ROUNDUP360

Oncology

New hope for skull base tumours

x-ref Spine

■ It is so obvious that it doesn't need stating. Skull base tumours represent one of the more tricky orthopaedic oncology diagnoses to manage – surgical inaccessibility and the radioresistance associated with skull base chordomas and chondrosarcomas lead to poor survival and disease free outcomes. Although traditionally considered radioresistant, there has been a fresh look taken by surgeons in **Toronto (Canada)** who have developed a technique for using image-guided intensity modulated radiotherapy (IG-IMRT) to address these poorly responding tumours. The study team designed a prospective study with the aim of assessing the utility of IG-IMRT in 42 consecutive patients with primary diagnoses of either chordoma (24 patients) or chondrosarcoma (18 patients), all of whom were treated at the same centre over an 11-year period.[1] The median follow-up was to just over three years and all patients underwent surgery initially (7% biopsy, 57% subtotal resection and 36% total resection). Patients received either 70 Gy or 76 Gy in 2 Gy fractions for chondrosarcoma and chordoma, respectively. Amazingly, overall five-year survival was high (85.6% chordoma; 65.3% chondrosarcoma), with an impressive local control rates of 88% in both groups. As might be expected, there were some adverse events, with a single patient suffering a radiation-induced malignancy and seven other late local effects. This study really does contribute knowledge to the management of these rare and difficult to treat tumours. The study team were able to demonstrate good local control rates for two tumours that are traditionally thought to be radioresistant. Furthermore, IMRT is now widely available, unlike Proton or Carbon Ion RT which is very expensive and not yet available in many countries (including UK). The higher doses of RT that can now be delivered with IMRT (76Gy) are similar to those given by protons.

Survival but at what cost?

x-ref Children's orthopaedics

■ Ewing's sarcoma is one of the most widely studied orthopaedic oncology diagnoses, with widely reported surgical outcomes and operative techniques. Like many oncology diagnoses, the emphasis of research and reporting in studies is focused on survival, an emotive issue in a paediatric diagnosis. It is not that surprising, therefore, that little is known about the longer-term treatment outcomes for Ewing's sarcoma. With survival now much improved, researchers in **British Colombia (Canada)** took the opportunity to study the long-term treatment outcomes and, perhaps more interestingly, the long-term complications of what is after all a relatively common primary bone sarcoma. They conducted a retrospective study of over 100 patients with diagnoses of Ewing's sarcoma and achieved a follow-up of 13.5 years.[2] The research team use the time-honoured method of Kaplan-Meier survival analysis with Cox regression analysis to calculate the usual benchmarks of disease-free survival and overall survival. In addition to addressing prognostic factors, the research team also set out to address the previously unanswered questions surrounding quality of outcomes in this cohort of patients. The study cohort presented with predominantly lower extremity (33%), pelvic (24%) and thoracic (18%) tumours, with around half of patients being managed operatively. Whilst the overall survival was good at the five-year mark (85% for localised and 73% for metastatic disease), there were high rates of complications reported. These good survival rates were achieved at a cost – 77% of survivors had long-term complications, with half in the musculoskeletal system. With improving odds of survival for osteosarcomas, and long-term complications predominantly affecting the musculoskeletal system, these patients represent a lifelong challenge for orthopaedic surgeons in managing the survivors of Ewing's sarcoma.

Synovial sarcoma beginning to be cracked?

■ One of the difficulties with studying rare tumours (such as synovial sarcoma) can be that there are rarely enough cases gathered together in a single place to allow for a decent comparative study of outcomes to be undertaken. The advent of large pan-continental studies has, however, begun to change all of this. The latest in a long line of large prospective studies, the European Paediatric Soft Tissue Sarcoma Study Group have presented a large prospective comparative non-randomised study exploring the outcomes of paediatric synovial sarcoma.[3] Incredibly, the study group were able to report the outcomes of 138 patients with this rare tumour, managed in 60 centres across nine different countries in a seven-year time span. The research team report the results of a comprehensive treatment strategy based on multimodal therapy including ifosfamide-doxyrubicin therapy. At a median follow-up of 52 months, the event-free survival was just over 80%, and the overall survival was an impressive 97.2% at three years and 90.7% at five years. The study team attempted to determine prognostic factors and their risk score was associated with changes in predicted overall survival. There were no relapses in the 24 'low risk' patients (completely resected tumour < 5 cm in size) treated with surgery alone. This risk stratification-based model yielded impressive survival rates for children with this rare soft-tissue sarcoma. International collaboration allows results to be obtained that could never be achieved in small centres. Further study is certainly required here but the first steps to cracking the treatment of synovial sarcoma have been well and truly taken.

Wound complications facing soft-tissue sarcoma surgeons

x-ref Research

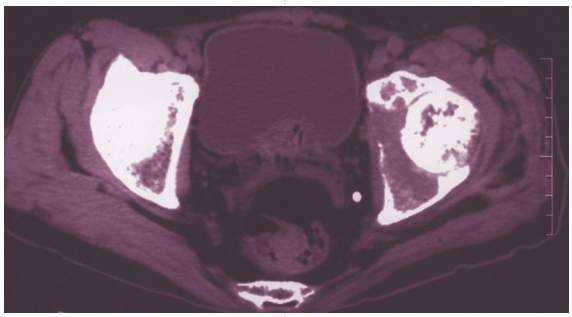
The treatment of large soft-tissue sarcomas usually involves extensive surgery and adjuvant chemo- or radiotherapy. The onset of wound complications (infection, dehiscence, etc) is one of the most catastrophic complications described in this group and is associated with poor outcomes following surgery. A study team in **Montreal (Canada)** set out to explore the factors associated with major wound complications following surgery for soft-tissue sarcoma. They explored a number of potential associated factors in a series of 256 cases operated for a diagnosis of soft-tissue sarcoma.[4] The research team were able to demonstrate associations between tumour factors (large diameter, high grade and location) and pre-operative radiotherapy. Whilst these in themselves are not surprising associations, what is surprising is that patient factors traditionally associated with poor outcomes (diabetes, smoking and obesity) were also associated with risks of major wound complications but closure method was not. It seems that wound complications are, to a certain extent, predictable, and in patients with risk factors undergoing aggressive resection in irradiated tumours they are more likely to run into problems. It seems possible that a more aggressive soft-tissue reconstruction strategy may be advantageous in these patients with significant associated risks.

Amputation may offer no survival benefit over reconstruction

With the push in recent years towards limb reconstruction through use of either limited excision and biological reconstruction or endoprostheses, there has been concern in some quarters that although limb salvage may improve functional outcomes, it may hamper longer-term survival with higher local recurrence rates. Although it certainly won't put this argument to bed, researchers from **Nashville (USA)** have added a valuable piece to this puzzle. They designed a study with the intention of establishing if amputation offered a survival benefit over limb reconstruction in patients where close excision margins were necessitated by salvage strategy. Their study of 360 patients included those who had a poor response to chemotherapy and underwent either limb salvage with poor margins or amputation, using a mix of surgical tactics.[5] The cohort includes 127 patients treated with amputation and 233 treated with salvage (36 with intralesional margins and 197 marginal margins). Local recurrence rates varied somewhat (36% in patients with intralesional margins; 20% in 'marginal margins'; 0% in amputation), however, there were non-significant differences in longer-term survival (46% intralesional margins; 28% marginal margins; 36% for amputation). This paper may go some way towards answering the question of whether it is safe to carry out limb salvage on patients with large tumours that do not appear to be responding to chemotherapy. Although not a trial, these results do suggest that amputation may not offer a survival advantage despite the worryingly high rates of local recurrence, especially in patients with an intralesional margin. This observation may in part be explained by the inherent selection biases associated with this kind of study. It is likely that many of the amputation patients had more locally advanced disease and hence unsalvageable limbs.

Giant cell tumour in the longer term

Treatment of giant cell tumours is routine surgery for the orthopaedic oncologist – simple curettage and cement augmentation is a widely accepted and successful technique. What is not quite so clear is how, in the longer term, the cement may affect the joint. We simply do not know. Researchers from **Sao Paulo (Brazil)** set out to establish precisely what the correlation between arthrosis and the presence of cement adjacent to the articular cartilage might be in addition to the final functional outcomes of joints in the presence or absence of radiographic arthrosis. The research team completed a study encompassing the results of 46 patients, all treated for a primary diagnosis of giant cell tumour between 1975 and 1999.[6] All patients were treated in a fairly standard manner with diagnosis by biopsy followed by curettage and cement augmentation. The study team reviewed the radiographs and functional outcomes of all patients and attempted to establish any patterns of outcome associated with either radiographic appearance of arthrosis or functional score and the distance of the cement from the joint surface. Whilst the authors established that the distance of the cement to the subchondral bone was associated with a greater risk of radiographic arthrosis, there were no detectable differences in the musculoskeletal tumour society scores between those with and without arthrosis. It does appear that with no longer-term measurable effects on functional outcome, surgeons can continue, with a clear conscience, to use cement to augment resection in giant cell tumour!



Intralesional treatment comparable with excision in GCT of the radius?

x-ref Wrist & Hand

Keeping with the theme of giant cell tumours (GCT), researchers in **Chicago (USA)** took a fresh look at the various different methods of treatment for GCT in the distal radius. They report their study of patients treated in two regional oncology centres over a 25-year period.[7] The study reports the results of 32 patients (of 39 initially identified as being treated for a GCT in the distal radius). Within the cohort there was a mixture of treatment strategies, with 20 intralesional excisions, 15 resection and radiocarpal arthrodesis, and four resections with osteoarticular allograft. The study team reviewed radiographs and obtained clinical outcomes in terms of examination and functional scores at a minimum follow-up of one year. The authors did not report any significant differences in pain or functional scores between the two groups in the main, although range of movement (as would be expected) was improved in the intralesional excision group. There was, however, a higher rate of recurrence (n = 6/17) in the intralesional group when compared with the *en bloc* resection (n = 0/15), and a higher re-operation rate. The authors concluded that resection for giant cell tumour of the distal radius, with distal radial allograft arthrodesis, was associated with a lower recurrence rate, lower re-operation rate, and no apparent differences in functional outcome compared with joint salvage with intralesional excision. However, they do observe that given that arthrodesis after recurrence functions similarly to those with initial resection and arthrodesis, there is probably no harm (and better movement) in the joint preserving options.

Imaging prior to oncological referral

While the fate of patients following oncological referral is well documented in the medical literature, as are the consequences of non-referral, there is little known about the fate of patients prior to referral to the tertiary centre. In an interesting and unique study, researchers in **Florida (USA)** set out to establish how useful evaluation prior to referral (particularly with a focus on imaging) actually is. The authors designed a prospective study to evaluate the utilisation of pre-referral complex imaging.[8] The authors reviewed all of the imaging obtained prior to referral and, using a consensus method with two musculoskeletal radiologists and two orthopaedic oncologists, determined if the imaging was appropriate using fairly tight criteria. Imaging was deemed inappropriate if they were either not indicated for diagnosis or treatment or a sufficient interval had passed by the time of referral such that the imaging needed to be repeated. The study reports an evaluation of 298 consecutive patients, and the headline result is of nearly a third of patients underwent inappropriate imaging of musculoskeletal tumours prior to referral. Teasing the data apart revealed unfortunate trends of ordering advanced imaging studies (MRI scans and CT scans) without a radiograph. Amazingly, a third of CT scans performed were inappropriate (most commonly ordered in error for evaluation of a soft-tissue mass). Over a quarter of MRI scans were inappropriate either due to being requested to evaluate a bony lesion or to image a clearly benign bone lesion. The situation was worse with bone scanning, where nearly 50% were inappropriate. This excess of inappropriate additional imaging equated to excess spending of $150 per patient evaluated. Besides representing a substantial cost to the patient and healthcare system, over-investigation in the community setting leads to a potential delay of referral, an increase in radiation exposure, and identification of other incidental findings.

And finally...

Schwab and colleagues from **Boston (USA)** have updated the review 'what's new in primary bone tumours' to include all significant papers over the last calendar year. A very worthwhile update for the general orthopaedic surgeon.[9]

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