ROUNDUP360

Oncology

Eyeball as good as microscope for tumour margins!

One of the only consistent prognosticators in tumour surgery is that of negative margins. Not surprisingly, if you don't completely resect the tumour the outcome is poorer. Various strategies including pre-operative planning, intra-operative fluoroscopy, computer navigation and intra-operative histopathology have been described to improve resection margins. Intra-operative frozen bone marrow section is a time- and resource-intensive technique as, due to the laboratory time, the patient may be occupying the operating theatre for longer periods than are strictly necessary. Researchers in **Boston (USA)** were slightly sceptical of the benefits of bone marrow frozen section so designed a prognostic study to establish if frozen section has any advantages over 'eyeball inspection'. The retrospective study design was intended to establish what the correlation was between histological frozen section, what clinical decision was made with discrepancy and ultimately how accurate both assessments were with regards to final pathological assessment.[1] The research team were able to include an impressive 195 margins from 142 patients (mean age 12.8 years). There was a 95.6% negative and 38.5% positive agreement between both techniques. In the 16 cases of disagreement all treatment decisions were based on eyeball inspection of the split gross specimen. In this practice all 195 intra-operative decisions were made based on gross specimen inspection, which agreed in all cases with the final pathologic examination. It certainly appears from the results presented here that a gross examination of a split resection specimen may be a more successful method of assessment than a histological one.

When is best to stabilise femoral metastases? Xref

There is usually little crossover between the world of oncological surgery and trauma surgeons. However, metastatic bone disease is often treated by general orthopaedic and trauma surgeons as well as trauma and tumour specialists. In patients with disseminated metastatic disease where a cure or primary control cannot be achieved with excision, the treatment of choice is often intramedullary nailing. The Mirels'-score is almost universally accepted as the best prognosticator for impending fracture, and many units use this to prophylactically stabilise those patients who are likely to fracture in the near future. Researchers in **Madrid (Spain)** wished to establish if the practice of prophylactic nailing confers any advantage over treatment of pathological fracture in a retrospective cohort series. The series included 65 patients, all with femoral metastasis, treated over a 16-year period. All patients were treated with the same reamed intramedullary Gamma nail. Outcomes were assessed through survival, radiological and functional outcomes. The research team divided the cohort into those that underwent prophylactic nailing (Mirels'-score > 7) and those undergoing nailing for pathological fracture. The short-term mortality was surprisingly high in both groups (5% prophylactic *versus* 11.4% fracture). The functional outcomes were also markedly different, with all patients who were prophylactically nailed able to mobilise after surgery, whereas just 76% of the fracture group were able to do so. While the mean survival time was similar in both groups, the prophylactic nailing group had a lower transfusion requirement (1.4 *versus* 3.0), mobilised earlier (day 4.0 *versus* 10) and had shorter hospital stays (8 *versus* 16 days).[2] The results of this study are quite clear. For patients with metastatic cancer, prophylactic stabilisation was a far more successful treatment with lower mortality and better functional outcomes. It seems that early stabilisation for patients at risk of fracture is nearly always the correct thing to do.

Fluorine does not cause bone tumours Xref

Conspiracy theorists and concerned mothers rarely have much in common, but on the topic of artificial fluorination in drinking water they do share some significant common ground. While initially instigated as a public health measure, there has been much controversy over what should be a simple intervention to improve dental health care. The controversy surrounds a number of issues, but one area of particular concern for orthopaedic surgeons is the suggestion that artificial fluorination of drinking water may induce bone cancer. Given the almost universal approach to fluorination, this has been a difficult allegation to prove or disprove. Researchers in **Oxford (UK)** used an ingenious study design to assess the risk played by fluorination in water. They utilised UK-wide population-based cancer registries to establish case data on osteosarcoma and Ewing's sarcoma over a 25-year period, and accessed data on fluoride levels in drinking water in England and Wales through regional water companies and the Drinking Water Inspectorate. Using a carefully constructed negative binomial regression, the relationship between sarcoma incidence and fluorination level in drinking water was explored.[3] The study population included 4216 patients (2566 osteosarcoma and 1650 Ewing's sarcoma cases) and the researchers were unable to find an association between osteosarcoma risk and fluoride in drinking water (RR = 1.001) or Ewing's sarcoma (RR = 0.929). In a relatively exhaustive epidemiological study, the question surrounding fluorine and cancer risk seems to have been conclusively answered.

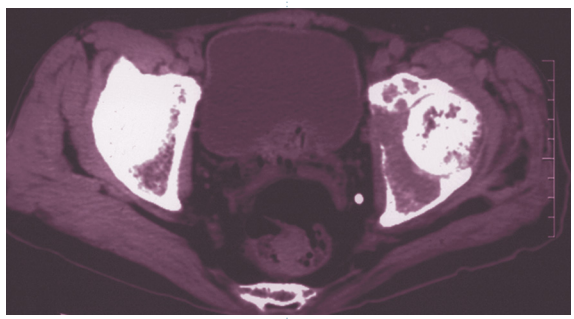
Is giant cell tumour of the proximal femur ever successfully managed?

Joint preserving management is essential to maintaining function in the proximal femur. However, this can be a challenging approach in giant cell tumours, a rare tumour of the proximal femur. Researchers

in **Birmingham (UK)** set out to assess the efficacy of joint sparing surgery (curettage and grafting) in a series of 24 cases managed over a 35-year period. Although this is a small series of patients, the research team attempted joint preserving surgery in the ten patients in whom it was clinically feasible to perform joint preserving surgery. Of the initial patients, cure was achieved in 79% of cases. Of the recurrences, two were treated by hip replacement and with curettage. There were no cases where an endoprosthesis was required. The authors conclude that 18 of 24 patients ultimately had a replacement and just six (25%) kept their native hip joint. Although these prostheses will provide reasonable or even excellent function in the medium term, eventual revision is almost inevitable.[4] The question foremost in our minds here at *360* is whether surgery will remain the mainstay of treatment, or the advent of drug therapy (in particular denosumab) will transform the management of giant cell tumour of bone and help retain host bone for eventually better oncologic and functional outcomes in these young patients.

Extraskeletal osteosarcoma revealed

Extraskeletal osteosarcoma is a rare soft-tissue sarcoma about which little is known. This article represents one of the largest series to shed light on this rare tumour. As would be expected for such an unusual tumour, the researchers in **New York (USA)** designed a retrospective case series with the aims of establishing the typical clinical features, natural history and factors affecting outcomes. The series includes 53 patients (42 with localised disease, two with metastatic disease, and nine recurrences). Patients presented at an average age of 64 years, for the most part with high grade lesions in the extremities. The average survival for patients with localised disease was nearly four years from diagnosis, with 18 patients suffering further events (two local recurrences, ten metastases, six recurrences and metastases). The authors note that for patients presenting with localised extraskeletal osteosarcoma, three-year event-free survival was higher for patients with superficial tumours and negative margins at resection. Due to the small numbers the authors were unable to provide any treatment advice, although they comment that radiation and chemotherapeutic treatment were not associated with a lower incidence of death or a longer event-free survival.[5] The authors stress in the discussion section the importance of distinguishing extraskeletal osteosarcoma from primary osteosarcoma of bone. The lesions are histologically indistinguishable and it is tempting to attribute a similar pathophysiology to both diseases. While there may be a rationale to use bone osteogenic sarcoma chemotherapy, it is important to remember that this is a distinct lesion and likely to behave in a unique manner.



Osteosarcoma treatment in summary

Here at *360* we would thoroughly recommend this paper from **Münster (Germany)**, which provides a bird's eye view for the general orthopaedic surgeon of the current status of management of osteosarcoma.[6]

Modular lower limb tumour reconstruction

Modular tumour reconstruction systems have been around for a number of years and the evidence is accumulating to support their use in a range of tumour reconstruction procedures. However, there are few large series detailing outcomes over mid-term follow-up. While not groundbreaking, research surgeons in **Bologna (Italy)** have reported exactly this. They present a retrospective analysis of 295 current-generation Global Modular Replacement System (GMRS) modular tumour endoprostheses for the lower limb in primary and secondary implantation procedures. The outcomes were reported at a mean of 4.2 years' follow-up.[7] Of the 295 patients, there were 197 primary implants and 98 revision procedures. The majority of procedures were surrounding the distal femur (60%, n = 199) and proximal tibia (20%, n = 60). Overall results were good with an average functional score of 81.6% (24.5) and an overall failure rate of 28.8%, with failure occurring at a median of 1.7 years. There was a significant difference in implant survival of all modes of failure between primary and revision implants, leading the authors to conclude that mid-term results with GMRS are promising, with good functional results and low incidence of complications for primary implants.

Observational studies the basis for most bone tumour treatment

As exemplified by last month's *360*, the evidence for orthopaedic surgery has progressed no end, with higher quality randomised studies informing practice in everything from trauma to arthroplasty surgery. However, not all orthopaedic disciplines find it as easy to conduct randomised studies. Surgeons from **Hamilton (Canada)** set out to establish what the state of play is in orthopaedic tumour surgery. Specifically, the authors hoped to determine what overall levels of evidence were for articles published on the management of lower extremity bone tumours. The study team also wished to assess the quality of reporting of evidence using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist and try to establish what the most common weaknesses were in reported studies. The study team undertook a massive review of all studies describing surgical management of lower extremity primary bone tumours over a ten-year period. The study team identified 1387 studies and included 607 that met the eligibility criteria. There were no Level I studies, two Level II studies, 47 Level III studies, 308 Level IV studies, and 250 Level V studies. The articles only managed to achieve 53% of the STROBE checklist points, with the most common pitfalls being failures to justify sample size, examine sensitivity, account for missing data, and discuss sources of bias. Amazingly, just two thirds of studies discussed follow-up or precision of outcomes, while around half addressed eligibility criteria and methodological limitations.[8] Currently, bone tumour surgery is guided by evidence that is predominantly based on observational studies with numerous reporting deficiencies. In tumour surgery it is incredibly difficult to perform randomised controlled trials due to small patient groups and heterogeneity of diagnoses. However, improving reporting of evidence in print and including comparison groups would significantly improve the evidence basis within the constraints that exist in the specialty.

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