ROUNDUP360

Oncology

For other Roundups in this issue that cross-reference with Oncology see: Research Roundups 5 and 6.

Metaphyseal and diaphyseal osteosarcoma subtly different beasts

Osteosarcoma is one of the most common primary tumours of bone and represents much of the workload for bone tumour surgeons. Occurring predominantly in the metaphysis, it is occasionally also seen in the diaphysis and although the different presentation patterns are well recognised, the differing characteristics seen between those with a diaphyseal and metaphyseal location are not well studied. Researchers from the Bone Tumour Unit in **Birmingham (UK)** have designed a study with the intention of characterising these more unusual tumours.[1] Their study included patients identified as part of their tumour registry with newly diagnosed high-grade osteosarcoma of the long bones. Their dataset included 974 patients with a new diagnosis of osteosarcoma, of whom 36 patients had diaphyseal osteosarcoma and formed the study group. These patients were matched three to one with a control group from the remaining patients, giving a control group of 108 patients to form a comparison. Outcomes were assessed in terms of adverse events, complications and the usual five-year overall and disease-free survivals. Patients presenting with diaphyseal osteosarcoma were found to have significantly larger lesions at diagnosis, (13.5 cm vs 10 cm) and a much higher pathological fracture rate (28% vs 12%). This said, there was an improved five-year disease-free (74% vs 40%) and overall survival (68% vs 46%) rate in this cohort. The proximal and distal metaphyseal fractures were not found to have any differences in survival in this study. The occurrence of a pathological fracture significantly worsened outcomes in the diaphyseal fracture cohort. The authors conclude that in their study, patients with diaphyseal osteosarcomas, despite presenting with significantly larger tumours and demonstrating higher pathological fracture rates, had superior five-year metastasis-free and overall survival. A pathological fracture significantly decreased the survival of the patients with diaphyseal osteosarcoma.

Sports not out of the question in endoprosthetic reconstruction of the knee x-ref Knee

Not so long ago, the concept of even asking whether patients following treatment for osteosarcoma could participate in sports would have been laughable. It shows how far limb reconstruction options have come that surgeons from **Vienna (Austria)** feel the time has arrived to assess what sporting activity levels can be expected following surgical resection and reconstruction for osteosarcoma around the knee.[2] The surgical team decided to evaluate the eventual functional results for patients who had received endoprosthetic reconstruction of the knee for osteosarcoma and were a long-term survivor. Sadly, the surgical team were only able to recruit 27 of the 120 patients they had treated over a ten-year period into this study, with the remainder being removed from the cohort through death (n = 25, 21%), amputation (n = 6, 5%), non-German speakers (n = 39, 32%), and loss to follow-up (n = 14, 12%). As this study was designed to evaluate clinical outcomes in surviving patients, the research team used a combination of a self-reported sports participation questionnaire and two activity scores (UCLA Activity Score and Weighted Activity Score) which were assessed retrospectively. While we have some concerns about the retrospective application of activity scores over the long retrospective periods in this study, it is refreshing to see at least some attempt at longitudinal data collection in this kind of paper. The cohort of 27 patients consisted of 16 distal femoral and 11 proximal tibial tumours, and the investigators established that a surprisingly high number of patients were able to perform sports activities. Patients reported at one year (89%, n = 24), three years (33%, n = 9), five years (74%, n=20) and by final follow-up (around 90%), that most were able to perform sports activities in some way. The best predictor of post-operative activity levels appears from this relatively small series to be the patients' pre-operative activity levels. The investigators noted that impact sports activities dropped in frequency and that the development of complications had no effect on the ability to take part in sports activity. Reassuringly, there were no sports activity-related complications found in this series, although there was a high revision rate of 51% which may reflect the high activity levels seen in this series. Although a small cohort and sadly also a small subgroup of the available population, this is a novel study and demonstrates effectively that in long-term survivors of osteosarcoma, high levels of sports activity can be achieved. The information yielded in this study is important and allows surgeons to give realistic expectations for long-term survivors of osteosarcoma of the knee.

Is curettage without tissue diagnosis sensible in cartilaginous tumours?

Much has been made in recent years of the importance of avoiding the 'whoops' manoeuvre – biopsy or surgery to a malignant lesion without proper staging or recognition of the underlying pathology. Most of this concern relates to osteosarcoma and there is little evidence one way or the other to support the traditional triple assessment followed by excision for cartilage-based tumours. Given the diagnostic difficulties associated with distinguishing cartilaginous tumours (specifically enchondroma; low and high grade chondrosarcoma), researchers in **Stanmore (UK)** asked if a tissue diagnosis is required prior to undertaking curettage of the lesions based on radiological diagnosis of a 'low-grade' lesion.[3] The study team

initially set out to establish what the accuracy of radiological diagnosis is using an MDT, given just history, examination findings and radiology. They then went on to assess the rate of recurrence following confirmation of histology in those lesions managed with curettage that subsequently turned out to be high-grade chondral lesions. Due to the rarity of this condition, even at a large specialist centre like the Royal National Orthopaedic Hospital, just 53 patients with chondral lesions were treated between 2001 and 2012. The majority of these were in the femur (n = 20), humerus (n = 18) and tibia (n = 9), with just six in other bones. The tumour team were able to reach a consensus of diagnosis in 35 patients without the need for a tissue diagnosis and consequentially these patients underwent primary curettage. In the remaining 18 patients, a tissue diagnosis was obtained. There were only two high-grade chondrosarcomas identified (3.7%), with the majority of lesions being low-grade chondrosarcoma (92.6%). There were four cases of disease recurrence (three low-grade and one high). The single high grade recurrence was treated with prosthetic replacement and overall a 7.5% recurrence rate was seen at 4.7 years. It appears from the data presented here that the proposition of treating tumours that appear to be low-grade cartilaginous tumours on imaging alone can safely be managed as low grade without pre-operative histological diagnosis. Though a few of these may demonstrate pockets of high grade features on final histological review, the rates of recurrence are not affected. The low risk of local recurrence and metastatic disease allows a more conservative surgical approach for low grade tumours, with curettage providing an effective treatment that permits preservation of the limb and decreased morbidity.

Autoclaved autograft in bone tumour reconstruction

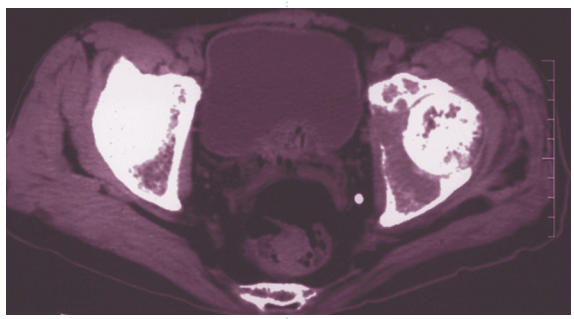
x-ref Children's orthopaedics

■ Bone tumour reconstruction is a difficult problem in the developing world. In addition to the problems associated with decision making, longevity and recurrence rates in this challenging group of patients, expensive reconstruction options are potentially financially unachievable. Amputation may be socially stigmatising and in many nations the lack of even basic orthotic services can result in severe loss of function for the patient following amputation. Surgeons in **Karachi (Pakistan)** have raised an interesting option in the resource-challenged environment of the third world.[4] Irradiated/sterilised autotumour graft is a well described reconstructive option. They report their experience of 40 paediatric patients who underwent resection for malignant tumours followed by subsequent biological reconstruction using re-implantation of their own resected autoclaved tumour bone. All the patients underwent a similar surgical procedure with a wide en-bloc resection of the tumour followed by curettage of the tumour from the resected bone, eight minutes of autoclaving, then re-implantation along with fibular graft (both vascularised and non-vascularised). The surgical team were able to report that by 18 months of follow-up, 38 patients successfully achieved a solid bony union between the graft and recipient bone and, amazingly, 31 of these recovered without any complication. The authors' reported infection rate of less than 10% is commendable. Outcomes were assessed with functional evaluations (MSTS scoring system) and recurrence rates. There was a remarkably low recurrence rate, with two patients suffering local recurrence and two nonunions. While these clinical results are probably partly a reflection of the expertise of the surgical team treating the patient groups, we are inclined to agree with the authors that this approach does offer a proven, robust method for treating patients with bone tumours.

Vascularised graft a step too far in bone defects?

x-ref Trauma

■ In common with trauma surgeons, tumour surgeons are often faced with large bone defects to reconstruct. The use of vascularised fibular graft has been variably popular, with some surgeons being huge proponents of it and, certainly on the face of it, providing a bulk autograft of vascularised bone has a great number of potential advantages. There are, however, detractors who argue that the additional operative time, microvascular skill set requirement and potential exposure to another set of complications may outweigh the theoretical advantages. Researchers in **Vienna (Austria)** have examined the differences between vascularised and non-vascularised bulk fibular grafting in a large series of 53 patients, all of whom underwent reconstruction following bone tumour excision over a 22-year period at a single centre.[5] The surgeons were able to report their experience of 53 patients, all with diaphyseal defects treated with a roughly 50:50 split between the two allografting techniques. Outcomes assessed included oncological, functional and complication-related outcomes, with Kaplan-Meier survival analysis used to estimate complication-free survival. The patients were followed up to a mean of 53 months and overall 75% of patients achieved primary union (n = 40). Although not significant, there were higher rates of union in the non-vascularised group (42% vs 34% of united grafts). While the results reported do suggest that both methods of reconstruction provide a reliable method of addressing any potential issues with bone defects, there was a marked difference in the survival without a complication between the groups. Unsurprisingly, a 60% revision rate was seen overall and these complications were much more likely to be in the vascularised graft group. There was a mean 36 months of complication-free survival in the vascularised group as compared with the non-vascularised graft group of 88 months. While in a relatively small case series it is difficult to draw definitive conclusions, there certainly doesn't seem to be the expected survival and complication advantage associated with the vascularised graft method.



Interdigitated neoadjuvant chemoradiotherapy in high-grade sarcoma

■ The outcomes for patients presenting with high-grade soft-tissue sarcomas are sadly very poor. There are few patients who manage with surgery alone, and careful planning of neoadjuvant therapies has resulted in longer survivals than would have been expected a few years ago. Amongst the various neoadjuvant regimes is interdigitated neoadjuvant chemoradiotherapy. While a potentially potent mix, this allows for the potential for improved tumour control at the risk of increased local and systemic complications. The oncology team at Johns Hopkins Hospital in **Baltimore (USA)** have been using a protocol of treatment with three cycles of neoadjuvant chemotherapy, interdigitated pre-operative radiation therapy (44 Gy administered in split

courses with a potential 16 Gy post-operative boost), and three cycles of post-operative chemotherapy in patients presenting with high-grade soft-tissue sarcomas.[6] Even at a large centre such as this, just 16 patients were available for review treated over a three-year period. Outcomes were assessed as oncological survival at three years following surgery. Of the 16 patients included, there was a median tumour size of 14.6 cm and age at presentation of 53 years. All of the patients successfully received the interdigitated regime and, impressively with this protocol, the surgical teams were able to achieve 100% local control with a three-year disease-free survival of 62.5% and overall survival of 73.4%. These impressive mid-term outcomes, albeit in a small number of patients, demonstrate what can be achieved even with high-grade sarcomas with a combined modality approach.

Predicting life expectancy in patients with painful metastasis

■ Perhaps one of the most crucial and simultaneously difficult questions to answer is, 'how long will I live doctor?'. Not just on the human side, but also on the professional side, an unknown longevity can make decision making in patients extremely difficult. While in primary bone tumours this is complex enough, throw in the additional difficulties of metastatic tumours and things become really tricky. The tried and tested Mirel's score can be used relatively reliably to predict fracture in patients with metastasis – but how does one predict longevity? The optimum treatment of bony metastasis can only reliably be decided if both the risk of fracture and likely longevity are known. Researchers in **Utrecht (The Netherlands)** set about attempting to plug this gap by designing a prognostic score with the specific intention of giving a reliable estimation of patient survival in the group of patients with painful bony metastasis.[7] The study team set out to use simple prognostic factors (patient and tumour characteristics, Karnofsky performance status (KPS), and patient-reported scores of pain and quality of life) to design a prognostic score in this highly disparate group of patients with painful bony metastases. The team used the Dutch Bone Metastasis Study and included 1157 patients who were all treated with radiation therapy for their painful bone metastases. The ubiquitous Cox proportional hazard analysis was used to design a prognostic model to predict longevity in a patient presenting with a metastasis. Once the model had been designed, an external validation exercise was undertaken with a separate dataset of 934 patients who were all treated with radiotherapy for vertebral metastases. The patient cohort was representative of those usually presenting with bony metastasis (breast (39%), prostate (23%), and lung cancer (25%)). Survival at 142 weeks of final follow-up was poor, with just 26% of patients still alive. The hazards modelling suggested that factors of gender, primary tumour type, metastases, and both the KPS and patient-reported outcomes were predictive of survival. Interestingly, when the researchers excluded the other factors, the model using just the KPS and patient-reported outcome measures was equally predictive. This simple and easy to administer predictive model can be used to aid decision making in patients presenting with painful bony metastasis. The sad reality is that most likely this score will be lost in the quagmire of hundreds of scores published each year predicting almost everything. However, for us here at *360* it has all the desirable characteristics of an accurate estimation of a difficult to predict clinically relevant event in a simple and easy to use manner. If someone would produce an 'App' we are sure this would take off!

Osteolytic lesions of the hands and feet

x-ref Foot & Ankle, Wrist & Hand

■ Regularly neglected due to their rare and often unusual presentations, osteolytic lesions of the hands and feet have been given a thorough review by the team at the Himalayan Institute of Medical Sciences **Dehradun (India)**.[8] Using their unique position as the only tertiary referral centre in their province in India, the team felt they were able to collate a geographically complete sample representing a cross-sectional study of patients with osteolytic lesions of the extremities. Over a period of seven years, the orthopaedic surgeons at the tertiary referral centre were able to report the demographic details of 52 referred lesions. Their sample population consisted of 25% symptomatic lesions, with the majority representing benign (38%) and borderline (38%) lesions. Nearly one in five was an inflammatory or post-traumatic lesion, with just three patients (5%) presenting with malignant lesions. The authors note that there were no malignant lesions of the phalanges in their series, and that the most common presentations were those of giant cell tumour and aneurysmal bone cyst. Although compellingly argued, this paper does have some significant limitations. India is not a developed healthcare economy, with many patients not having the means, transport, nor desire to seek medical help at their nearest facility, let alone travel to a tertiary referral centre. As such this sample is very unlikely to represent a true cross section of the population. It does, however, convey some very important points. Given the rarity of these lesions and low chance of a primary malignant diagnosis, appropriate work up and referral to a specialist centre is clearly nearly always required.

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