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Oncology

Bone sarcoma in children, adolescents, and young adults X-ref

■ It is rare that a child with an orthopaedic tumour actually presents to an oncology service. In fact, the majority present either to a fracture clinic following an incidental injury and continuing tumour-related pain or to the paediatric service following an outpatient referral. Given the rarity of these diagnoses and the rapidly changing field that is paediatric orthopaedic oncology, it can be difficult to know what to do with the patient at first consultation (beyond the obvious referral to a tumour centre) and, for both the patient and the orthopaedic surgeon, this can be a real challenge. We would encourage any surgeon who is involved in a general orthopaedic practice, or those seeing paediatric or paediatric trauma patients, to spend a little time reading this review from **Tampa, Florida (USA)**.[1] The authors concisely reach a consensus as to what represents current best practice in a difficult and rapidly changing field.

Denosumab: for how long? X-ref

■ The orthopaedic world has been buzzing with reports of denosumab - "the wonder drug" - and its remarkable efficacy in the treatment of giant cell tumours of bone (GCTB). The giant cell tumour relies on activation of the RANK receptor via its ligand (RANKL) and denosumab is a RANKL inhibitor. It has been so remarkably effective in metastatic and unresectable lesions that, for many, this has become the 'go-to' treatment with exceptional tumour kill rates. Patients are managed with a short 'treatment' course for the first four weeks, and then a long-term once-monthly suppression regime. The difficulty, of course, is that although the efficacy against the giant cell tumour is well documented, the drug has not been in use for long enough to establish whether there is a long-term cytotoxic profile. Although denosumab is certainly a useful addition to the armoury, it seems to have raised as many questions as it has answered. Surgical oncologists in **Bologna (Italy)** have reported their outcomes from a series of 97 patients, all of whom were treated with long-term denosumab.[2] In 43 cases, the surgical team achieved resection of the tumour with a subsequent denosumab treatment course of 12 months (6 to 45). However, 54 patients had unresectable giant cell tumours and, as such, were treated with denosumab alone. Of this more advanced disease cohort, around a quarter presented with lung metastases, a third had a primary spinal tumour on diagnosis and, perhaps unsurprisingly given they were all unresectable, around two thirds were relapses following previous surgery. In this group, patients had an average of 54 months (9 to 115) of denosumab treatment. As one would expect, there was a clinical response in all cases taking denosumab, however, when discontinued around 40% of patients suffered tumour progression. This is in line with data from other series, and highlights the often long-term requirement for this drug. There were relatively few side effects, with denosumab being, in general, well tolerated. There were six patients who developed osteonecrosis of the mandible, and around 10% of long-term treatment patients experienced peripheral neuropathy and a cutaneous rash, both of which are recognised complications. Perhaps most reassuringly, there were only two cases each of hypophosphataemia and atypical femoral fractures. These authors have conclusively shown that prolonged treatment with denosumab yields sustained activity in GCTB, including pain reduction and radiological disease control, and has a mild toxicity profile. They recommend careful and strict monitoring of patients who need prolonged treatment because of the dose-dependent toxicity observed.

Articular surface and curettage for epiphyseal chondroblastoma? X-ref

■ In an interesting study from **Buenos Aires (Argentina)** researchers ask the question: what happens to the articular cartilage following aggressive intralesional curettage?[3] Although there is much written on the treatment of epiphyseal tumours, it all concerns revision and relapse rates. There is surprisingly little literature that addresses the long-term sequelae in terms of joint degeneration and functional outcomes after aggressive intralesional curettage. These authors identified 53 patients, all treated with aggressive intralesional surgery for their primary diagnosis of epiphyseal chondroblastoma. The initial cohort of 53 patients were evaluated at a final follow-up of 77 months, and outcomes assessed were joint complications. There were 26 local complications seen in 22 patients, of which the most common was degenerative change in the joint (77%; n = 20/26 complications), although four patients suffered local tumour recurrence. Other complications reported in this series include acute fracture and infection. Overall, the authors report a somewhat disappointing 74% joint survival at ten years (90% at five years), although this did vary by joint, with proximal femoral tumours only reaching survivals of 44% at five years. The authors conclude that osteoarthritis was a frequent complication of aggressive curettage of epiphyseal chondroblastoma, and tumours located in the proximal femur appeared to be at particular risk of secondary osteoarthritis and prosthetic replacement. As chondroblastoma is a tumour which disproportionately affects younger patients, the patient and surgeon should be aware that arthroplasty at a young age is a potential outcome for treatment of proximal femoral chondroblastomas. This cohort was actually slightly under-representative in terms of skeletally immature patients, where surgery may result in growth arrest. It is likely that this underestimates this important

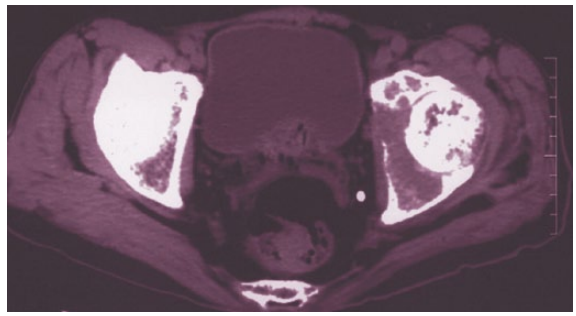
complication. Combine this with the relatively short follow-up and a number of asymptomatic patients exhibiting signs of joint degeneration reported in the study, we are sure here at *360* that the reported failure rates will rise as this series comes to maturity.

Hindquarter amputation for sarcoma: is it worth it?

Hindquarter amputations or external hemipelvectomies are considered to be one of the most morbid of any operation. The rehabilitation time is long and the complication rate, including mortality, is high. Therefore, most specialised sarcoma centres recognise that patient selection is of vital importance, and opinion is somewhat divided as to who will benefit, and who will not. The problem with patient selection is compounded by the relative rarity of the condition, with few individual surgeons having enough experience to develop their own feeling for who does well or poorly from this extensive operation. This study from **Toronto (Canada)** evaluated 78 patients who underwent a hindquarter amputation for a diagnosis of either bone or soft-tissue sarcoma.[4] The median hospital stay was 24 days, almost half of patients had wound complications and 6% of patients died prior to discharge from hospital. Overall survival for patients with metastases at presentation was significantly poorer than for those patients with only localised disease at presentation, with a five-year survival of 0% *versus* 41%, respectively. For patients treated for localised disease, age (over 65 years) and larger tumour size (> 15 cm) were the two significant determinants of poorer metastasis-free survival and overall survival. The authors concluded that younger patients are more likely to benefit from hindquarter amputations in terms of survival and functionality. It does, however, seem that for older patients and those with large tumours the hindquarter amputation might be excessively morbid.

The ilium resection in patients with a sarcoma: should the pelvic ring be reconstructed?

Although this may appear to be an obscure question to those readers who don't undertake sarcoma excision in the pelvis, it is one that is repeatedly debated by orthopaedic oncologists. There have been a range of options available for many years including fibular grafting, irradiation and re-implantation, and even the hemipelvic replacement which is now available as a custom-manufactured implant from planning CT scans. This study from **Birmingham (United Kingdom)** adds some vital information to the debate. The authors evaluated 64 patients who underwent excision of a tumour involving the ilium between 1976 and 2015.[5] A total of 35 patients underwent complete resection, of whom 24 were reconstructed with a non-vascularised fibular graft, and four with *en bloc* resection, extracorporeal irradiation and re-implantation. The remaining 29 patients underwent a partial tumour resection. The authors compared functional outcomes using the Toronto Extremity Salvation Score (TESS) between the various groups to establish what the expected outcome is following resection of the ilium at final follow-up. The patients who underwent total resection with reconstruction generally fared much better than those who did not undergo reconstruction (mean TESS 72.0% (17% to 100%) *versus* 53.3% (20% to 90%)). Those patients who only underwent a partial resection did better than the complete resections (mean TESS 76.3%), however, the rate of local recurrence was 42.2%. There was nothing to choose between the groups in terms of surgical complications. A major limitation of this study, which should be clearly borne in mind when interpreting the results, is that functional outcome data were available for only 27 patients (42%) which will undoubtedly have injected some bias into



the study. The authors went on to conclude that, given the high rate of local recurrence following excision of a tumour from the ilium, obtaining wide surgical margins should be a priority even if this requires more aggressive surgery. When total resection of the ilium is considered, reconstruction should also be looked at as it confers a higher functional outcome than total resection without reconstruction.

Inadvertent positive margins following soft-tissue sarcoma resection

The aim of any tumour surgery, whether wide local excision, limb salvage or amputation, is to reduce the risk of local recurrence. Soft-tissue sarcomas, as with other tumours, have a higher risk of recurrence when the surgeon inadvertently leaves positive excision margins. This study from **Toronto (Canada)** assessed the thorny issue of inadvertent positive margins, and the aetiology of incomplete excision from both a tumour- and surgery-related perspective.[6] The authors conducted a retrospective study of 25 years' worth of data and identified 2234 soft-tissue sarcomas that had been resected, with 13% having positive margins (n = 309) and 4% inadvertent positive margins. The authors followed the patients up to a year, finding that 55% were high grade and the average size was a little over 9 cm. The authors categorised the positive margins as either surgery-related in the majority (75%; n = 67) or tumour-related (25%; n = 22). The surgery-related positive margins were perhaps the most interesting, as this is where the potential learning is to be had. The majority of surgery-related positive margins involved the deep margin and were most frequently in muscle. The probability of local recurrence after an inadvertent positive margin was 28% at five and 37% at ten years, with a mortality rate of 38% at ten years. The type of inadvertent margin did not affect the outcomes in terms of mortality or local recurrence. These results will perhaps be most useful in terms of operative planning. They emphasise the need for care at deep margins, as well as margins within muscle, particularly in patients where larger tumours are being excised.

Dedifferentiated chondrosarcoma: surgery the only effective treatment

Dedifferentiated chondrosarcoma remains a difficult disease to treat and, in part due to its rarity, little is known about the most effective treatments. We were delighted to read this paper from **Maywood, Illinois (USA)** reporting the outcomes of those dedifferentiated chondrosarcomas on the Surveillance, Epidemiology, and End Results (SEER) dataset over a ten-year period.[7] Despite the size of the SEER database, just 159 cases were reported over the decade of this study, and overall five-year survival was 18% (disease-specific survival 28%). Perhaps surprisingly, those patients with appendicular skeletal tumours did much worse (HR 0.20) than those with axial skeletal tumours. Poor prognostic signs were the usual suspects (stage

III or IV, larger than 8 cm, and metastatic disease). In addition, those treated without surgical resection and those treated with limb salvage had the poorest prognosis with significant increases in mortality. This paper confirms the poor prognosis for this unpleasant disease and goes further to confirm that surgery with clear margins remains the only effective treatment at the present time.

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Children's orthopaedics

***X-ref** For other Roundups in this issue that cross-reference with Children's orthopaedics see: Spine Roundup 3; Oncology Roundups 1 and 3.*

Shortened mid-shaft clavicular fractures in adolescents? X-ref

■ If you haven't fixed a clavicle fracture in an adolescent, please don't; if you are doing so, please stop. This is essentially the take home message from this much needed paper from **Rochester, Minnesota (USA)**.[1] One of the difficulties with randomised controlled trials is that because they are designed to test a single primary outcome measure, they can often be misquoted or misunderstood, or the subtleties of the trial design missed by the casual reader. The oft-quoted COTS study, for example, (which demonstrates improved functional outcomes in the shoulder) only applies to adult males with mid-shaft, shortened clavicle fractures. However, clinicians tend to extrapolate and expand indications when the evidence is strong and convincing in one group to apply this to another. A perfect example of this is the adolescent clavicle fracture which was a no-brainer for conservative management until relatively recently. In some centres it is now being considered for operative intervention. This paper reports the outcomes of adolescents with displaced (> 1.5 cm of shortening) mid-shaft clavicle fractures to a minimum of nine months of follow-up. The authors were able to identify 16 patients (eight each in operative and non-operative groups) who met the inclusion criteria and were happy to undergo outcomes assessments. The children were, on average, 14 years old. They underwent a gamut of outcome measures, including radiological assessment, QuickDASH Score, Constant Shoulder Score, and questions regarding satisfaction with treatment. Quantitative isometric strength, range of motion, and abduction fatigue testing were performed on the involved and uninvolved sides for comparison. In short, there were no differences in outcomes in terms of appearance, satisfaction or functional scores. The differences observed all favoured the non-operative group, with clavicle fixation associated with poorer abductor function and a higher rate of symptomatic nonunion. This is another paper demonstrating equivalence in functional outcome and cosmesis between non-operatively managed and operatively managed isolated shortened clavicle fractures in adolescents; equivalence, that is, with the exception that in the operatively managed group there were two surgeries and significant additional cost was incurred by our overburdened healthcare system!

Radiology reports in paediatric orthopaedic clinic?

■ Here at *360*, we aren't sure of the value of radiology reporting in addition to reporting of the radiographs by paediatric orthopaedic surgeons themselves. There is little evidence one way or the other, however, reasoning that a 'radiology report' represents a significant input in terms of both time and resource, and is essentially duplicated work, these authors from **Pittsburgh, Pennsylvania (USA)** have set out to see if there is any value in this approach.[2] The authors undertook a retrospective review of patients presenting over a four-month period and compared the orthopaedic surgeon's note with the formal radiology report. In addition, the authors calculated the costs of the radiologist's reporting. There were 1570 consecutive patients included in the study who underwent 2509 radiographs. There were enough data available for inclusion in the study in 2264 cases. The radiologist's interpretation of the radiographs added useful information in just 23 cases (1.0% n = 23/2264), however, the radiologist failed to reach the diagnosis in 1.7% of cases (n = 38/2264). Overall, the cost for each 'positive read' was $3798. Given that the radiologists 'missed' more diagnoses than the paediatric orthopaedic surgeon, and the additional cost per positive diagnosis was nearly $4000, one does have to ask if there is any value in this intervention in these times of austerity.

The management of residual acetabular dysplasia: updates and controversies

■ This article from **Beirut (Lebanon)** is a review article, rather than a study, but shares interesting concepts and discussion.[3] The management of residual acetabular dysplasia is somewhat problematic, and there is much debate as to the indications for further surgery. These authors have succinctly reviewed the evidence, and their article is informative at all points in the treatment and decision-making pathway. The summary of what the current state of play is that essentially in a patient with persisting acetabular inclination of over 25° in children treated in infancy for developmental dysplasia of the hip should prompt all surgeons to think about further treatments or investigations. The authors consider the chondrolabral acetabular anlage a suitable intervention, and recommend MRI or arthrography as the appropriate investigation to aid decision making. If the results of these investigations are maintained normal morphology, then the