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Intraoperative cryotherapy as a local adjuvant after bone curettage in orthopedic oncology: A review of modern literature

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 October 2025 and was last updated on 25 October 2025.

INTRODUCTION

Review question / Objective This systematic review of the literature aims to evaluate the effectiveness of curettage and cryotherapy in treating benign and locally aggressive bone tumors. Our research focuses on investigating the oncological efficacy of the treatment in terms of local recur-rences, assessing the safety of the procedure, evaluating complication rates, and eva-luating functional outcomes in terms of pain control, functional scores, and motion per-formance after surgery. This effort aims to orient surgical decision-making and further define the role of cryotherapy in contemporary orthopedic oncological practice.

Condition being studied Patients with benign and locally aggressive bone tumors treated with intraoperative cryotherapy were considered.

METHODS

Search strategy A systematic review of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, using a PRISMA checklist and algorithm.
A comprehensive search was conducted across the PubMed and MEDLINE databases using various combinations of the keywords "cryotherapy," "cryosurgery", "bone tumor", and "sarcoma" [Search string: ((Cryotherapy) OR (Cryosurgery)) AND ((Bone Cyst) OR (Bone Tumor) OR (Sarcoma))]. We included papers published between January 2000 and January 2025. The research was conduced in August 2025. Two independent reviewers (E.I., A.D.A.) conducted the research separately, screening for all the original articles reporting on the surgical treatment of benign and locally aggressive bone tumors that have been treated with intralesional curettage and cryotherapy as an adjuvant treatment during

surgery. The investigators separately reviewed each publication. All articles were initially screened for relevance by title and abstract, excluding articles without an abstract. All potentially suitable articles were then obtained and closely read, with data extracted to minimize selection bias and errors. Only original articles from peer-reviewed journals were included.

Participant or population A systematic review of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, using a PRISMA checklist and algorithm.
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Intervention The year of publication was recorded for each article that met our inclusion criteria. The number of cases included in each study was reported, along with the histological diagnosis of each treated lesion. The mean lesion size (larger diameter) was mentioned when reported. The curettage technique and the eventual use of a high-speed burr or chemical adjuvants other than cryotherapy to clear the surfaces of tumor residuals were described. The technique of choice for cryotherapy administration was considered and recorded. The follow-up of all included cases was considered, and their mean duration was reported for each study. The occurrence and the diagnostic timing of recurrences were considered for each article when available. Functional outcomes, when reported according to the Musculoskeletal Tumor Society (MSTS) scoring system, were also recorded. Intra-operative or post-operative complications, when documented by the authors of the single articles, were recorded in number and type. The absence of information regarding complications, MSTS score, or data on patients' clinical conditions at their latest follow-up did not constitute exclusion criteria. However, mean and average values were calculated excluding articles that were missing such data.

Comparator The year of publication was recorded for each article that met our inclusion criteria. The number of cases included in each study was reported, along with the histological diagnosis of each treated lesion. The mean lesion size (larger diameter) was mentioned when reported. The curettage technique and the eventual use of a high-speed burr or chemical adjuvants other than cryotherapy to clear the surfaces of tumor residuals were described. The technique of choice for cryotherapy administration was considered and recorded. The follow-up of all included cases was considered, and their mean duration was reported for each study. The occurrence and the diagnostic timing of recurrences were considered for each article when available. Functional outcomes, when reported according to the Musculoskeletal Tumor Society (MSTS) scoring system, were also recorded. In-tra-operative or post-operative complications, when documented by the authors of the single articles, were recorded in number and type. The absence of information regarding complications, MSTS score, or data on patients' clinical conditions at their latest follow-up did not constitute exclusion criteria. However, mean and average values were calculated excluding articles that were missing such data.

Study designs to be included Pre-clinical studies, literature reviews, articles that did not mention or provide data on cryosurgical treatment, and papers written in languages other than English were excluded. Considering the limited number of articles and the low level of evidence in the few available articles, we included in our study articles ranging from Level I to Level IV. Reports on single cases were excluded.

Eligibility criteria Inclusion criteria were (1) a confirmed diagnosis of benign, locally aggressive, or low-grade malignant bone tumor, (2) curettage, and detailed use of cryosurgery as an adjuvant treatment, along with (3) details on the clinical and oncological outcomes of the received treatments. Pre-clinical studies, literature reviews, articles that did not mention or provide data on cryosurgical treatment, and papers written in languages other than English were excluded. Considering the limited number of articles and the low level of evidence in the few available articles, we included

in our study articles ranging from Level I to Level IV. Reports on single cases were excluded.

Information sources PubMed and MEDLINE databases; papers published between January 2000 and January 2025.

Main outcome(s) Twenty-two studies met our inclusion criteria. A total of 1451 cases with benign and locally ag-gressive bone tumors were recorded. After a mean follow-up of 55.7 months, the mean recurrence rate was 7.4% and the global complication rate was 8.7%. The mean MSTS score was 27.8. Thereby, the combination of curettage and intra-operative cryotherapy, administered with either open or closed contact techniques, can be effective in eradicating benign and locally aggressive bone tumors, has low complication rates, and a limited impact on patients' functionality.

Quality assessment / Risk of bias analysis To account for the heterogeneity in study design and methodology among the se-lected studies, the Joanna Briggs Institute (JBI) Critical Appraisal tools were employed to critically assess their quality for inclusion in this systematic review. Each item on the checklist is rated with one of four possible responses: "yes", "no", "unclear", or "not applicable".
Egger tests were used to determine the risk of publication bias for complications and recurrences.

Strategy of data synthesis The year of publication was recorded for each article that met our inclusion criteria. The number of cases included in each study was reported, along with the histological diagnosis of each treated lesion. The mean lesion size (larger diameter) was mentioned when reported. The curettage technique and the eventual use of a high-speed burr or chemical adjuvants other than cryotherapy to clear the surfaces of tumor residuals were described. The technique of choice for cryotherapy administration was considered and recorded. The follow-up of all included cases was considered, and their mean duration was reported for each study. The occurrence and the diagnostic timing of recurrences were considered for each article when available. Functional outcomes, when reported according to the Musculoskeletal Tumor Society (MSTS) scoring system, were also recorded. In-tra-operative or post-operative complications, when documented by the authors of the single articles, were recorded in number and type. The absence of information regarding complications, MSTS score, or data on patients' clinical conditions at their latest follow-up did not constitute exclusion criteria. However, mean and average values were calculated excluding articles that were missing such data.
Statistical analyses were carried out using Stata SE 13.1 (StataCorp LLC, College Station, TX, USA). The complication and local recurrence rates of each study were noted or calculated. The studies' heterogeneity was calculated, and forest plots were designed for both complications and local recurrences.

Subgroup analysis NA.

Sensitivity analysis To account for the heterogeneity in study design and methodology among the se-lected studies, the Joanna Briggs Institute (JBI) Critical Appraisal tools were employed to critically assess their quality for inclusion in this systematic review. Each item on the checklist is rated with one of four possible responses: "yes", "no", "unclear", or "not applicable".

Statistical analyses were carried out using Stata SE 13.1 (StataCorp LLC, College Station, TX, USA). The complication and local recurrence rates of each study were noted or calculated. The studies' heterogeneity was calculated, and forest plots were designed for both complications and local recurrences. The size, heterogeneity, and retrospective nature of the included studies discouraged us from setting our review as a meta-analysis; however, the authors conducted a random-effects analysis to examine complications and local recurrences across the researched studies. Egger tests were used to determine the risk of publication bias for complications and recurrences. Generative artificial intelligence (GenAI) (ChatGPT 5.0, OpenAI Inc., San Francisco, USA) has been used to generate graphics based on our collected data, and to double-check statistical analysis.

Language restriction Only articles written in english were included.

Country(ies) involved Italy.

Keywords Bone tumor; Complication; Cryoprobes; Cryosurgery; Liquid nitrogen; Recurrence; Fracture.

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