ROUNDUP360

Oncology

For other Roundups in this issue that cross-reference with Oncology see: Spine Roundup 2; and Research Roundup 5.

Achieving global collaboration

x-ref Research

Some conditions are so rare that defining an adequate treatment approach based on evidence is difficult; many bone tumours fall into this category. However, in order to improve outcomes, comparative randomised controlled trials are essential to establish the most appropriate and effective treatments. In what is one of the first genuine global collaborations, the importance of the **EURAMOS study** cannot be under estimated. Whilst the final clinical results are yet to be known, the collaboration has reported what is the first truly multinational trial of a rare orthopaedic condition. The logistics of this study were formidable but the study concluded successfully. Four international study groups were able to devise and complete two ambitious randomised controlled trials where patients were randomly allocated to one of two treatment regimens. Patients were randomised to their chemotherapy after treatment for resectable osteosarcoma; those with <10% viable tumour being randomised to either MAP or MAP with pegylated interferon while those patients with >10% viable tumour received either MAP or MAP with ifosfamide and etoposide. An amazing 2260 patients were registered in the study and 1334 were successfully randomised, with 50% of patients achieving 90% necrosis in the resected specimen.[1] This landmark study will continue to report for a number of years as the primary and secondary outcome measures become reportable at further follow-up. It is clear that more innovative studies like this are required to improve the outcomes of patients with rare cancers. EURAMOS-1 has proven that this is achievable.

A new standard for limb salvage

Reporting of failures in a standardised manner is hugely important in any branch of surgery, and non-standardised outcomes make comparison of different approaches difficult in addition to hampering efforts of review teams and those attempting to conduct meta-analysis of data. This problem is particularly acute in tumour surgery where the same diagnosis has multiple different approaches for reconstruction, all of which should be compared with regard to complications. There are few standardised approaches to this and in a landmark article published in The Bone & Joint Journal, surgeons from **Lebanon (USA)** present a new system that we believe at *360* should be the gold standard for all future reports.[2] The system is the result of the work by the International Society of Limb Salvage (ISOLS) which aims not only to focus on endoprosthetic complications but also to be more appropriate for biological reconstruction. Their system is based on an interesting approach of an evidence-based review of complications, stratification into five primary types of failure for endoprosthesis and complementary systems for biologic and paediatric reconstructions. This article should become the standard when reporting prosthetic failures for oncology reconstructions.

Inoperable chondrosarcoma: chemotherapy?

Chondrosarcoma, when advanced and unresectable, is widely considered a terminal diagnosis. These tumours usually present with a combination of advanced local invasion, metastatic spread, and large inaccessible tumours. Treatment options are limited with chondrosarcoma where chemotherapy and radiotherapy are not commonly regarded as effective. In an interesting two-year retrospective study researchers from **Leiden (The Netherlands)** give a slightly different perspective on the whole issue[3] The research team designed a study to take a fresh look at the outcomes for patients with inoperable chondrosarcoma. They included data from both **Bologna (Italy)** and Leiden treated over a 30-year period. Their data concern the outcomes of 171 patients with, as would be expected, appalling survival rates. Conditional-based survival was around 50%/year, year on year (48% one year; 24% two years; 12% three years; 6% four years and 2% five years). Interestingly, their survivors were patients with locally irresectable disease without distant metastasis. In addition, the research team identified that patients who underwent either doxorubicin-based chemotherapy or non-cytotoxic drug therapy (imatinib and sirolimus) had significantly improved survival when compared with no treatment. Radiotherapy was also associated with improved overall survival. These authors present interesting data on the outcome of patients with inoperable chondrosarcoma and the tantalising suggestion that chemotherapy may indeed have some role in this tumour which is generally considered to be chemoresistant. This kind of study should always be taken with a pinch of salt: there is, by definition, a selection bias and the improved outcomes could well be due to case selection. Perhaps a trial (like Euramos above) will provide that information.

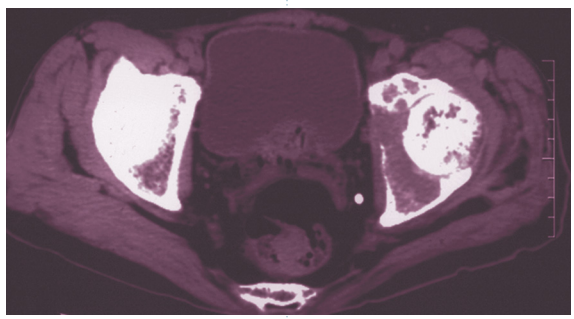
Soft-tissue sarcoma and adjuvant chemotherapy

There are few bone or soft-tissue malignancies that can be managed best with surgery alone and, as such, patients suffering from every conceivable form of musculoskeletal malignancy are subjected to surgery and then chemotherapy, radiotherapy or both, before and sometimes after surgery. While there is little doubt that in many diagnoses the morbidity associated with chemoradiotherapy is worth the patient investment as outcomes are so much improved, in some diagnoses there appears to be a certain amount of 'mission creep' and the improvement in outcomes is yet to be proven. Soft-tissue sarcomas (STS) are one such area where adjuvant chemotherapy for STS remains of unproven benefit (despite its wide adoption in many countries). In a re-analysis of two trials, both aimed to evaluate the efficacy of chemotherapy in treatment of soft-

tissue sarcoma, the multinational team of trialists from France, Italy and The Netherlands, among others, set out to review the results of two previously conducted clinical trials run through EORTC-STBSG.[4]The collaborative co-ordinated and completed two large trials evaluating the use of adjuvant chemotherapy in localised high-grade soft-tissue sarcoma. The study team pooled the results of both studies and were able therefore to draw on data from 819 participants with the aim of hypothesis generation and identifying prognostic factors that might predispose for a more successful outcome with adjuvant chemotherapy. Potential prognostic factors the research team investigated included tumour size, resection margins and histological grade. The research team were unable to identify any prognostic factors suggestive of an improved outcome in the adjuvant CT group. They identified that quality of initial resection and improved outcomes were predicted only by improved surgery and not the quality of adjuvant therapies.

Missed diagnoses and malpractice in sarcoma

The incidence of sarcoma is so low that reaching a diagnosis can sometimes take some time, and it is sadly not unheard of for the diagnosis to either be missed, or - even worse – for patients to undergo a surgical procedure without the diagnosis being reached beforehand. Litigation in these cases is relatively common and surgeons from **Nashville (USA)** set out to establish if there were any patterns in recent litigation that could provide a hint as to the factors most commonly resulting in litigation in sarcoma practice.[5] Over a 30-year period there were 216 cases of sarcoma-related litigation in the US where around 60% of verdicts favoured the plaintiff to the tune of $2.3 million per case. The most common issue leading to sarcoma-related litigation was, perhaps unsurpringly, delay to diagnosis (80%), with unnecessary amputation and misdiagnosis making up the rest. Although these data are from the US, very similar cases frequently arise in the rest of the world and it is likely that delay in diagnosis is the most common feature the world over. The message here seems deceptively simple: if a radiograph looks abnormal, get a second opinion or investigate it.



Radiofrequency in cartilage tumours?

There are a range of atypical borderline malignancy cartilage tumours that are usually treated with intralesional curettage as definitive treatment, however, this carries with it the potential for complications, including long bone fracture. The surgical oncology team in **Groningen (The Netherlands)** have set out to establish the potential role for a tantalising new application of radiofrequency ablation in the treatment of atypical cartilage tumours (ACTs).[6] The authors have conducted a pilot feasibility study as proof of concept, treating 20 patients with ACTs. The patients were treated with biopsy and radiofrequency ablation initially; an interval MRI scan and subsequent curettage allowed the surgical team to establish the safety and make an educated guess at the efficacy of such a treatment strategy. In a number of patients (n=14/20), an impressive 100% necrosis rate was associated with use of the radiofrequency ablation. In this small series the functional outcomes were improved after radiofrequency ablation when compared with the curettage, and there were no fractures following ablation but a 10% fracture rate following curettage. In this series the post ablation MRI scan was 91% sensitive for detection of residual tumour although the event rates were small and these results should be considered in that setting. This approach certainly has promise, and in selected cases it does look like radiofrequency ablation may offer kill rates similar to curettage but without the difficulties, morbidity and potential complications.

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