

Not applicable.

#### Ethical statement

Not applicable.

#### Funding

None.

#### Credit author statement

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#### Declaration of competing interest

No interests to declare.

#### Acknowledgment

None.

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