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Outcome of recycle bone reconstruction using liquid nitrogen in primary malignant bone tumor

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Abstract: Primary malignant bone tumors constitute a small but significant portion, accounting for 3–5% of childhood cancers. Cryosurgery, utilizing liquid nitrogen to induce tumor necrosis through extreme cold, emerges as a favorable surgical technique for bone tumor. This study delves into the clinical and radiological outcomes of individuals underwent cryosurgery. This descriptive study focused on patients with primary malignant bone tumors subjected to wide resection and cryosurgery with follow-up period from 6 up to 48 months from year 2018 - 2023. The data was collected from medical records and database, we evaluated the demographic data, clinical with Musculoskeletal Tumor Society (MSTS), radiological outcome with International Society of Limb Salvage (ISOLS) score, and the complications of cryosurgery observed. Among the 37 patients examined, 20 males and 17 females were averaging 21.7 years of age. 29 of 37 (78%) cases identified as osteosarcoma most common location in the epimetaphyseal of the long bone with Grade Enneking IIB. MSTS score averaged 25.35 ± 5.54, with more than 68% achieving excellent and good score. ISOLS for radiological score revealed 37.8% with an excellent score, 48.6% with a good score. The most common complication, reccurence, occurs in 6 cases (16.2%). Patients with primary malignant bone tumors who underwent cryosurgery showed successful clinical and radiological outcomes, as measured by MSTS and ISOLS scores. This underscores the significance of cryosurgery in primary malignant bone tumor as favorable and cost-effective treatment, showcasing improved functionality and positive radiological results.

Keywords: *Biological Reconstruction, Cryosurgery, Primary malignant bone tumor, Recycled bone reconstruction.*

1. Introduction

Primary bone tumors are rare neoplasms, constituting approximately 3-5% of all cancers in children and less than 1% in adults. Despite their infrequency, primary bone tumors exhibit higher mortality and morbidity rates compared to other malignancies. Current treatment modalities include both surgical and non-surgical approaches, with surgery aiming for wide or radical resection. The shift from limb amputation to limb salvage surgery, driven by advancements in surgical techniques, anesthesia, prosthetics, imaging, and pathology, has become prominent since the 1970s.[1-3].

Limb salvage surgery involves extensive tumor resection followed by reconstruction to restore function and appearance while preserving the affected limb. Ideal reconstruction should be durable, functional, aesthetically pleasing, compatible with early rehabilitation, and cost-effective.[4] Various non-biological and biological reconstruction methods exist, each with its own considerations. Non-biological reconstruction includes arthrodesis with cement and spacers, while biological reconstruction

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methods encompass free vascularized autografts, massive allografts, recycled bone, and composite graft prostheses.[5]

In hospitals located in developing countries and lack of access to cadaver bone banks, extracorporeal reconstruction methods, such as cryosurgery, offers good alternative due to its low cost and easy to obtain. Cryosurgery, using liquid nitrogen to induce tissue necrosis at temperatures as low as -196°C, has been applied since 1964 for palliative procedures and, more recently, for osteosarcoma management. Cryosurgery provides advantages such as superior osteoinductive and osteoconductive properties, compatibility in size and shape for reconstruction, and ease of procedural execution [1,3,6].

In the last five years, cryosurgery has been utilized for primary bone tumors at Dr. Soetomo General Academic Hospital, Surabaya. However, there is a lack of comprehensive studies evaluating the clinical and radiological outcomes of patients undergoing cryosurgery for primary malignant bone tumors. Therefore, further research is essential to investigate the clinical and radiological outcomes of primary bone tumor patients treated with cryosurgery [1,3,6,7].

Research in this area is crucial to provide insights into the effectiveness and safety of cryosurgery, contributing valuable information to enhance the treatment strategies for primary malignant bone tumors. Assessing both clinical and radiological aspects will enable a comprehensive understanding of the impact of cryosurgery on patient outcomes, facilitating informed decision-making for clinicians and improving the overall management of primary bone tumors.

2. Materials and Methods

The research adopts a concise case study design with a prospective approach to examine the clinical and radiological outcomes of patients with primary malignant bone tumors who underwent wide resection and bone recycling with liquid nitrogen at Dr. Soetomo General Academic and affiliated hospitals. The study encompasses the population of all patients with primary malignant bone tumors who underwent wide resection and bone recycling with liquid nitrogen at the specified institutions between 2018 and March 2023. This study has been approved by the ethical committee of Dr. Soetomo General Academic Hospital.

Research samples consist of patients meeting the criteria of having primary malignant bone tumors, undergoing wide resection, and bone recycling with liquid nitrogen at RSUD Dr. Soetomo and network hospitals within the specified timeframe. Sample size determination utilized the Slovin formula, resulting in a minimum sample size of 24. Inclusion criteria comprise 1) patients with primary malignant bone tumors up to stage IIB Enneking, 2) patients undergoing wide resection and bone recycling with liquid nitrogen, 3) patients willing to participate in the research, and 4) post-operative patients with a minimum 6-month follow-up. Exclusion criteria include 1) patients with primary malignant bone tumors at stage III Enneking (metastatic case), 2) patients with primary malignant bone tumors not exposed to liquid nitrogen, 3) patients unwilling to participate in research, 4) patients with a postoperative follow-up period of less than 6 months. The methodology involves 1) Searching the MST database and medical records for patients who underwent wide resection and reconstruction surgery for primary bone tumors using liquid nitrogen from 2018 to 2023, 2) Inclusion of patients meeting the specified criteria, 3) Conducting clinical and radiological evaluations using MSTS and ISOLS for 6 months post-surgery based on medical records and Surabaya MST database records.

This research design aims to comprehensively explore the outcomes of wide resection and bone recycling with liquid nitrogen in treating primary malignant bone tumors, offering valuable insights for improving treatment strategies and patient care.

3. Results

3.1. Sample Distribution

In total cryosurgery that was performed at Dr. Soetomo General Academic Hospital and network hospitals from 2018 to 2023, there were 46 patients. A total of 37 patients met the inclusion criteria in

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this study. All samples were obtained through follow-up of post-cryosurgery patients, between 6 months, to the longest, namely 48 months with a mean of 13 Months (Table 1) (Figure 1).

Table 1.
Sample demographic distribution.

	Patients (n=37)	Proportion (%)
Gender		
Male	20	54
Female	17	46
Age (Years)		
≤10	4	10.8
11-20	17	45.9
21-30	10	27
31-40	3	8.1
41-50	1	2.7
51-60	1	2.7
>60	1	2.7

Figure 1.
The imaging of the subject from preoperative to follow-up. A) Preoperative x-ray; B) Preoperative MRI; C) Postoperative x-ray; D) Final follow up x-ray.

Based on gender, there were 20 male patients and 17 female patients, with an age range from less than 10 years to more than 60 years, with a mean age of 21.7 years. Most patients were in the teenage range, namely 11 to 20 years old, 17 patients (45.9%). There were 4 pediatric patients (10.8%) aged less than 10 years, and 1 elderly patient aged more than 60 years (2.7%).

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In the results of the distribution of patients based on gender and age, it was found that the number of male patients was greater than that of female patients in all age categories. There were no female patients over 60 years of age who underwent cryosurgery (Table 2).

Table 2.
Sample distribution based on age per gender.

Age	Male patients (n=20)	Proportion (%)	Female patients (n=17)	Proportion (%)
≤10	1	5	3	17.6
11-20	10	50	7	41.2
21-30	6	30	4	23.5
31-40	1	5	2	11.8
41-50	0	0	1	5.9
51-60	1	5	0	0
>60	1	5	0	0

A total of 37 samples were included in this study. The study sample had an average age of 21.7 ± 12.04 years with 20 (56%) of them being men. Based on tumor type, there were Osteosarcoma (78%), Chondrosarcoma (14%), Ewing sarcoma (5%), and others (3%) (Table 3). A total of 37 samples were included in this study. The study sample had an average age of 21.7 ± 12.04 years with 20 (56%) of them being men. Based on tumor type, there were Osteosarcoma (78%), Chondrosarcoma (14%), Ewing sarcoma (5%), and others (3%).

Table 3.
Sample distribution based on tumor type.

Tumor type	Patients (n=37)	Proportion (%)
Osteosarcoma	29	78%
Chondrosarcoma	5	14%
Ewing sarcoma	2	5%
Others	1	3%

In this study, tumor cell viability was evaluated using a grading system based on Enneking. In this study, there were 1 subject who had Grade IA (3%) and 4 subjects with IB (11%), there were 2 subjects with Grade IIA (5%) and 30 subjects (81%) with Grade IIB.

The location of primary tumor distribution was more often found in long bones, which was divided into proximal locations found in 16 subjects (43%), diaphysis locations in 3 subjects (8%), and distal locations in 13 subjects (35%), in this study also Locations found in non-long bones were 2 subjects (5%).The complication after operative management were recurrence in 4 patients (10.8%), Infection in 6 patients (16.2%), Metastasis in 4 patients (10.8%), and nerve lesion was occurred in 1 patient (0.27%).

3.2. MSTS Score Results

The MSTS score in this study has an average of 25.35 ± 5.54. If detailed, it was found that 9 of the 37 samples (25%) had excellent scores, 16 samples (43%) had good scores, 9 samples (25%) had fair scores, and 3 patients (8.1%) had poor scores. This shows that patients who were treated surgically experienced a good improvement in function.

3.3. ISOLS Score Results

From the ISOLS score, it was found that 14 of the 37 samples (37.8%) had excellent score, and 18 of the 37 samples (48.6%) had a good score, and 5 of the 37 samples (13.5%) had a fair score. This shows that patients treated surgically experienced very good radiological results.

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4. Discussion

The use of ISOLS/MSTS as scoring systems to assess post-tumor resection outcomes has been widely adopted in previous studies.[4,5,8] The MSTS system assigns numeric values (0-5) to six categories for lower extremity operations, including pain, function, emotional acceptance, gait, support, and walking. Upper extremity categories include hand position, dexterity, lifting ability, pain, emotional acceptance, and function. Patient scores are determined through direct examination and clinical interviews, resulting in classifications of excellent, good, fair, or poor outcomes.[9–12]

MSTS has been validated and deemed reliable in previous research, showing consistent results among observers.[10] MSTS scores averaged 24.97 ± 6.44, with 26% of samples rated as excellent, 38% as good, 19% as fair, and 17% as poor. This indicates a generally positive improvement in patient function post-surgery. ISOLS scores showed that 33% of samples were excellent, 21% were good, 33% were fair, and 12% were poor. This suggests a reasonably good radiological improvement post-surgery. It's important to note the inherent differences between the two assessments: MSTS is objective, while ISOLS is subjective.[10,14,15]

Cryosurgery is an effective surgical technique for certain types of tumors at specific stages. In osteosarcoma, cryosurgery is effective, particularly for use in osteosarcoma Stage IIB and below. In developing countries with limited resources, cryosurgery could be a viable option due to its relative simplicity compared to extensive surgical procedures. Cryosurgery also provides superior osteoinductive and osteoconductive properties, compatibility in size and shape for reconstruction, and ease of procedural execution. However, it's crucial to consider factors such as the availability of skilled medical personnel, proper equipment, and follow-up care. Healthcare providers should assess each case individually and take into account specific circumstances before determining if cryosurgery is an appropriate first-line treatment for a primary bone tumor. As medical knowledge and practices evolve, it is advisable to consult with an orthopedic oncologist for the most up-to-date and context-specific information.

Chen et al. disclosed that soft tissue injury associated with Cryotherapy typically manifests within a few weeks after surgery. Skin necrosis poses a significant risk if freezing affects the superficial layers. Continuous irrigation of neighboring tissues with warm saline helps mitigate the likelihood of skin necrosis. The infection rate stood at 1.40%, comparable to reported cases by Marcove RC, Gage AA, and Souna BS, where infection rates after bone cryotherapy ranged from 0% to 8%.[17–20] In our cases, Infection was occurred in 4 from 37 patients (10.8%).

Chen et al. also addressed the contentious issue of tourniquet utilization in cryosurgery. Some studies advocate for tourniquet application to reduce circulation and induce bone necrosis, while opponents argue that tourniquets may reduce vascularization to the skin and nerves, potentially leading to skin necrosis or nerve damage. However, our findings did not indicate an increased risk of soft tissue complications when employing a tourniquet. Prophylactic antibiotics were uniformly administered, akin to other tumor surgeries, and cryoablation did not correlate with increased infection rates.[17]

Sheng et al. observed no significant disparity in therapy response for bone metastases between groups at the 12-month mark post-treatment, suggesting that primary tumor treatment via cryosurgery has no impact on bone metastases. Additionally, their study indicated that patients undergoing cryosurgery experienced fewer local complications.[21]

Bickels et al. expounded on the concept and methodology of cryosurgery in benign and malignant bone tumor treatment. Cryosurgery extends the efficacy of curettage, rendering it comparable to wide resection. Compared to alternative techniques, cryosurgery with composite fixation not only preserves joint function but also markedly reduces local tumor recurrence rates. Despite being relatively straightforward, cryosurgery can lead to considerable morbidity if not executed correctly. Safe and effective procedures necessitate sequential steps including adequate tumor cavity exposure, meticulous curettage and burr-drilling, soft tissue mobilization and protection prior to liquid nitrogen introduction, internal fixation of the tumor cavity, and protection of the operated bone throughout the healing phase.

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Meller et al demonstrated an overall local recurrence (LR) rate of 8% in 440 cryo procedures, with over 90% occurring within the initial two years post-operation.[22] In our case the percentage of recurrence values was found to be higher with 16.2%. This can be thought to be caused by some patients not routinely following the postoperative chemotherapy protocol.

The study has limitations, such as not comparing the MSTS and ISOLS, the completion of chemotherapy, and not including the histopathological margin postoperative. However, the study provides a theoretical basis for future studies, emphasizing the necessity of incorporating both clinical and radiological aspects in postoperative assessments or using combined scoring systems, as the two aspects may not be directly related.

5. Conclusion

Patients with primary malignant bone tumors who underwent wide resection and reconstruction with recycled bone using liquid nitrogen had good clinical and radiological outcomes as measured by MSTS and ISOLS. This shows that patients treated with surgery have improved function and good radiological results, which should be heavily considered as a treatment option for primary malignant bone tumors particularly in the developing country with limited resources.

Ethical Clearance:

This study has been approved for ethical clearance by the Research Ethical Board of Dr. Soetomo General Academic Hospital number 2165/107/3/V/2023.

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Table 1.
Sample distribution-based post operative complication.

Post operative complication	n	Percentage (%)
Infection	4	10.8
Recurrence	6	16.2
Metastasis	4	10.8
Neve lesion	1	0.27