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Research Article

Nerve Palsy following Reconstruction around the Knee in Musculoskeletal Oncology – A Single Institutional Experience of 30 Cases in a Quarternary Cancer Centre from India

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Introduction

The 21st century has shifted the paradigm in surgical management of most limb malignancies, making limb salvage not just an option, but the norm, as a result of effective adjuvant therapy, superior imaging, improved surgical technique and advanced biomaterials and mechanics [1]. Nowadays, more than 80% of the patients are treated with limb salvage surgery without critically compromising oncological principles [2]. The knee region, consisting of the proximal tibia, distal femur and the surrounding soft tissue, is the commonest site of predilection for primary bone tumors. In the knee, the distal femur is the most common site, followed in descending order by proximal tibia [3-7].

In limb-salvage surgery for bone tumor, there are 3 main ways to reconstruct the bone defect after tumor resection: auto graft or allograft, inactivation and re-implantation, and artificial prosthesis replacement [8]. Allografts and endo prostheses are the most commonly used replacements for the osteo articular defect resulting from en bloc resection of primary malignant bone tumors from the distal femur or proximal tibia [9-11].

Mastering limb salvage procedures are technically demanding endeavors, with a long learning curve. The knee is an anatomically complex site, which requires the surgeon undertaking a limb salvage procedure in this region to have an intricate knowledge regarding the musculoskeletal anatomy as well as the neurovascular course. Pre-operative radiological planning is essential in determining the complete extent of the tumor, ascertaining course of the neurovascular structures with respect to tumor, and involvement if any within the tumor. Visualizing the best approach for excision of tumors with adequate margins and at the same time making sure that neurovascular bundle is safe and adequate soft tissue is left behind for reconstruction for an optimal functional outcome is key.

In spite of the strides made in the execution of limb salvage surgeries, there are a host of complications that have been reported in the literature, including infection, wound necrosis, nerve palsy, nonunion, mechanical implant failure, and vascular compromise [12-13]

Nerve palsy following limb salvage for tumors around the knee joint are one of the most jeopardizing complications seen from a functional outcome point of view. Anatomically, the major motor nerves affected in this region are the sciatic nerve and its components tibial and common peroneal nerve (CPN) [14]. Literature on this specific complication is scarce and with this paper we aim to dive into the aspects and natural course of this specific complication so as to give surgeons just starting out in the field of musculoskeletal oncology a perspective.

Materials and Methods

This study was conducted in HCG Cancer Centre Bangalore, a tertiary care cancer center. Retrospective search of the sarcoma registry was done. Out of a total of 8124 operated cases of sarcoma, approximately 3000 cases of limb salvage cases were isolated, and 815 of these involved tumors around the knee. 31 cases met our inclusion criteria.

Based on the pathology, patients were either started on standard neo-adjuvant chemotherapy or were planned for upfront surgery.

Preoperative planning was done with radiological evaluation consisting of CT and MRI, and the neurovascular bundle course was ascertained with respect to tumor. All surgeries were performed by a single team, in accordance with the principles of limb salvage surgeries.

Based on intraoperative findings with regards to the proximity of the nerve to tumor, we devised a classification system for nerve dissection – "Pramod and Abrar" Classification of nerve dissection.

Type of Nerve Dissection/Isolation	Description
Retracted	No intraop requirement to isolate/separate and visualise nerve, nerve away from field
Isolated	Nerve in close proximity to lesion, requirement for isolation and visualisation to excise tumor with wide margin
Separated	Incomplete nerve encasement by tumor, seprated with intact epineurium
Perineural Dissection	Nerve completely encased by tumor, proximal and distal end of nerve freed and intralesional perineual dissection done with epineurium excised as margin

Table 1 – Classification of nerve dissection

Image 1 – 29/M with an Ewings sarcoma of the proximal tibia, wherein nerve was "Retracted" in preparation of a pedicled autograft recycling with liquid nitrogen.

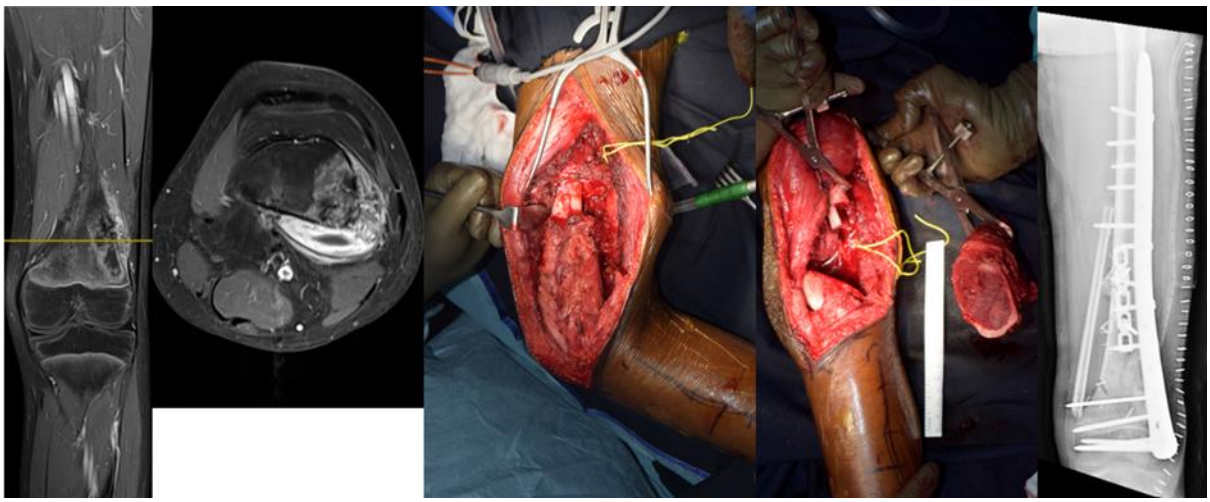

Image 2 – 11/M with an osteosarcoma of the distal femur, wherein nerve was “Isolated” in preparation for an autograft recycling and reconstruction with ECRT.

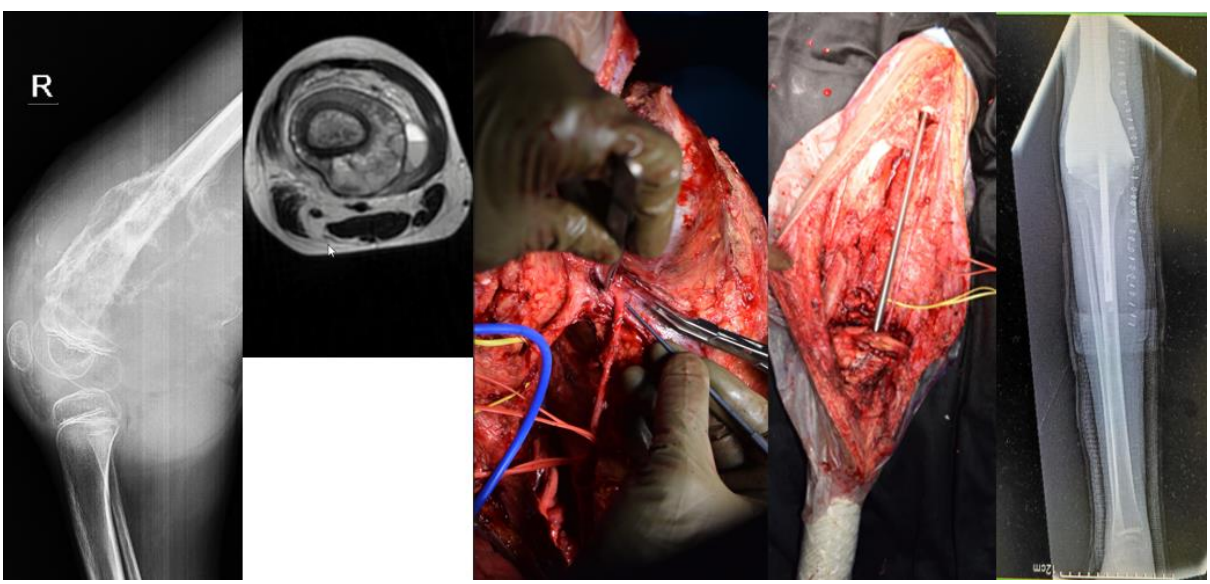

Image 3 - 8/M with an Osteosarcoma of the distal femur,completely involving the quadriceps wherein the nerve was “Separated” from the tumor margin followed by a nail cement spacer

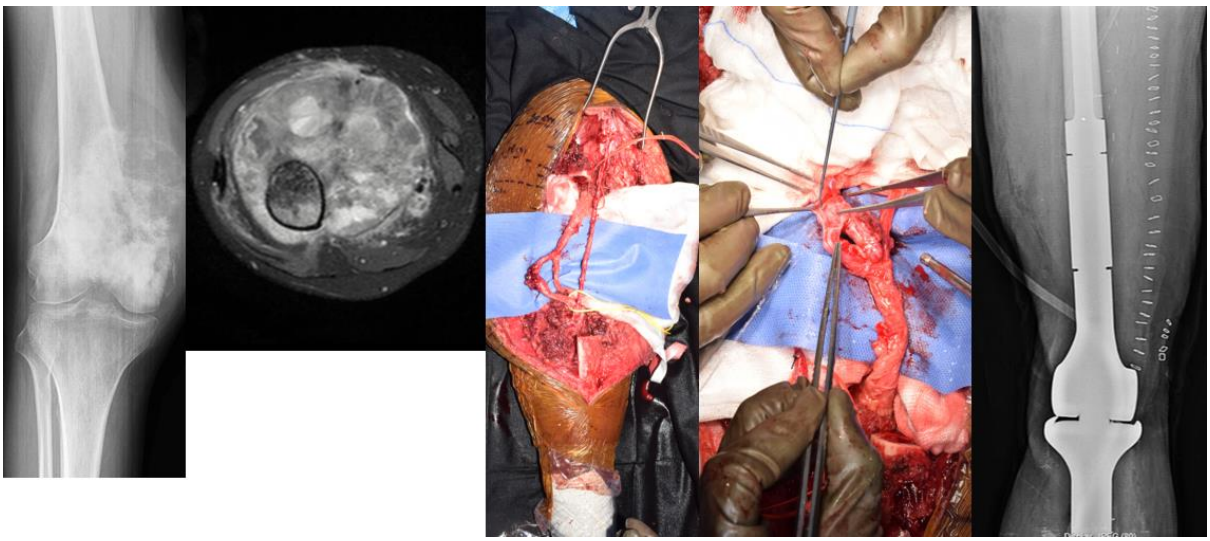

Image 4 – 22/M with an osteosarcoma of the distal femur and proximal tibia, completely encasing the sciatic nerve wherein "Epineural dissection" was done followed by implantation of tumor prosthesis

Functional outcomes, oncological outcome and complications were evaluated by Musculoskeletal Tumor Society score[22], clinical and radiological examinations.

Score	Pain	Function	Emotional acceptance	Supports	Walking ability	Gait
5	No pain / no medication	No restriction / no disability	Enthused / would recommend to others	None / no supports	Unlimited / same as preoperative	Normal / no alterations
4	Intermediate	Intermediate	Intermediate	Intermediate / occasional use of brace	Intermediate	Intermediate
3	Modest / non-disabling / non-narcotic analgesic	Recreational restriction / minor disability	Satisfied / would do again	Brace / mostly brace	Limited / significantly less	Minor cosmetic / cosmetic alterations only
2	Intermediate	Intermediate	Intermediate	Intermediate / occasional cane/crutch	Intermediate	Intermediate
1	Moderate / intermittently disabling / intermittent narcotics	Partial occupational restriction / major disability	Accepts / would repeat reluctantly	One cane or crutch / mostly cane/crutch	Inside only / cannot walk outside	Major cosmetic / minor functional deficit
0	Severe / continuously disabling / continuous narcotics	Total occupational restriction / Complete disability	Dislikes / would not repeat	Two canes or crutches / always cane/crutches	Not independently / can walk only with assistance or wheelchair bound	Major handicap / major functional deficit

Table 2 – MSTS scoring system

Study Design:

Type of study – Retrospective study

Sample size - All patients who underwent tumor resection and reconstruction around the knee joint with postoperative nerve palsy were included in the study.

Selection of subjects:

Inclusion criteria –

1. Patients who underwent limb salvage surgery and reconstruction for tumor around the knee joint, and had postoperative nerve palsy, and with a minimum of 2 years follow-up.

Exclusion criteria –

1. Patients with pre-operative nerve palsy
2. Patients who had previously undergone oops surgery
3. Patients with a pathological fracture at presentation

Study Protocol:

All surgeries were performed by a single surgeon, in adherence to general principles of limb salvage surgery, with affected bone removed with a cuff of muscle and along with biopsy tract, and reconstruction performed. All patients gave written informed consent for participating in the study in their own native language. Study approval was obtained from our institutional review board. Regular follow up was done and essential imaging and clinical assessments were done time to time.

Statistical Analysis:

The data was analyzed with SPSS software version 21.0. Interpretation and analysis of obtained results was carried out using descriptive statistics. Functional outcomes, oncological outcome and complications were evaluated by Musculoskeletal Tumor Society score, clinical and radiological examinations.

Source of Funding – None

Results

31 Patients who underwent limb salvage surgery and reconstruction for tumor around the knee joint, and had postoperative nerve palsy, and with a minimum of 2 years follow up were included in the study.

The mean age was 22± 13.8. 17 (54.8%) were females and 14 (45.2%) were males.

Out of 31 patients, 21(67%) were diagnosed with osteosarcoma, 4(12.9%) were diagnosed with Ewing's sarcoma, 3 (9.7%) were diagnosed with Giant cell tumor, 2(6.5%) with fibromyxoid sarcoma and 1(3.2%) with chondrosarcoma.

These tumors involved Proximal tibia in 16(51.6%) cases, distal femur in 13(41.9%) cases and both proximal

tibia and distal femur in 2(6.4%) cases.

As part of the limb salvage surgeries, 14(45%) patients underwent biological reconstruction (allograft/recycled auto graft), 12(38.7%) patients underwent endo prosthetic reconstruction, resection followed by nail cement spacer was done in 3(9.6%) patients and curettage with cementing and plate fixation in 2(6.4%) patients.

As per our classification of nerve dissection, the nerve was epineurally dissected in 2(6.5%) of patients, separated in 10(32.3%) of patients, isolated in 13(41.9%) patients and retracted in (19.4%) patients.

Nerve isolation	Time(median(IQR))	p-value
Separated(N=10)	9(1.5)	0.009*(<0.05)
Retraced and Isolated(N=18)	6(3)	

Table 3 - Comparison of nerve isolation in terms of time till recovery

Both patients in whom epineural dissection was performed, there was no recovery from palsy observed at 2 years.

Patients in whom the nerve was “separated” took a mean time of 9±1.5 months until recovery and the patients in whom the nerve was “retracted/isolated” took a mean time of 6±3 months until recovery.

Mean duration of surgery was 324±73 minutes. Mean blood loss was 410±170ml.

19(61.3%) patients developed immediate postoperative nerve palsy, while 12(38.7%) patients developed palsy on the following day.

Interval	Time(median(IQR))	p-value
Postop(N=16)	9(2.2)	<0.001*(<0.05)
POD1(N=12)	5(1.7)	

Table 4 - Comparison for interval in terms of time till recovery

The mean±sd for time till recovery is 7±2.8.

Mean time till recovery in patients developing nerve paly on POD1 was 5±1.7 months, whle in patients who developed pot op palsy it was 9±2.2 months.

26(83.8%) of patients were given standard chemotherapy for their specific sarcoma, while 5(16.2%) did not receive any chemotherapy.

Chemotherapy	Time till recovery(median(IQR))
Yes(N=22)	8(2.7)
No(N=6)	3(6.5)

Table 5 – Mean time till recovery in chemo and non-chemo patients.

Mean time till recovery in patients developing nerve palsy postoperatively and who were receiving chemotherapy was 8±2.7 months, while in patients who were not on chemotherapy it was 3±6.5 months.

Chemo	MSTS(median(IQR))	p-value
Yes(N=25)	25(2)	<0.001*(<0.05)
No(N=6)	28(0.7)	

Table 6 - Comparison of chemo in term of MSTS score

The mean±sd for MSTS score is 25.3±1.9.

Mean MSTS score in patients developing nerve palsy postoperatively and who were receiving chemotherapy was 25±2, while in patients who were not on chemotherapy it was 28±0.7.

Gender	**Counts**	**% of Total**
F	17	54.8 %
M	14	45.2 %

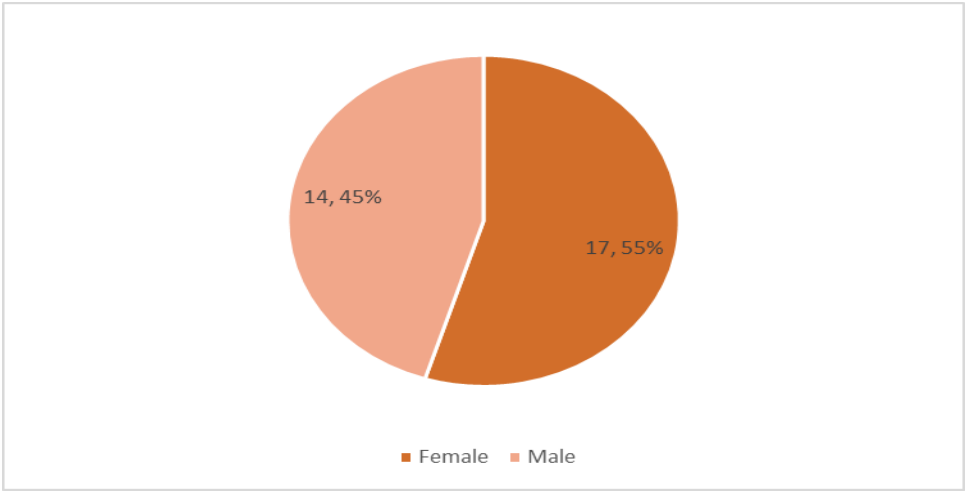

Fig 1

Table 1: Frequencies of Diagnosis

Diagnosis	Counts	% of Total	Cumulative %
OSTEOSARCOMA	21	67 %	64.5 %
FIBROMYXOID SARCOMA	2	6.5 %	71.0 %
GIANT CELL TUMOR	3	9.7 %	80.6 %
EWINGS SARCOMA	4	12.9 %	93.5 %
CHONDROSARCOMA	1	3.2 %	96.8 %

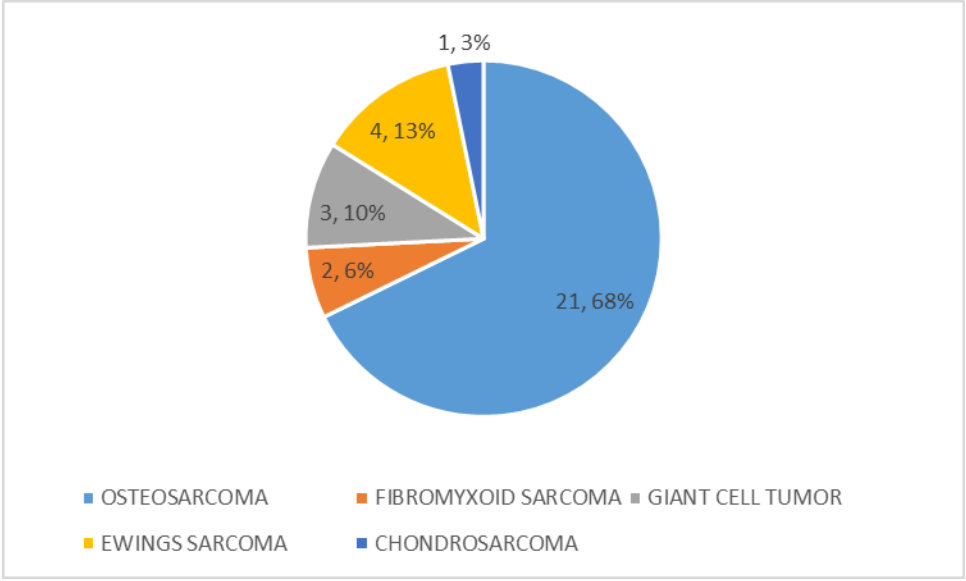

Fig 2: Frequency for Bone involvement

PALSY	Counts	% of Total
PROXIMAL TIBIA	16	51.6 %
DISTAL FEMUR	13	41.9 %
DISTAL FEMUR AND PROX TIBIA	2	6.4 %

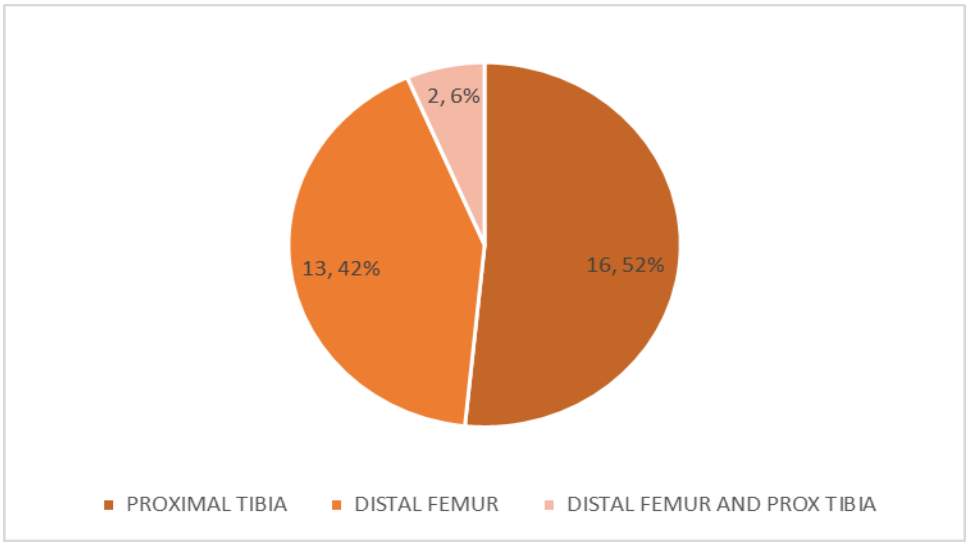

Fig 3: Palsy

Procedure	Counts	% of Total
WLE+AUTOGRAFT RECYCLED RECON	14	45.1 %
WLE+RECON WITH MEGAPROSTHESIS	12	38.7%
RESECTION WITH NAIL CEMENT SPACER	3	9.6 %
ETENDED CURETTAGE+CEMENT+PLATE	2	6.4 %

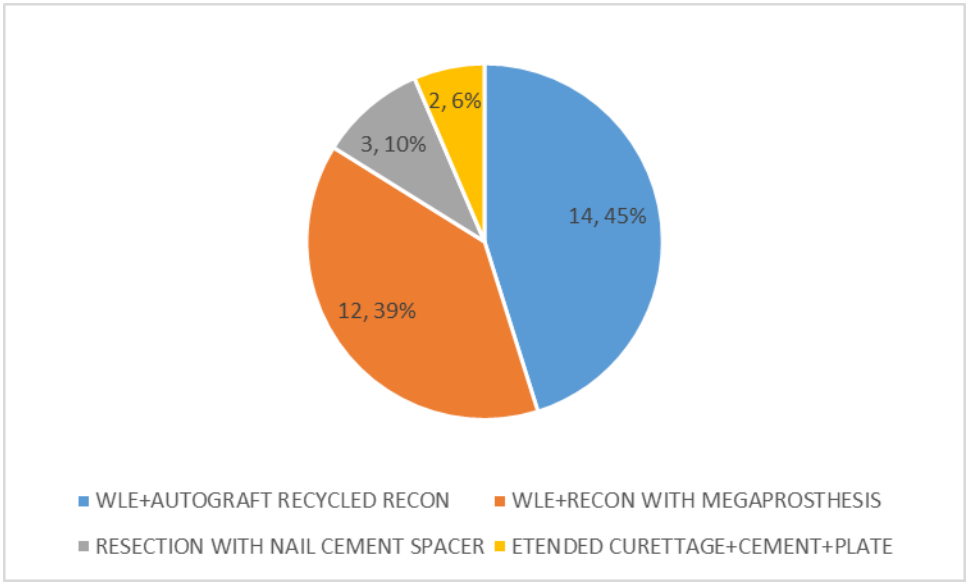

Fig 4: Procedure

Nerveisolation	Counts	% of Total
ISOLATED	13	41.9 %
SEPARATED	10	32.3 %
RETRACTED	6	19.4 %
EPINEURAL DISSECTION	2	6.5 %

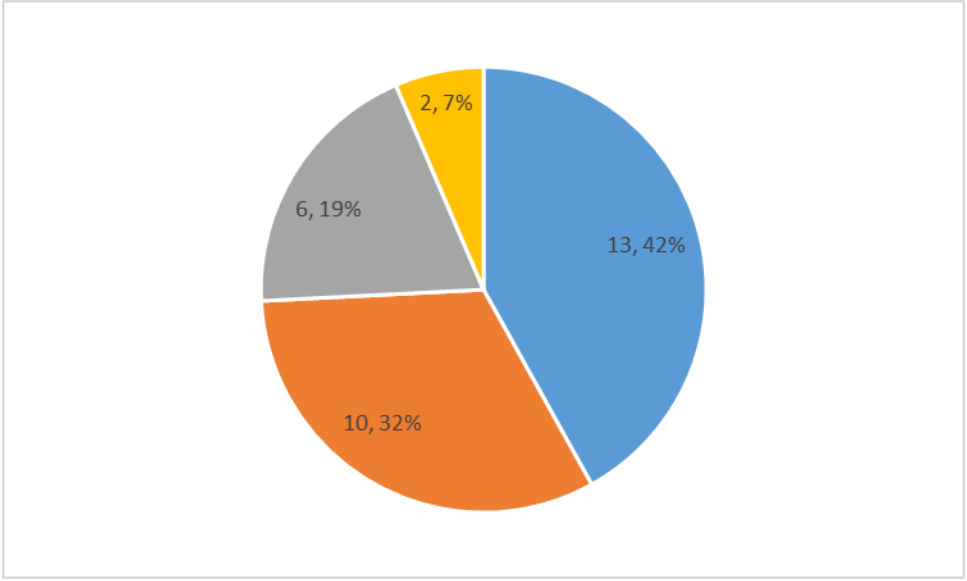

Fig 5: Nerveisolation

Interval	Counts	% of Total
POD1	12	38.7 %
POST OP	19	61.3 %

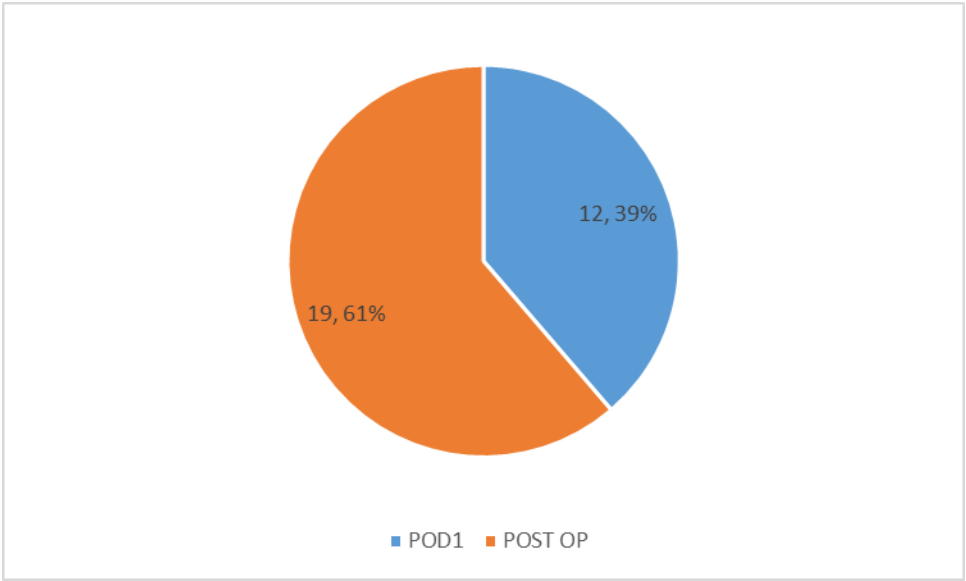

Fig 6: Interval

Interval	isolation2	Counts	% of Total
POD1	ISOLATED	7	22.6 %
	SEPARATED	0	0.0 %
	RETRACTED	5	16.1 %
	EPINEURAL DISSECTION	0	0.0 %
POST OP	ISOLATED	6	19.4 %
	SEPARATED	10	32.3 %
	RETRACTED	1	3.2 %
	EPINEURAL DISSECTION	2	6.5 %

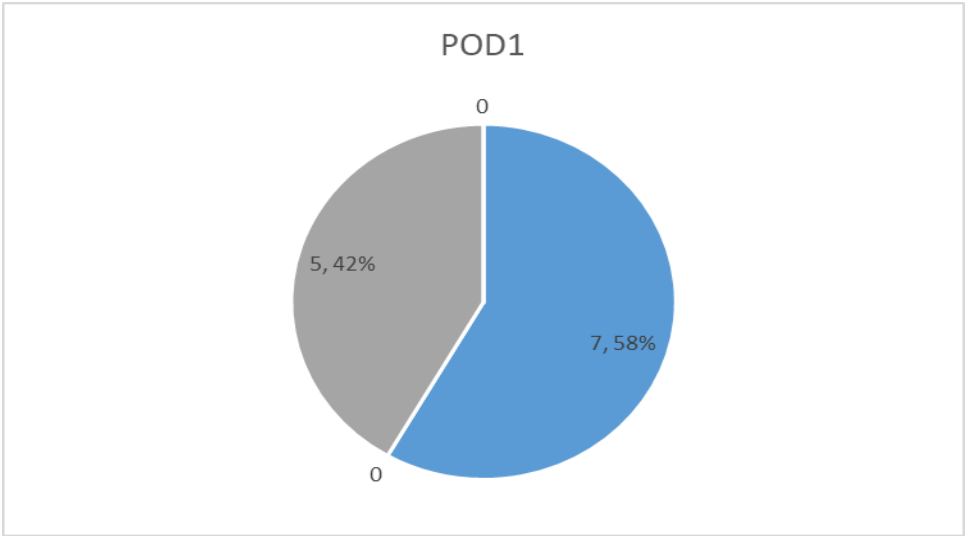

Fig 7: POD1

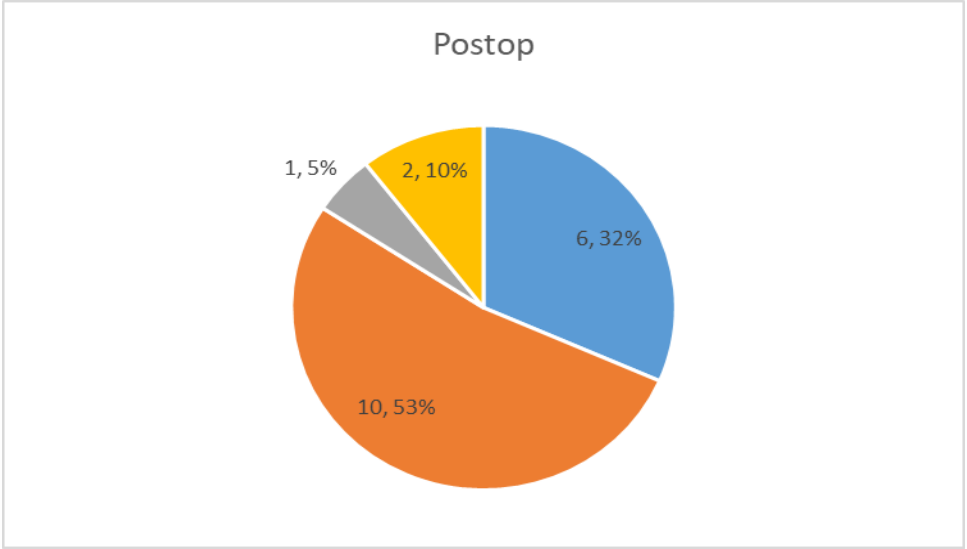

Fig 8: Post Op

Frequencies of Chemo

Chemo	Counts	% of Total	Cumulative %
MAP	17	60.7 %	60.7 %
NONE	5	17.9 %	78.6 %
VAC IE	4	14.3 %	92.9 %
CISPLAT-DOX	2	7.1 %	100.0 %

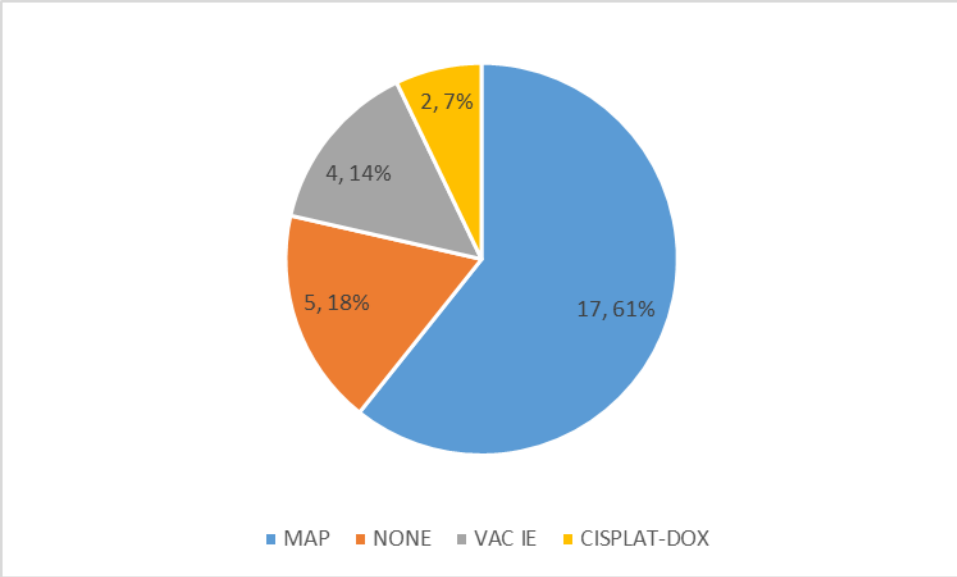

Fig 9: Frequencies of Chemo

Inferential Statistics

The test used for comparing nerve isolation, interval and adj. chemo in terms of time till recovery and MSTS score is the non-parametric Mann Whitney test.IQR gives the spread of data, i.e, how much dispersed is the other data points from the median.

Discussion

Tumors about the knee present one of the greatest opportunities for limb salvage, because this is the region most usually affected by the osteosarcoma and because it is the joint where reconstruction is practical to achieve after limb salvage resection [18]. Approximately 60-80% of osteosarcomas are located around the knee [19].

On retrospective analysis of our sarcoma registry, of a total of 815 cases of tumors around the knee were isolated, with 31 of these cases developing postoperative nerve palsy after tumor excision and reconstruction around the knee (3.8%).

W.Sim et al performed a retrospective analysis of consecutive resections and endo prosthetic reconstructions for tumors around the knee between 1996 and September 2005 performed at St Vincent's Hospital, Melbourne. Fifty consecutive cases were reviewed, with a median follow-up of 24.5 (range, 2-124) months. There were five cases of postoperative nerve palsies (10%), with four affecting the common peroneal nerve and one involving the deep peroneal nerve. In the latter case, the nerve was sacrificed due to tumor envelopment. A multidisciplinary approach to management was adopted with physiotherapy, occupational therapy and

orthotics being involved. An ankle-foot orthosis was provided to aid patients with foot drop. There was resolution within six months of initial surgery in three cases [1].

Zimri FK et al in his descriptive case series documented the clinical presentation of tumors around the knee and explored the outcome of lower limb salvage with oncological resections and mega prosthetic reconstructions, observed over a follow up period of 5-years with the study spanning over a period of 13 years. Out of 73 patients, there were 43 (58.90%) males and 30 (41.09%) females. Their ages ranged between 16–53 years with a mean of 32.97±10.68 years. The tumors included giant cell tumors (n=41), osteosarcomas (n=24), Spindle cell sarcoma (n=5), chondrosarcoma (n=2) and Ewing's sarcoma (n=1). The average postoperative musculoskeletal tumor society (MSTS) score was 84.65%. Various complications encountered included superficial infections/ delayed wound healing among 9 (12.32%) patients, local recurrence in 6 (8.21%), deep infections among 5 (6.84%) and transient palsy of peroneal nerve in 3 (4.10%) cases. [15]

Neuropraxia is the simplest form of nerve injury and is most likely to result in complete recovery. With this injury pattern, the nerve's myelin covering is damaged, hence the diminished signal. However, the actual nerve pathway is not harmed. Once the Schwann cells rebuild the myelin sheath, the nerve function should fully recover. It is this type of nerve injury that results in a palsy in patients in whom the nerve was "isolated" or "retracted".

The intermediate nerve injury level is axonotmesis. Here the actual nerve pathway, as opposed to the covering only, is damaged. The surrounding nerve sheath is still intact, but there is axonal discontinuity. Wallerian degeneration occurs, and partial to full recovery can be expected. It is this type of nerve injury that results in a palsy in patients in whom the nerve was "separated".

Finally, neurotmesis occurs when the axon, myelin, and connective tissue components are damaged, disrupted, or transected, and is the most severe form of nerve injury. Recovery from neurotmesis requires surgical intervention, and the likelihood of full recovery is much lower. Tran- section of a nerve with a surgical saw blade or cautery would cause this devastating nerve insult [23]. It is this type of palsy that usually manifests in patients in whom the nerve was "epineurally dissected".

To decrease the risk of making the nerve "angry" and development of a postoperative palsy as a result of dissection, we recommend a "no holding" technique of nerve dissection wherein a jet of normal saline is sprayed with the help of a syringe and needle hub cap onto the nerve soft-tissue interface while at the same time pushing the nerve using a small periosteum, separating it from adherent tissue.

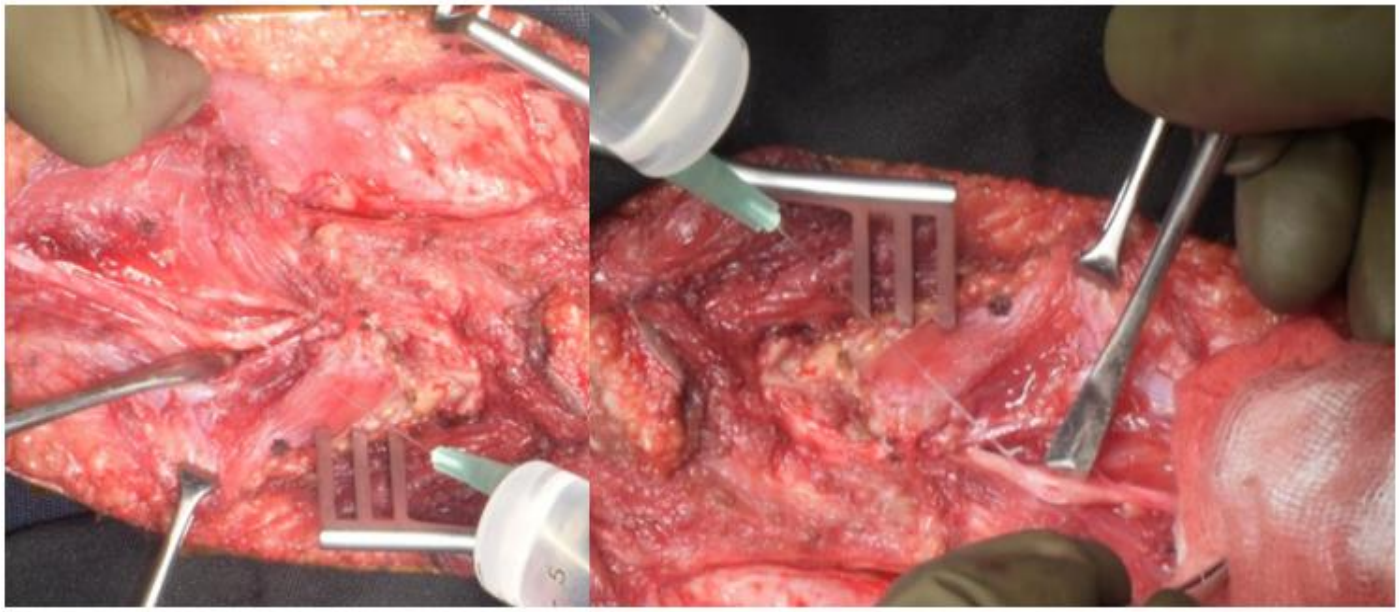

Image 5 – Nerve dissection technique.

In case of postoperative nerve palsy, detected either immediate postoperatively or on the next day, we advise to follow our "Post Nerve Palsy Checklist".

This includes loosening of the dressing, to eliminate any constriction effect, keeping the knee in a flexed position of 15º, to reduce nerve stretch and application of a derotation boot, especially in cases where rotating platform prosthesis are implanted, to prevent external rotation of limb and undue pressure on nerve at the level of fibular head.

Neuromodulators such as vitamin B12 and pregabalin (300mg per day) should be commenced. Pregabalin is effective in the treatment of peripheral and central neuropathic pain[(24)]. Steroid medication inhibits the inflammatory response and consequently the recruitment of macrophages. The presence of such cells close to the site of damage has been shown to accelerate nerve regeneration in the short term[(25)].

In all cases of nerve palsy, clinical evaluation for the presence of compartment syndrome must be done and in case of any doubt, CT angiography must be performed at the earliest, or re-exploration in low resource setting.

POST OPERATIVE NERVE PALSY CHECKLIST
☐ Loosen Dressing
☐ Knee Flexed to 15degree
☐ Application of derotation boot
☐ Neuromodulators
☐ Steroids
☐ Signs of compartment?-Immediate CT Angio

Table 7 – Post Operative Nerve Palsy checklist

Conclusion

Nerve palsy following tumor excision and reconstruction around the knee joint, from a functional long term perspective, is a demoralizing complication, both for the surgeon as well as the patient. With the results of our study, surgeons just starting in the field of orthopedic oncology must understand that most nerve palsies recover completely, albeit delayed in patients receiving chemotherapy. Intricate preoperative planning, with use of modern tools such as 3D segmentation, and with the help of our radiology colleagues must be done, to map out the course of the neurovascular bundle with respect to the tumor, to mitigate inadvertent injury. Nerve dissection itself should be gentle and in case of postoperative nerve palsy, our "Post Palsy Checklist" must be followed.

Patient education in the form of thorough preoperative counselling must be done, to keep them well informed of a potential of risk of nerve palsy postoperatively.

Further research is warranted in the form of prospective studies, using the modality of nerve conduction studies and other advanced studies, to deepen our knowledge on the pathophysiology and natural course of this complication, and also to ascertain the cause of the enigmatic palsy that sets in the day after the surgery (POD1).

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