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Is Pre-Operative Angio-Embolisation an Effective Modality to Control Intraoperative Blood Loss in Extremity Bone Tumors?

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Abstract

Introduction: *Bone tumors of the extremity and metastatic lesions of the long bones are hypervascular lesions. Limb salvage is besieged with a number of complications and the earliest to occur is inadvertent and unexpected blood loss during surgery. Pre-operative angio-embolization has been offered as a rescue treatment to prevent or minimize blood loss during surgery. The benefits of this technique are in the form of reduced blood losses, less need for autologous transfusions, better surgical resections and improved patient survival.*

Material and Methods: *A prospective study was undertaken wherein 12 patients who had pre-operative embolization for an extremity tumor were subsequently operated upon. The intra operative blood loss was calculated as per established protocols in literature.*

The factors taken into consideration were tumor volumes, efficacy of the embolization procedure, duration of surgery and intra-operative blood losses. Each variable was independently calculated against the actual blood loss. Statistical analysis of the data was performed to calculate the significance of individual variables by calculating the p values.

Results: *Out of 12 cases, 6 patients underwent wide resection, 4 patients underwent margical resection and 2 patients had intra-lesional resection.*

In all cases, pre-operative embolization led to significant decrease in actual blood losses as compared to estimated losses. The blood loss was higher when the tumor volumes exceeded 400cm3 and the duration of surgery exceeded 270 minutes.

In 50% cases, the duration of surgery was >270 min and the actual losses were 1174+_ 492 ml. Actual losses were 556+_171ml for surgeries lasting 270 min. The statistical correlation for this observation was significant (p value 0.003).

Discussion: *Pre-operative angio-embolization where the vascular tumor bed is occluded with the help of embolic agents has come to be recognized as an effective method to achieve this goal. Though other factors like tumor volume, duration and complexity of the surgical exercise and degree of devasculaization achieved also contribute to the overall blood loss, embolization is helpful in decreasing iintra-operative blood loss.*

Keywords- *bone tumors, angioembolization, intra-operative blood loss.*

Introduction

Bone tumors of the extremities include a variety of lesions, both primary and metastatic. Surgical resection of primary tumors coupled with adjunctive modalities is the treatment of choice [(1)]. Pre-operative selective/ super-selective intra-arterial embolization is an effective method to decrease the tumor vascularity in hypervascular tumors of the bone and soft tissues of the extremities [(2,3)].

Feldman et al described the use of selective arterial embolization for treating bone tumors in 1975[(1,2)]. In order to control intra-operative blood loss it was performed pre-operatively. The indications for the procedure are reducing the risk of intra-operative and post-operative bleeding in hypervascul; arised tumors, simplifying the manipulation of tumors, better definition of tissue planes at surgery facilitating wide resection and hence reduced recurrences [(4,5)].

Tumor embolization is defined as blockage of the vascular supply to a tumor. This is usually performed via an endovascular approach using the Seldinger technique[(6)]. The procedure is usually performed in a single session with diagnostic arteriography[(7)]. Angiography is performed prior to embolization to identify the tumor feeding vessels and to determine the safety of embolization[(4)]. Ideally an embolic agent will block very small vessels within the tumor but spare the adjacent normal tissue. Relatively larger particulate agents like polyvinyl alcohol (PVA) and Gel foam do not penetrate deeper regions of the tumor but are less likely to cause damage to adjacent normal tissues[(1,7,8)]. Liquid embolic agents such as acrylic or ethanol and powdered particulate materials can penetrate the smallest of blood vessels but can also damage normal tissues extensively if the vessel identification is faulty [(7,8,9)]. The basic premise in trans- arterial embolization is occlusion of most of the capillary bed of the tumor. The occlusion of only the major feeders is ineffective because of numerous collaterals [(1,4)].

Primary bone sarcomas, giant cell tumors of extremities, aneurysmal bone cysts, hemangiomas and solitary metastatic lesions of the bone are some of the tumors affecting the skeleton that are amenable to surgical resection [(10,11,12)]. Majority of these lesions are hypervascular in nature and can cause considerable blood loss during surgery thus threatening the survival of the extremity or the patient. Preoperative endovascular embolization decreases the overall blood supply to a tumor thus reducing it's size and making the surgical exercise relatively easier with reduced blood losses [(13, 14)].

Material and Methods

The institutional ethics committee approved this study. Informed consent was obtained by all a ptients before angio-embolization and again before surgery after explaining the procedures and their complications.

A prospective study involving 12 patients was undertaken to evaluate the results of pre-operative angio-embolisation on intraoperative blood loss. All patients had radiologically and histopatholo-gically confirmed bone and soft tissue tumors. In 6 cases, a wide resection of the tumor was deemed feasible on pre-operative imaging. In benign cases and metastatic lesions of the skeleton, the surgical exercise was aimed at achieving local control by intra-lesional or marginal resection.

Calculation of tumor volume

Tumor volume was calculated using one of the two formulae as applicable. For ellipsoidal masses, the volume was calculated as (Volume= π/6 x length x depth x width) where there was a large soft tissue component. For tumors with discrete soft tissue component the formula (Volume= length x depth x width x 0.735) was used [(15, 16)].

Technique of pre-operative embolization

Arterial catheterization was performed after femoral/ radial artery puncture under local anesthesia using the Seldinger technique[(4,6)]. Catheterization was done using a coaxial catheter system comprising of a large 4-6 French catheter and a microcatheter (2.7 French) was used for

selective arterial access. Angiography was performed to identify the major vascular supply of the extremity and the feeding vessels to the particular tumor. As all patients were planned for surgical resection, only temporary occlusion of the tumor blood supply was desired and this was achieved with gel foam or a combination of PVA particles/coils. Tumor devascularization was identifiable on a post embolization angiogram as residual tumor staining and was graded as: Total/near total (none or upto 10%); Subtotal (10-30%); Partial (30-70%) and incomplete/failure where no devasculization was visible [5,6].

Calculation of anticipated blood loss

Estimation of anticipated blood loss was derived from historical references wherein blood loss values were available. We used references where nearly similar tumors were operated in relation to size, site, volume, duration of surgery and reconstruction methods used and the values for actual blood loss were documented [3,17,18,19].

Calculation of intra-operative blood loss

Intra-operative blood loss was calculated using the gravimetric method. The loss was quantified by measuring the difference between the dry and wet weight of surgical gauges and sponges and the total amount of sterile irrigation fluid used during the procedure. Blood loss was determined as the difference between the sterile irrigation fluid used and the volume in the suction container plus the net weight of blood and saline in all the gauges and sponges used. Additional 150-200ml was added for each change of the soiled drapes. We measured the losses immediately after surgery to minimize the evaporated losses [20].

Statistical Analysis

Chi Square test, Fischer's Exact test were used for univariate analysis of categorical variables in different subgroups. A p value of <0.05 was considered significant.

Observation and Results

This prospective study was conducted to ascertain whether pre-operative angio-embolisation of extremity bone and soft tissue tumors translated into reduced intraoperative blood loss.

Out of the 12 cases available for evaluation, 6(50%) underwent wide resection of the tumor, 4 patients underwent marginal resection (3 benign lesions and 1 metastatic lesion) and 2 patients had intralesional resections (both metastatic lesions).

We identified various factors determining the amount of intraoperative blood loss. These were tumor volume, type of embolization, duration of surgery and post-operative collection in suction drains. The mean expected blood loss was 1633+_660 ml (range 700-2500ml). The blood loss was more when the tumor volume exceeded 400cm3 and the duration of surgery exceeded 270 min (p value=. 001) (Fig 3, 4). Pre-operative embolization decreased blood loss across all tumors irrespective of the tumor size (p value=. 001) (Fig 5).

In 66% of cases, a complete or near total tumor devascularization could be achieved (Fig1, 2). In these cases, the mean estimated blood loss was 1825+_723ml and the mean actual loss was 950+_449ml. In the subtotal/partial group, the mean estimated loss was 1250+_289ml and the mean actual loss was 694+_342ml. No statistical significance could be derived from the observation (p value= 0.34).

In 50% of cases, the surgery was performed within 72 hours of the embolization procedure. All cases were operated within a week of the embolization. In the first instance the actual intraoperative blood loss was 873+_478ml whereas it was 856+_399ml in the second group. The p value calculated was 0.94 that was not statistically significant (Fig 6).

In 50% of the cases, the duration of surgery was >270mim and all these patients had wide resection of the tumor and skeletal reconstruction with tumor megaprostheses. The mean estimated blood loss was 2083+_492ml while the actual loss encountered intra-operatively was 1174+_359ml. the surgeries that could be completed in less than 270min, the actual loss was 556+_171ml against a

mean estimation of 1183+_479ml. the p value of 0.003 was found to be statistically significant.

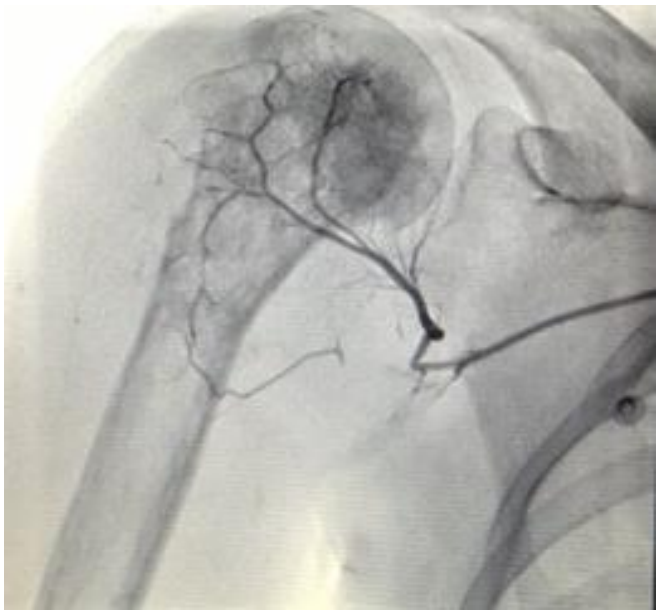

Fig 1 Pre embolization angiogram of a 22-year-old male patient suffering from Ewing's sarcoma of the proximal humerus. The angiogram shows rich vascularization of the lesion due to tumor neoangiogenesis

Fig 2 Post embolization angiogram of the same patient showing a successful blockage of tumor vascularity with a tumor blush due to retained dye.

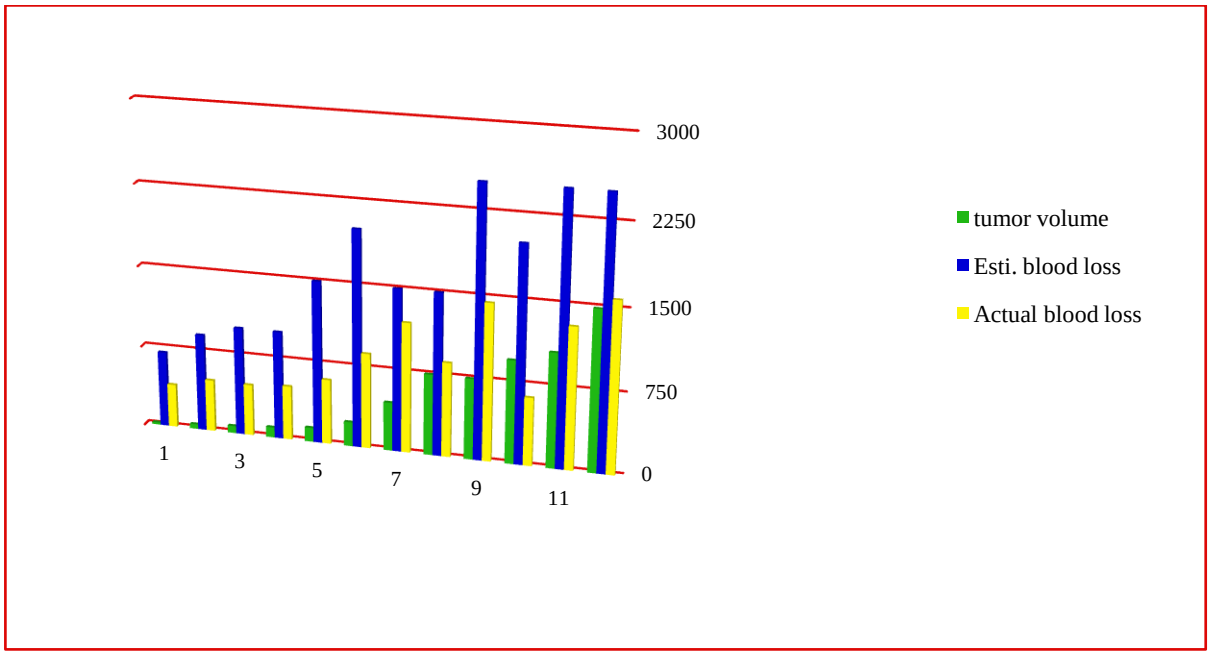

Fig 3 Chart showing correlation between tumor volume, estimated blood loss and actual blood loss. Both the estimated and actual blood losses increase as the tumor volumes increase. There is a uniform reduction in actual blood losses post embolization.

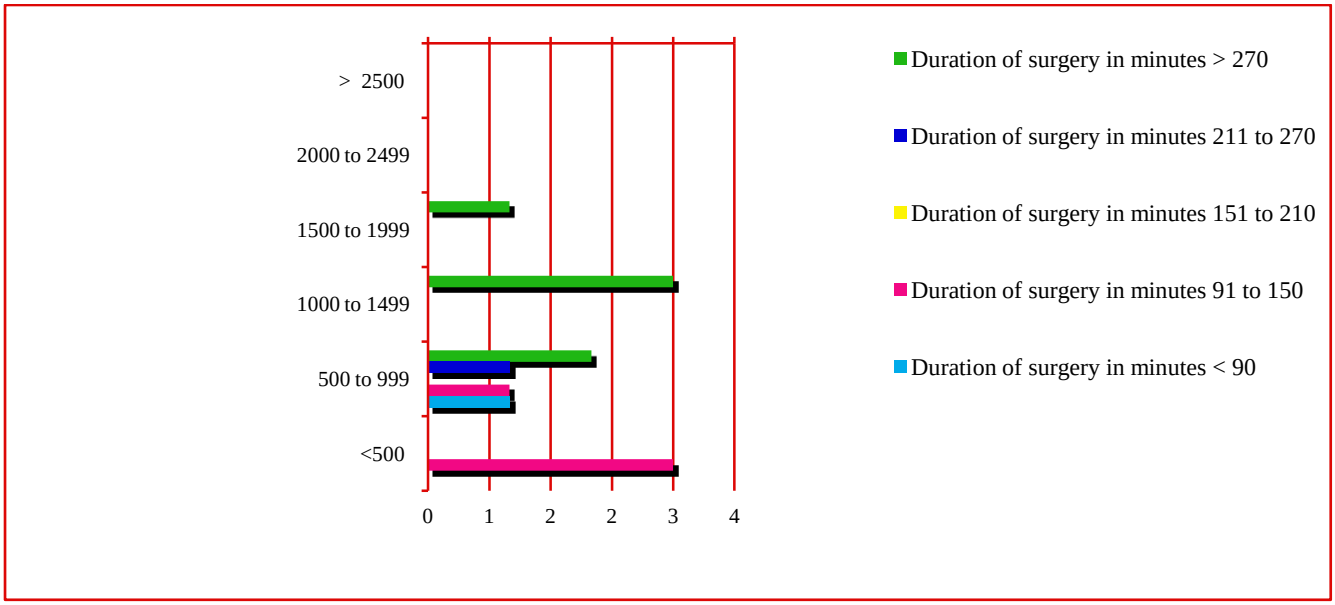

Fig 4 Chart showing relationship between duration of surgery and blood loss. Higher losses were calculated for surgeries where the duration exceeded 270 minutes.

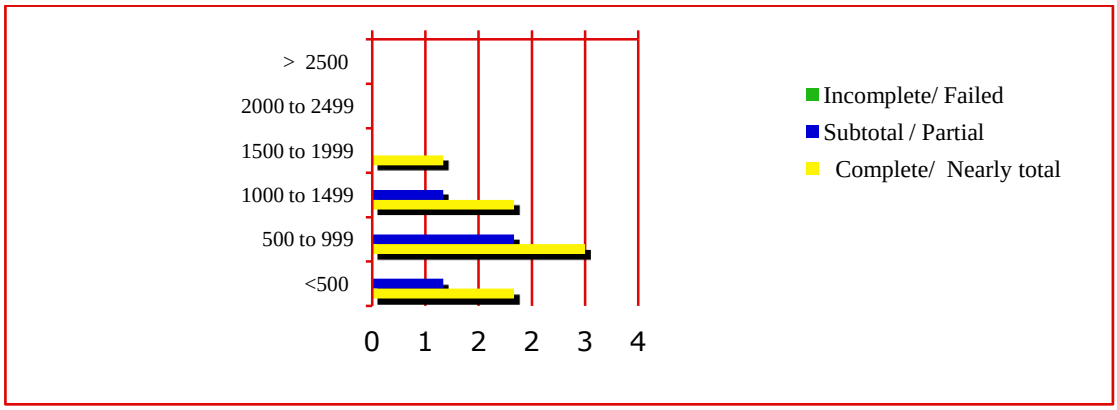

Fig 5 Chart showing relationship between degree of tumor devascularisation achieved and intra-operative blood loss.

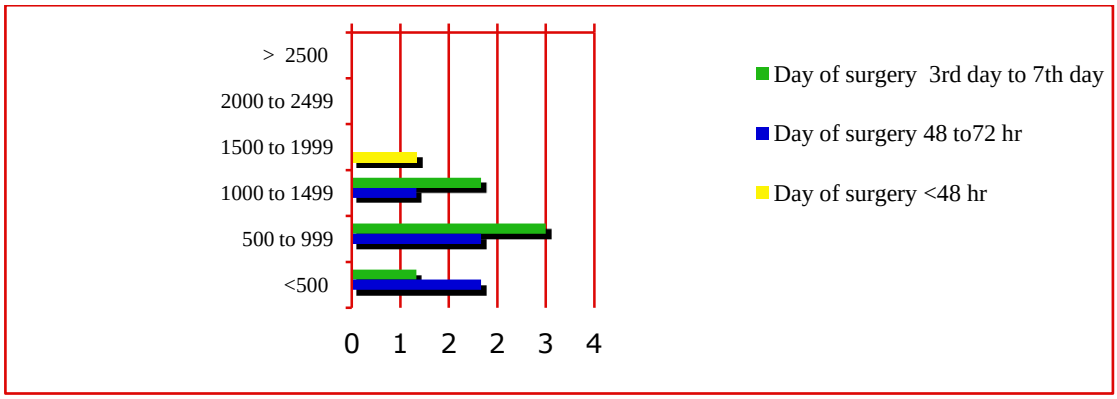

Fig 6 Chart showing correlation between blood loss and interval of embolization and surgery

Discussion

Limb salvage is an accepted alternative to amputation in primary bone tumors. Improvement in surgical techniques and reconstructive options has made limb salvage feasible in majority of patients with primary bone tumors who are non metastatic at presentation[21,22]. Wide resection of primary limb sarcomas is the first step in this

endeavor. However, this entails significant blood loss intra-operatively[13,23]. Wide resection of the tumor and reconstruction is time consuming and the average duration of surgery may extend to beyond 270mim. Significant blood loss through an exposed resection bed may add to the anticipated blood loss during resection[13,14].

Metastatic bone disease is the commonest type of skeletal malignancy treated by orthopedic surgeons. Pain from bone metastases can be due to pressure or mass effect of tumor tissue within the bone and bone destruction causing mechanical instability with impending or existing pathological fracture[4]. Embolization is useful in the treatment of metastatic bone disease either as a preoperative adjunctive therapy before palliative surgery or as serial embolization for cases deemed unfit for major surgical intervention [13,17]. Since all metastatic bone lesions are hypervascular, all patients should be considered appropriate candidates for tumor embolization[4]. Surgical excision of solitary bone metastasis is reported to translate into a better lifespan and quality of life [24].

The blood supply to a tumor is derived from multiple vessels of small to medium calibers that arise directly from a major vascular pedicle to the extremity and then arborize in the tumor substance. The aim of embolization is to occlude as many of these vessels as possible without occluding or damaging the normal vascular tree. Selective catheterization and embolization of the pathological feeding arteries is expected to be successful in majority of cases [25]. This helps in decreasing the size of the tumor and reduction in the vascularity of the tumor. The margins between the tumor and the surrounding tissues become better-delineated thus facilitating surgically safe resection and also reduce the operative time thereby decreasing the intra-operative blood loss [26,27]. This is particularly important that high transfusion requirements in patients undergoing tumor resection is complicated by coagulopathy. When performed with a curative intent the surgical exercise should be undertaken within 48-72 hours of the embolization procedure because tumor neoangiogenesis happens soon thereafter [28].

Preoperative angio-embolization has been demonstrated to decrease intraoperative blood loss, decrease the need for autologous blood transfusion and operative time[29]. There is however one study that seems to contradict this claim, majority of studies in literature support the view that pre-operative embolization reduces intraoperative blood loss and need for transfusions [30]. It has been postulated in literature that preoperative embolization of spinal tumors could significantly decrease intraoperative morbidity by decreasing losses to the tune of 30-50% [31,32]. In our series, the intraoperative blood loss was less as compared to mean estimated loss and this was statistically significant (p value= 0.001).

We were also able to establish a relationship between the percentage of tumor devascularisation achieved and the intra-operative blood loss. In 66% of cases where complete or near total devascularization was achieved the mean intraoperative loss fell by as much as 50% (1825ml/ 950ml). However, no statistical significance could be established for this observation. In literature, there have been conflicting results with no correlation found between degree of devascularization and intraoperative hemorrhage, especially for metastatic non-spinal skeletal disease [33].

In our series 50% of patients underwent surgical resection within 72 hours and all cases were operated within a week of the index embolization procedure. We could not establish a statistically significant relationship between the time elapsed after embolization and intraoperative blood loss. In literature however, the beneficial effect of embolization is reported to wane off after the first 48-72 hours because of rapid neoangiogenesis and establishment of blood flow to the tumor from collaterals and sprouting of new feeders. In literature there has been conflicting data in this regard. No statistical difference could be found between surgeries performed early (within 24 hours) against delayed (36-120 hours) in patients

who underwent preoperative embolization using polyvinyl alcohol particles and coils[25,29]. Others have reported increased incidence and intensity if intraoperative hemorrhage if the surgery was delayed after embolization using gel foam[34,35]. So, rather than the interval between embolization and surgery, the blood loss could be determined by the type of embolic agent used (PVA, Coils Vs. Gel foam). Traditionally, gel foam has been used as an embolic agent of choice as neoadjuvant therapy because of it's cost but that may also be influencing the intraoperative blood loss if for some reason the surgery is delayed beyond 48 - 72hours. It seems that tumor neovascularization is faster if gel foam has been used as an embolic agent.

We were also able to identify tumor volumes and operative time as predictors for intraoperative blood loss. Tumor volumes greater than 400cm3 and operative times greater then 270 min were associated with higher intraoperative blood losses ($p = 0.001$). Larger tumor size has been correlated with greater estimated blood loss ($r= o.451$; $p< o.oo1$)[29]. Tumor volumes greater than 200cm3 have been associated with lager amounts of intraoperative blood loss in sacral tumors (odds ratio 3.381) [36].

We have found pre-operative angio-embolization as a useful adjunct to operative intervention in malignant and metastatic bone tumors.

Conclusion

Preoperative embolization of extremity bone tumors is a safe technique and significantly decreases intra-operative hemorrhage in limb salvage surgery.

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