Original Research Paper

Volume - 13 | Issue - 03 | March - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Radiology

ROLE OF PREOPERATIVE EMBOLIZATION IN BONE TUMORS- A case control study

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ABSTRACT Preoperative embolization of bone tumor is a minimally invasive angiographic intervention technique and effective adjuvant treatment option for bone tumors. In 1975, Feldman was the first to use the pre-operative arterial embolization technique to downstage the vascularity of bone tumors, thus reducing blood loss during surgery. Surgery remains the mainstay treatment option for bone tumors. Embolization reduces tumor vascularity and hence decreases intraoperative blood loss and intraoperative blood transfusion. It enables more accurate delineation of tissue planes during surgery, resulting in complete removal of the bone tumor. The most frequent bone tumors that typically need preoperative embolization are those difficult to operate on because of their huge size, high degree of vascularity, proximity to critical tissues, or difficult surgical access. PVA particles are regarded as a workhorse in preoperative transarterial embolization and thus used commonly as an embolizing agent. It is safe procedure and therefore can be used as part of the multidisciplinary approach to the management highly vascular bone tumors.

KEYWORDS : Preoperative embolization, Intraoperative blood loss, Intraoperative blood transfusion, DSA- Digital subtraction angiography, bone tumors

INTRODUCTION:

Bone tumors can develop as a result of either abnormal growth of bone tissue or soft tissue, or both. Bone tumors can be classified into benign and malignant or primary and secondary. Primary malignant lesions are around a hundred times less prevalent than benign bone lesions.(1) Depending on the type of tumor, there are many treatment options. Surgery along with other therapy is typically the best treatment option. However, certain bone neoplasms may be difficult to operate on because of their huge size, high degree of vascularity, proximity to critical tissues, or difficult surgical access.(2)

Embolization of bone tumor is a crucial adjuvant therapy and in rare circumstances, it may even be the only and most effective option. In 1975, selective artery embolization was first used by Feldman et al. to treat bone malignancies in order to reduce intraoperative blood loss(3) Preoperative transarterial embolization has been proven to be successful in treating both primary and metastatic bone tumors. The tumor's vascularity and intraoperative blood loss are decreased by preoperative transarterial embolization. Additionally, it lessens the necessity for blood transfusions and the likelihood of post-operative problems. It enables more accurate delineation of tissue planes during surgery, resulting in complete removal of the bone tumor. The exact targeting of the tumor feeding arteries and tumor capillary bed is the fundamental idea behind embolization of bone tumors.(4)

The most frequent bone tumors that typically need preoperative embolization are those that are hypervascular in nature such as giant cell tumors, aneurysmal bone cysts, telangiectatic osteosarcomas, vertebral hemangiomas, osteoblastomas and vascular metastatic lesions, notably from thyroid or renal cell.

AIM:

To study the role of pre-operative embolization of bone tumors in relation to intraoperative blood loss, intraoperative blood transfusion and surgical time.

MATERIALS AND METHODS:

Prospective study was conducted in 17 patients with radiological and histopathological proven cases of bone tumors (15 primary and 2 secondary) at Gauhati Medical College and Hospital, Guwahati from May 2021 to April 2022 with approval of institutional ethics committee.

Informed consent was obtained from all patients before angio-embolization after explaining the procedures and their complications. In this study, patients with primary and secondary bone tumors of the extremities suspected to have highly vascularized lesion on radiological imaging and amenable to limb salvage surgery were included.

Every patient had X-ray of the affected area, computed tomography scan and magnetic resonance imaging scan utilizing various pulse sequences in various planes.

TECHNIQUE OF ANGIOGRAPHY AND EMBOLIZATION:

Before two days of the procedure, patient's viral markers and other routine blood investigations including serum creatinine, PT-INR, BT, clotting time, RBS were done.

A single interventional radiologist with more than three years of expertise performed the angiography and embolization using Siemens artis zee biplane DSA machine under MAC (monitoring under anesthetic care) with the use of local anesthesia.

Transfemoral route was used in all patients, right femoral route was used in 10 patients while the left femoral route was used in 7 patients using cross over technique. The femoral artery was punctured using the seldinger technique. Once the mini-guide wire was inserted into the artery lumen, the cannula was removed. Over the short guide wire, the arterial sheath was then inserted.

All patients underwent pre-embolization angiograms to determine the extent of tumors vascularity and the tumor feeding arteries.

Through the artery sheath, the Terumo guide-wire (0.035" angled) and guiding catheter (C2-Cobra/MPA) was inserted.

Under fluoroscopic guidance, the catheter and guide wire were manually manipulated to enter the parent artery from which the tumor feeder arteries were suspected to arise.

The tumor's parent and feeding arteries were then injected with contrast material. To determine the hypervascularity of all bone tumors and to pinpoint the primary feeding arteries and matching tumors blush, selective arteriogram was performed on each patient.

When a stable selective catheter position is achieved a microcatheter (Progreat 2.7 – 2.9F) was introduced through the selective catheter.

The selected embolic agent was administered through the microcatheters into the feeding arteries and tumors capillary bed. Eleven embolization were carried out solely using PVA particles (sizes of 300–500 and 500–700 microns), whereas six embolization used a combination of gelfoam and PVA. The choice of embolizing material was done on the basis of personal preference, catheter size, position of catheter tip and diameter of the feeding vessel.

One advantage of employing microcatheters, which are frequently advocated, is that the delivery of the embolic agent away from the parent channel which may reduce the likelihood of non-target embolization.

It was determined that the goal of embolization would be near total obliteration of the tumors blush and the embolization of the all feeding arteries supplying the tumors.

Lastly post-embolization angiogram was obtained to detect the technical success of embolization and graded the devascularization into 3 groups on the basis of degree of devascularization. Devascularization more than 75% was taken as grade I, 50 to 75% as grade II and less than 50% was considered as grade III. (5)

By manually compressing the puncture site after the procedure, homeostasis was established and pressure bandage was applied.

Within 048 hours of embolization, tumor stabilization and resection surgery were performed on all patients. All surgeries were conducted by two orthopedic surgeons with experience of more than ten years.

The surgical procedures carried out on the study group's patients included tumor resection and implant fixation in 7 cases, curettage and bone cementing in 4 cases, and tumor resection, bone grafting, and plate fixation in 6 cases.

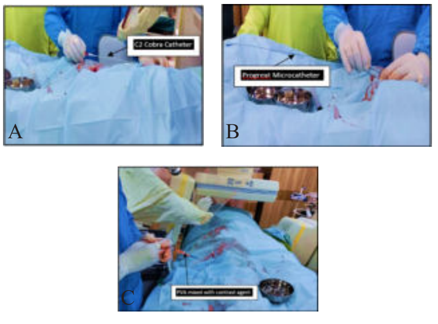


Figure 1: Showing the procedure of embolization (A) C2 Cobra catheter with guide wire advanced through arterial sheath, (B) Introduction of progreat through the selective catheter, (C) Administration of embolizing agent (PVA particles) through the progreat microcatheter.

Calculation of intraoperative blood loss:

The volume of overall sterile irrigation fluid utilized during the surgery and the difference between the dry and wet weight of surgical gauges and sponges were used to quantify the intra-operative blood loss. The amount of blood loss was calculated using the difference between the volume of the suction container and the sterile irrigation fluid utilized, plus the combined net weight of blood and saline in all gauges and sponges employed. Intraoperative blood transfusion volume and surgical time taken were also noted from the surgical note.

In this study, parameters recorded were intraoperative blood loss, intra operative blood transfusion and surgical time from the surgical notes in each patient.

Statistical analysis:

For statistical analysis, the hospital records of 17 patients with a comparable histological diagnosis who had previously undergone surgery without preoperative embolization (control group, n = 17) were retrieved. The most prevalent histological type among these 17 patients was GCT, which accounted for 6 patients (35.3%).(4)

We also recorded the parameters such as intraoperative blood loss, blood transfusion and surgical time from the surgical notes of the 17 patients of the control group operated in past without undergoing any preoperative embolization.

Statistical analysis was performed using SPSS Version-21 software. P-value was obtained. With regard to intraoperative blood loss, intraoperative blood transfusion and surgical time, statistical comparisons were made between the embolization group and the non-embolization group (data were taken from the hospital medical record). Chi square and fisher's exact test was used to examine the differences between the two groups.

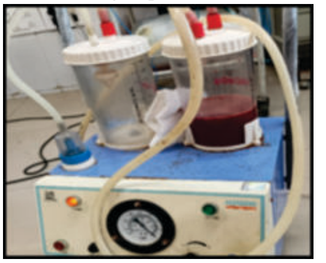


Figure 2: showing suction bottle to measure the blood loss during surgery.

RESULTS:

In our study, 17 patients had undergone preoperative embolization of bone tumors of the extremities and pelvis which includes GCT (n= 5), Osteosarcoma (n=4), ABCs (n =2), Chondrosarcoma (n=2), Ewing sarcoma (n=2), metastasis from thyroid carcinoma (n = 1) and metastasis from RCC (n = 1). GCT was the most common tumor undergone embolization followed by osteosarcoma. Patient aged ranges from 11 to 65 years of both genders.

Table 1: Patient demographics and tumor histology of study population.

Characteristic	Number (%)
Age group (years)	
<20	5(29.4%)
20 - 40	7(41.1%)
41 - 60	3(17.6%)
>60	2(11.8%)
Sex	
Male	8(47%)
Female	9(53%)
Histopathological Diagnosis	
GCT	5(29.4%)
Osteosarcoma	4(23.5%)
Chondrosarcoma	2(11.7%)
ABC	2(11.7%)
Metastases	2(11.7%)
Ewing sarcoma	2(11.7%)

PVA particles were utilized exclusively in 11 patients, while Gelfoam and PVA were mixed in 6 patients. After embolization, tumor blush was reduced by more than 75% (grade I devascularization) in 12 patients (70.6%) and was reduced by 50% to 75% (grade II) in 2 patients (23.5%).

Table 2: Comparison of mean intraoperative blood loss, mean intraoperative blood transfusion and mean surgical time between embolization group and non-embolization group.

Group	Embolization group (n=17)	Non- embolization group (n=17)	P- value
Mean intraoperative blood loss (in mL)	950	1508.8	<0.001
Mean Blood Transfusion (mL)	494.12	988.24	<0.001
Mean Surgical Time (Minutes)	201.47	210.29	0.423

Embolization group (n = 17)

The mean intraoperative blood loss in this study was 950 mL (range: 250–1650 mL), and mean intraoperative blood transfusion needed was

494.12 mL (range 0-1050 mL). In single individual, no blood transfusion was necessary. The mean surgery time required was 201.47 minutes (range 155-250 min).

Non-embolization group (n = 17)

The mean intraoperative blood loss was 1508.8 mL (range: 550–2200 mL), and mean requirement of intraoperative blood transfusion was 988.24 mL (range 350-1750 mL). The mean surgery time required was 201.47 minutes (range 180-260 min).

In our study, statistically significant ($P < 0.001$) difference was found on comparing mean intraoperative blood loss and intraoperative blood transfusion between embolization group and non-embolization group. No statistically significant ($P=0.423$) difference was found on comparing mean surgical time needed between embolization group and non-embolization group.(Table 2)

It was possible to achieve complete or almost complete tumor devascularization in 70.5% of individuals In these cases, average amount of blood lost was 895.8 ±358.9 ml. The mean loss was 1080 ±292.8 ml in the partial/incomplete group. From the observation, no statistically significant conclusions could be drawn (p value = 0.329). (Table 3).

Table 3: Shows completeness of devascularization compared to mean intraoperative blood loss.

Devascularization after embolization	Number of patients	Mean intraoperative blood loss (mL)	SD	P value
Complete/ near total	12	895.83	358.949	0.329
Partial/ incomplete	5	1080.00	292.831	
Total	17	950.00	342.783	

In our study, no major complications during and or after the procedure. Three patient suffered minor complications, 1 with puncture site hematoma and 2 with post embolization syndrome which were managed conservatively.

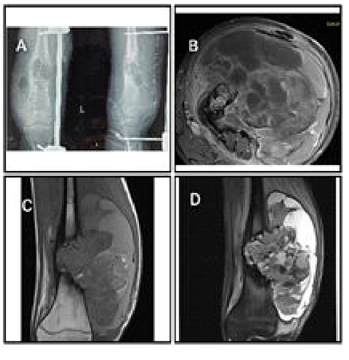


Figure 3: Telangiectatic Osteosarcoma at distal diaphysis of femur

X-ray AP and lateral view (A) showing an expansile lytic lesion in distal diaphysis of femur with cortical breach. On coronal T1WI (C) and PDFS image(D) lesion is iso to hypointense and heterogeneously hyperintense with adjacent marrow edema and large exophytic component with fluid-fluid levels within. On post contrast axial image (B), lesion is heterogeneously enhancing.

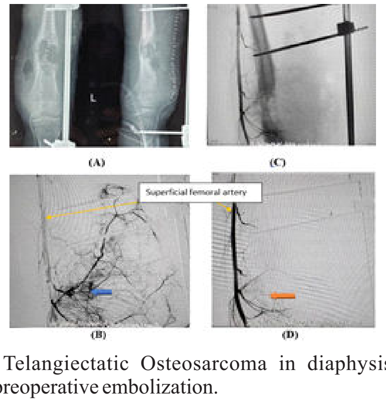


Figure 4: Telangiectatic Osteosarcoma in diaphysis of femur underwent preoperative embolization.

(B) Pre-embolization DSA image of left superficial femoral artery show multiple feeders arising from branches of superficial femoral and popliteal arteries are supplying the tumor with marked tumor blush (blue arrow). (C) and (D) Post embolization DSA image shows > 90% reduction in tumor blush (red arrow). (DSA: Digital substraction angiography)

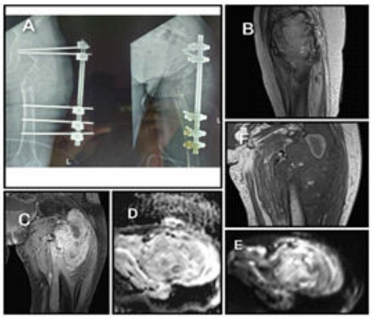


Figure 5: Metastatic carcinoma of thyroid in metadiaphyseal region of left femur. AP and lateral view of X-ray (A) shows a large expansile lytic lobulated lesion involving the metadiaphyseal region of the left femur with wide zone of transition, cortical destruction and aggressive periosteal reaction. The is pathological fracture at the diaphysis. On sagittal T2WI of MRI (B) lesion is heterogeneously hyperintense and on T1WI (F) isointense with internal areas of hemorrhage. On post contrast image (C), lesion is heterogeneously enhancing with internal areas of necrosis and large soft tissue component. On DWI (D and E), the lesion shows diffusion restriction.

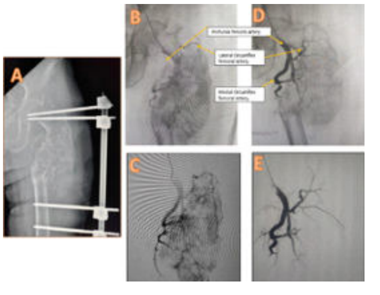
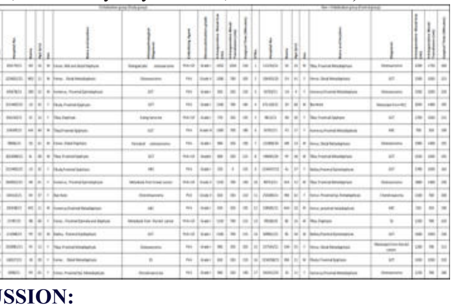


Figure 6: Metastatic carcinoma of thyroid in metadiaphyseal region of left femur. (B) and (C) Pre embolization DSA image of left femoral artery shows multiple feeders arising from branches of profunda femoris artery supplying the tumor with marked tumor blush (D) and (E) Post embolization DSA image shows > 90% reduction in tumor blush.

Table 4: Patient demographics, histological diagnosis, location of the tumor, blood loss, transfusion requirement and surgical time of the study group and control group for entire study and control population. (GCT= Giant Cell tumour, ABC= Aneurysmal bone cyst, ES= Ewing Sarcoma, PVA= Polyvinyl alcohol, GF= Gel foam)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DISCUSSION:

Surgical resection is still the primary form of treatment for primary bone tumors, whether they are benign or malignant. However, heavy, uncontrollable blood loss during surgery has been a typical issue, necessitating numerous transfusions. Preoperative embolization has greatly decreased intraoperative blood loss and improved the separation of the tumor's margins from its surroundings, making it easier to remove the tumor. The goal of embolization is to cut off the tumor's vascular supply.

In our study, preoperative embolization was performed on 17 patients; the most prevalent age range was 20 to 40 years with a slight female predominance. The most common type of tumor embolized was GCT (n = 5) followed by osteosarcoma (n = 4).

PVA particles are regarded as a workhorse in preoperative transarterial embolization and thus used commonly as an embolizing agent. It is a fine substance that may easily be administered and is reasonably priced. It has the ability to obstruct the tumor blood supply. In present study, only PVA particles were used in 11 patients (64.5%) and PVA combined with gel foam were used in 6 patients (35.5%). In a study conducted by Jha et al. (4) only PVA particles were used in 46% cases, PVA combined with gel foam was used in 50 % and only Gel foam were used in 4% of the patients. Along with gelfoam and PVA particles, Radeleff et al.(6) also used embosphere and liquid embolizing materials including cyanoacrylate lipoidal mixture and ethibloc in their research.

After the embolization was completed, a final angiogram was conducted and the degree of tumor devascularity was subjectively judged. Percentage of reduction of tumor blush was categorized into three groups as mentioned in previous studies; > 75% devascularization as Grade I, 50% 75% devascularization as grade II and < 50% devascularization Grade III. It represents the completeness of the embolization procedure. In present study, we found that >75% devascularization achieved in 12 patients (70 %), 50%75% devascularization achieved in 4 patients (25.5%), and <50% devascularization achieved in only 1 patient (5.8%). Findings of our study were in concordance with the findings of Thiex et al. (7). where they found 59%, 3.6 % and 5 % of the patient achieved > 75%, 50% to 75% and < 50% devascularization respectively. In other study conducted by Jha et al.(4) more than > 75% reduction of tumor blush was achieved in 24 patients (92%), and 50%75% in 2 patients (8%). Five of the eleven patients in a research by Börüban et al.(8) showed 80%–100% devascularization.

In our study, the mean intraoperative blood loss and blood transfusion in embolization group were 950 mL and 494.12 mL whereas mean intraoperative blood loss and blood transfusion in non-embolization group were 1508.8mL and 988.24mL respectively which shows the difference was statistically significant.

In 20 patients who underwent surgery without preoperative embolization, Barton et al.(9) reported blood loss of 2000–18500 mL (mean 6800 mL), however when preoperative embolization was carried out and operated on within 72 hours, only 500–1500 mL blood loss occurred. Their study also found that blood loss increased if surgery was not performed soon after embolization. In our study, all the cases were operated within 48 hours of embolization.

In a study conducted by Jha et al.(4) on preoperative embolization of primary bone tumors, they found mean intraoperative blood loss in embolization group and non- embolization group was 1300 mL and 1800 mL and mean intraoperative blood transfusion in embolization group and non- embolization group was 700 mL and 1400 mL respectively. They found statistically significant ($P < 0.001$) difference between embolization group and non- embolization group for the amount of blood loss and requirement of blood transfusion which was in concordance with our study.

When compared to the control group, the study group's mean surgical time was less (201.47 min), but no statistical significant ($p = 0.42$) difference was found between these two groups.

In our study, grade I devascularization was considered as complete or near total and Grade II and III devascularization was considered as partial embolization. Mean intraoperative blood loss in patients with complete or near total embolization was 895 mL while 1080 mL in patients with partial embolization in our study. Although mean amount of blood loss in complete or near total embolization was less than partial embolization, no statistical significance could be derived from the observation (p value= 0.329). This was concordance with the study done by Aggarwal et al. where the mean estimated blood loss was 950 ± 449ml in complete/near totally embolized patients and 694 ± 342ml in partially embolized patients with no statistically significant difference (p value= 0.34). According to a study conducted by Sun and Lang et al.(10), they discovered that the intraoperative estimated blood loss relies on the tumor blush's remaining area and patients with incomplete embolization experienced considerably more intraoperative blood loss than individuals with fully devascularized tumors.

Most studies found in the literature revealed that embolization was carried out using local anesthesia, as it was in our study.

Embolization of bone tumours may result in complications such as femoral artery dissection at the puncture site, discomfort from tumour ischemia necrosis, unintentional embolization of non-tumor feeding arteries, infections, and post-embolization syndrome.(8,11) No serious complications were recorded in our study, which is consistent with earlier studies that also found no major complications.

Limitations of our study were small sample size, no comparison of each type of tumor undergone preoperative embolization and no long term follow up to evaluate the tumor recurrence and survival rates.

CONCLUSION:

Our study concluded that preoperative embolization of bone tumors when carried out 0 to 48 hours before surgery reduces the intraoperative blood loss and need for intraoperative blood transfusion volume. Preoperative embolization, which significantly lowers the intraoperative blood loss and intraoperative blood transfusion, allows patients to undergo limb-savage surgery rather than amputation in many highly vascular bone tumors, which was beneficial for patients. As seen in our study and in numerous similar other studies around the world, preoperative embolization has proven to be a safe procedure and therefore should be used as part of the multidisciplinary approach to the management highly vascular bone tumors. However, it must be stressed that a large number of patients must be included in prospective randomized studies before a clear conclusion and generalize it for bone tumor resection.

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