ROUNDUP360

Oncology

Allograft composite superior to megaprosthesis in massive reconstruction

Limb-preserving surgery relies on the use of mega- or tumour-prosthesis to replace large sections of excised bone and soft tissue. Within the femur there are two slightly competing philosophies; the use of a prosthesis alone which results in detachment of both the abductors and iliopsoas but only reconstruction of the abductors *versus* an alternate prosthesis-allograft composite reconstruction when it is customary to reconstruct both tendon insertions offering a potential functional benefit. Surgeons from **Bologna (Italy)** conducted a prospective comparative case series, comparing femoral reconstruction with either a modular prosthetic replacement or an allograft prosthesis composite. The outcomes were assessed at a minimum follow-up of 2.5 years, using both gait analysis and the Muskuloskeletal Tumour Society Score. Although the functional score did not detect a difference between the two groups, there were consistent and measurable differences with gait analysis. There was a decreased walking speed in both groups and a difference in hip extensor function in late stance. Surface EMG identified a more evident muscle co-contraction during gait in the modular prosthetic group. The authors conclude that the use of an allograft-prosthesis composite, and the muscle reattachment options it offers, are likely to benefit patients through more efficient gait patterns.[1] This study raises an interesting and perhaps under-recognised problem. With objective evidence of an altered gait between the two groups, surely there is an argument in favour of the allograft-implant construct? But in the setting of no difference in outcome scores does this still hold true? The difference is obviously a genuine one but with no differences in a validated outcome measure, one has to ask whether it really matters, as functionally neither patient group appears more disabled than the other.

Pain from glomus tumours

A research team in **Chiba (Japan)** has undertaken a basic science study to evaluate the origin of pain from glomus tumours. These benign hamartomas are characterised by painful spasms which is often the presenting clinical sign. Little previous work has been undertaken on the mechanism of pain production, although substance P has been previously identified in the tumour itself. The research team used an immuno-histochemical approach to evaluate the presence of S100 protein, substance P, cyclo-oxygenase-2 expression and prostaglandin-E2 in eight glomus tumour samples in combination with regular histology techniques to confirm the identity of the lesion. They successfully identified S100, cyclo-oxygenase-2 and prostaglandin-E2 in all the samples they tested while substance P was identified in five of the eight samples tested. The authors hypothesise that given the high levels of cyclo-oxygenase-2 and prostaglandin-E2, which function as a vasodilator, the pain could be caused by increases in intracapsular pressure. Of course, the presence of S100 and COX-2 also points to a potential inflammatory mechanism for pain.[2]

Thromboembolism and orthopaedic malignancy

Top of the medico-political agenda in many developed healthcare systems is that of venous thromboembolic disease (VTE), fuelled by multiple large randomised controlled trials. The risks of VTE are known to be significantly higher in some patient populations, and particularly those with cancer who undergo orthopaedic surgery. Despite a global focus on prevention there is precious little data surrounding particular high risk populations. Investigators in **Changwon (South Korea)** set out to identify potential risk factors for post-operative VTE in patients undergoing surgery for musculoskeletal tumours of the lower limb. They enrolled 168 consecutive patients into their cohort and their outcome measure was a proven VTE within 90 days of surgery. Halfway through their study recruitment, a chemical thromboprophylaxis regime was instituted and 76 patients were treated without chemical thromboprophylaxis. The authors used a prospective database to collate 28 potential predictive variables covering patient, surgical and tumour related factors. Of the patients included in the study there were eight incidences of DVT and a single fatal PE. The researchers identified older age, higher ASA score and metastatic tumour as potential risk factors for VTE. The authors also note that there were no significant differences in rates of VTE pre- and post-institution of thromboprophylaxis.[3] While there are some very interesting assertions in this paper, it is important to remember that the number of patients evaluated was tiny, and the number of significance tests quite large. One would expect 1.5 false positive tests (as 28 were done) and with just four events, even if thromboprophylaxis cut the event rate in half, the results would not be significant. We welcome more data on this hotly debated and thorny topic but would caution leaping to conclusions based on such a low number of actual events.

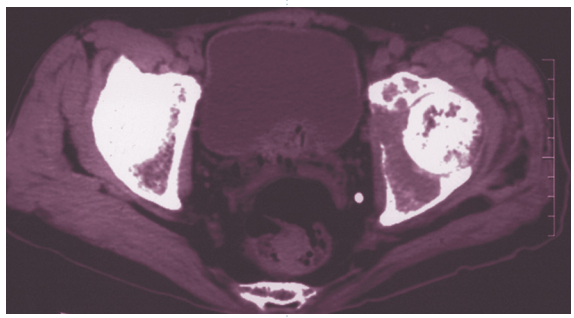
Bone marrow aspirate no help in cavity lesions

A well recognised treatment strategy for benign cavity lesions is open curettage followed by grafting. An alternate to autologous bone graft in common use is porous calcium phosphates. Researchers in **Syracuse (USA)** recognised that while reducing the morbidity associated with graft sites, graft incorporation is very slow. Not resting on their laurels, these industrious surgeon-scientists devised a randomised controlled trial to test the efficacy of adding bone marrow aspirates to Ultraporous β-tricalcium phosphate (TCP) prior to grafting. Their study included 55 patients, all with benign bone lesions, randomised to curettage and graft-

ing alone (n = 26) or curettage and grafting + bone marrow (n = 29). As would be expected in a randomised controlled trial there were no differences in baseline characteristics, and follow-up was with regular radiographs in addition to a CT scan at 12 months. In both groups there were radiological signs of significant increases in trabeculation and resorption over time, with the graft persisting but gradually resorbing throughout the study. There were, however, no detectable differences in any of these parameters between the two groups.[4] In this particular case, the addition of bone marrow aspirate has been clearly demonstrated to have no beneficial effect on graft incorporation. It is nice to see such a well conducted study answering such a simple question.

Metastasectomy in osteosarcoma

Despite the relative frequency of pulmonary metastasis associated with osteosarcoma and soft-tissue sarcomas, there is little evidence surrounding the benefits (or otherwise) of different treatment modalities. Surgeons in **Amman (Jordan)** aimed to establish the efficacy of metastasectomy and chemotherapy in resectable pulmonary metastasis. The investigators reviewed all patients retrospectively following presentation to their unit with an isolated pulmonary metastasis. They identified 71 patients presenting with pulmonary metastasis (32 osteosarcoma and 39 other sarcomas). Of these at presentation, 25 were unresectable and 46 resectable. The treating teams offered metastasectomy to 29 of the resectable lesions while the remaining 17 received a chemotherapy regime. Patients with resectable lesions who underwent metastasectomy had a significantly better disease-free survivorship throughout the course of the study than those who did not have resection (8 *versus* 4.3 months) and those with unresectable tumours (2.2 months). These results were also reflected in the overall survival rates, with the surgical group surviving 40 months compared with the chemotherapy group (20 months) and unresectable group (7.8 months). Interestingly, the authors found on subgroup analysis that this survival benefit was exclusively in the osteosarcoma patients and not reflected in the soft-tissue sarcomas.[5] Although this study in all likelihood suffers from a significant selection bias, it does provide some comparative data and may be useful in subsequent decision making. Given the potential for significant survival benefit for osteosarcoma patients, an appropriately designed RCT is definitely called for.



Prognosticating spinal giant cell tumour

Giant cell tumour (GCT) is a benign aggressive lesion characterised by giant cells in the stroma. Unusually with benign lesions, giant cell tumours have relatively high recurrence rates and metastatic potential and, as such, prognostication becomes more important than in other benign lesions. Researchers in **Shanghai (China)** noted the relative paucity of information and the unusual need for prognostication in a benign lesion occurring in the spine where recurrence can be disastrous. The authors used Kaplan-Meier survivorship analysis with recurrence-free survival as their end point and then subsequent multivariant analysis using a cox proportional hazards model. The study team identified 102 patients presenting with GCT of the mobile spine, with an impressive follow-up of nearly 40 months. During the period of the study, 38 patients developed recurrence and following the detailed statistical analysis the authors assert that young age (under 40), total spondylectomy and bisphosphonate use are favourable prognostic factors. The authors identified the same favourable characteristics of *en bloc* and piecemeal total spondylectomy.[6] This is, in our opinion, a superb little study. It sets out to, and answers, some specific research questions. Patients presenting with a mobile segment GCT can expect a more favourable prognosis if young, managed with a total spondylectomy and administered long-term bisphosphonate therapy.

Post-atomic strike sarcoma

On 6th August 1945 'Little Boy' was dropped over Hiroshima, killing between 90,000 and 166,000 people, and three days later 'Fat Man' was dropped over Nagasaki, killing a further 60,000 to 80,000 people, effectively ending the Second World War. The majority of those died on the day of the explosions. While exposure to very high levels of ionising radiation is known to cause soft-tissue sarcomas, the effects of lower levels are unknown. Investigators in Hiroshima and **Nagasaki (Japan)** used the Life Span Study of 80,180 atomic bomb survivors from those first nuclear attacks. The cohort has been prospectively followed and the lifetime risk of sarcoma development related to exposure to radiation (colon dose gray (Gy)) and subject demographics, age-specific, and survival parameters recorded. Of the 80,180 patients there were 104 soft-tissue sarcomas developed in patients with a mean colon dose of 0.18 Gy. The sarcomas developed over a mean 37-year period and had just a 39% five-year survival rate. The investigators established a linear dose response model between radiation exposure and risk of developing sarcomas with a relative risk of 1.01 per Gy and an absolute risk of 4.3 per 100,000/year/Gy.[7] While the appalling loss of life in both Hiroshima and Nagasaki can never be condoned, the ongoing population study of those that survived the blasts has contributed vastly to our understanding of the effects of radiation exposure. This data represents the largest and longest study of the effects of ionising radiation. The unique finding that lower doses of radiation than previously thought may contribute to the development of soft-tissue sarcomas is an interesting one.

Superficial sarcomas have higher post-operative infection rates

The use of adjuvant and neo-adjuvant radiotherapy has revolutionised survival in soft-tissue sarcomas. While survivals are similar with both pre- and post-operative radiotherapy, the complications associated with the treatment are not. Patients undergoing neo-adjuvant treatment have higher rates of wound complications but lower rates of fibrosis, stiffness and limb oedema. Reliable prediction of the risks of wound complications would allow for selection of the most appropriate radiotherapy strategy on a patient by patient basis. The research group in **Boston (USA)** conducted a prognostic study in the hope of identifying one or more prognostic factors that would be predictive of major wound complications in this cohort of patients. The researchers identified 103 patients treated at a single centre over a five-year period. All patients were treated with surgery and pre-operative radiotherapy, and wound complications were defined as those requiring operative treatment or prolonged dressings. In all cases patients were treated with

wide excision or radical resection for tumours with a median size of 84 mm (2 cm to 25 cm), with 70% of cases achieving primary closure but 27% requiring a vascularised flap; just 3% required a split skin graft. Major wound complications occurred in 35% of patients, and predictors of complications included diabetes, larger tumours (> 10 cm), those lying very superficially (< 3 mm from the skin surface) and those requiring flap closure.[8] Major wound complications are a common occurrence in patients with soft-tissue sarcomas, occurring in one out of three patients. We would agree, here at *360*, with the authors, that consideration should be given to either different radiotherapy regimes or pre-emptive steps to decrease wound complication rates in patients with high-risk superficial large tumours.

REFERENCES

1. **Benedetti MG, Bonatti E, Malfitano C, Donati D.** Comparison of allograft-prosthetic composite reconstruction and modular prosthetic replacement in proximal femur bone tumors. *Acta Orthop* 2013;84:218-223.
2. **Yanai T, Tanaka T, Ogawa T.** Immunohistochemical demonstration of cyclooxygenase-2 in glomus tumors. *J Bone Joint Surg [Am]* 2013;95-A:725-728.
3. **Kim SM, Park JM, Shin SH, Seo SW.** Risk factors for post-operative venous thromboembolism in patients with a malignancy of the lower limb. *Bone Joint J* 2013;95-B:558-562.
4. **Damron TA, Lisle J, Craig T, et al.** Ultraporous β-tricalcium phosphate alone or combined with bone marrow aspirate for benign cavitary lesions: comparison in a prospective randomized clinical trial. *J Bone Joint Surg [Am]* 2013;95-A:158-166.
5. **Salah S, Fayoumi S, Alibraheem A, et al.** The influence of pulmonary metastasectomy on survival in osteosarcoma and soft-tissue sarcomas: a retrospective analysis of survival outcomes, hospitalizations and requirements of home oxygen therapy. *Interact Cardiovasc Thorac Surg* 2013;(Epub ahead of print) PMID: 23599187.
6. **Xu W, Li X, Huang W, et al.** Factors affecting prognosis of patients with giant cell tumors of the mobile spine: retrospective analysis of 102 patients in a single center. *Ann Surg Oncol* 2013;20:804-810.
7. **Samartzis D, Nishi N, Cologne J, et al.** Ionizing radiation exposure and the development of soft-tissue sarcomas in atomic-bomb survivors. *J Bone Joint Surg [Am]* 2013;95-A:222-229.
8. **Baldini EH, Lapidus MR, Wang Q, et al.** Predictors for major wound complications following preoperative radiotherapy and surgery for soft-tissue sarcoma of the extremities and trunk: importance of tumor proximity to skin surface. *Ann Surg Oncol* 2013;20:1494-1499.