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Oncology

Predictors of venous thromboembolism in patients with primary sarcoma of bone

■ Venous thromboembolism (VTE) is known to be independently associated with both orthopaedic surgery and malignancy. However, although patients undergoing surgery for musculoskeletal malignancies are at an increased risk of thromboembolism, there is very little in the way of evidence on which to base practice in this group. In this retrospective study from **Boston, Massachusetts (USA)**, the authors report the outcomes of 379 orthopaedic oncology patients with at least 90 days of postoperative follow-up from the index surgery.¹ In this cohort, 21 patients (5.5%) had a clinically symptomatic, and radiologically confirmed, VTE within 90 days of index surgery (12 had a deep vein thrombosis (DVT); nine had a pulmonary embolism (PE)). The reported rate of VTE in this series represents only those that were clinically symptomatic and treated at their primary institution. This is therefore the lowest estimate of the actual rate, as it will not include subclinical events or those treated at outside institutions. The median time to event was 27 days. Although this cohort contained just 21 events, to our knowledge, here at 360, it is by far the largest series of patients exploring VTE following orthopaedic oncology surgery

and, as such, the authors went on to explore what they could glean from the series in terms of potential risk factors. They undertook an analysis of potential risk factors and report that a higher preoperative white blood cell count (possibly a reflection of haemoconcentration, which *per se* is prothrombotic in nature) and postoperative wound complications were found to be independent risk factors for VTE. There were no differences in this series in terms of efficacy among the various available antithrombotic medications. Nonetheless, the risk of wound complications increased significantly in patients who received chemical thromboprophylaxis (odds ratio (OR) 2.21). This observation prompted the authors to make the suggestion that aggressive DVT prophylaxis may actually increase the risk of thromboembolic events. They argue that prolonged immobilization and additional surgical interventions are likely to be required when addressing postoperative wound complications. They then make the reasonable recommendation that prospective randomized trials comparing different medications in combination with compressive devices are needed to assess efficacy with the lowest complication profile, and that simpler protocols may increase patient compliance with prophylactic treatment. This, of course, is a tall order in

the normal orthopaedic populations, and some observers may feel it is near impossible in the much rarer surgical oncological patients.

Carbon fibre-reinforced intramedullary nailing in bone metastasis X-ref

■ Traditional intramedullary nailing makes use of titanium cannulated interlocked nails, a venerable technology that has evolved through the past few decades. Nevertheless, despite the almost universal dominance of titanium nails, there are several other options available. One of the newest is carbon fibre-reinforced (CFR) nailing, which involves polyetheretherketone (PEEK) and has a couple of significant advantages. The carbon fibre enables a controlled response when stresses are applied to the implants in an anisotropic manner, which is much more difficult to achieve with titanium, and the radiolucency of the implant allows for surveillance of the fracture and metastasis. This series from **Italy** reports one of the few series on the use of these nails in musculoskeletal tumour surgery, with the longest available follow-up.² The authors report 53 adult oncology patients, all of whom had either pathological fracture or impending fracture requiring stabilization. The surgery in every case was undertaken using a CFR nail. The patients in this series

included the usual distribution of long bones (humerus, n=35; femur, n=11; tibia, n=7). The appearance of callus, the response to radiotherapy, and the clinical status of the patient's tumour were recorded. Hardware survival and failure, breakage, and need for implant revision were also reported as secondary outcomes. In terms of adverse events, the authors report a relatively high rate of intraoperative (13.2%) and postoperative (7.54%) complications. Eight patients had local progression and one developed a stress fracture proximally to the distal static screw. The chief advantage of CFR implants in orthopaedic oncology is that, unlike metal implants (titanium or stainless steel), they are radiolucent and, therefore, fracture reduction and healing can be assessed more easily. In oncology patients, the use of CFR-based implants enables monitoring of the consolidation of the pathologic fracture, local recurrence, progression, or response to therapies without obstruction of the metallic implant. Moreover, because of their low atomic number and radiation properties like the surrounding tissues, the CFR devices are inert to ionic radiation and give minimal disturbance on the irradiation dose distribution during radiotherapy. The potential disadvantages are that CFR nails are not contoured, humeral nails are not cannulated due to the

small diameter of the implant – and therefore guide wire insertion is not possible – and their use in fracture fixation is limited to straight diaphyseal fractures. Moreover, the radiolucent nature of the biomaterial precludes a direct visualization at fluoroscopy and, therefore, the interlocking screw fixation, although aided by some radio-opaque markers, can be difficult.

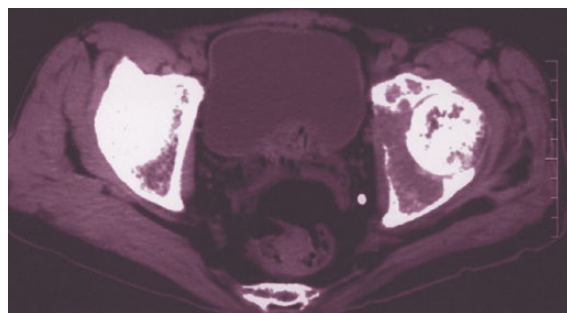
Long-term outcomes of cement-in-cement technique for revision endoprosthesis surgery

■ With increased patient survival, the incidence of failed endoprostheses after primary sarcoma surgery has risen, often leaving complex problems as the implants wear and loosen. With 25-year implant survival rates reported to be at approximately 50%, an increasing number of patients will require revision of their endoprosthesis over the coming years. Removal of the implant from stress-shielded bone is often fraught with challenges and the ease of simply ‘cutting above’ the cement mantle is tempting for surgeons. The cement-in-cement (CiC) revision offers a technically challenging but attractive option in these difficult cases. Not relying on removal of more bone, nor resulting in proximal stress shielding and further bone loss, the CiC revision – when handled correctly – allows for exchange of a loose component without further damaging the local bone stock. This is a retrospective review of 54 lower limb implants from **Santa Monica, California (USA)**, all revised with a CiC technique, and for which the authors have reported the long-term results.³ During the period of the study, the centres involved collated an endoprosthesis database of 512 consecutive cemented endoprosthetic reconstructions performed for oncologic diagnoses between 1980 and 2014. Overall, there were 54 of these procedures performed as first-time CiC revisions; 31 were performed as second CiC revisions.

This gave 54 limbs in 54 patients with 85 CiC procedures. The authors report their outcomes in terms of prosthesis survival, revision surgery, complications, and functional scores. At a usefully long interval of 15 years, these authors were able to report a Kaplan–Meier calculated survival rate of just 34% for initial revision, and 39% for subsequent revision implants. The mean revised Musculoskeletal Tumor Society (MSTS) Score was 27 at the latest follow-up, and there was an appreciable but low infection rate of 2% for the initial revision and then 9% and 13% for second and third revisions, respectively. The overall limb salvage rate, however, was excellent at 87% for the duration of the follow-up. The authors concluded that at long-term follow-up, endoprostheses revised with the CiC technique showed consistent 15-year survival from initial (34%) to subsequent (39%) revision. The fact that survival of subsequent revisions was equal to that of the initial CiC revision, they suggest, provides optimism in the reproducibility and durability of this technique. However, with just over a third of patients surviving with their revision implants to 15 years, one does question whether an improvement in the technology is going to be needed here. The number of patients with a megaprosthesis is increasing exponentially, with more and more bone sarcoma survivors joined by the increasing number of patients who are having excision and reconstruction of solitary bony metastasis.

Additional excision after unplanned excision

■ Sadly, even in the age of instant second opinions and electronic tertiary referral pathways, we still see a number of patients who have unplanned excisions of their soft-tissue sarcomas. This is sometimes due to mistaken diagnosis, but is more often just due to not ‘thinking sarcoma’ at the initial presentation. There are plenty of patients in whom, sadly, an initial unplanned



excision has been performed, after which the tumour unit is left with a referral. These patients continue to be of interest for a number of reasons. The first question to consider is whether the patient should have a revision excision, the second is how one might expect these patients to do, and the third is: How does this occur, and what can we learn about referral patterns and reaching rapid diagnoses in those in whom this is initially missed? A surgical oncology team from **Tsu City (Japan)** have focused on the second question – what can the expected outcome be if a second excision is required?⁴ They were able to draw on a series of 197 patients, all with a diagnosis of soft-tissue sarcoma in whom an unplanned excision was undertaken and a revision excision required. These patients had a mean age of 54 years and a mean primary tumour size of 4.7 cm. The tumour was classified as superficial in 132 patients, with the remaining 65 being classified as deep. There is a clear message here that revision excision is a positive thing to do, with 58% of patients (n=115/197) having residual tumour cells visible on histology at their second surgery, and a surprising 105 patients (53%) requiring plastic reconstruction at the time of revision excision. The longer-term outcomes were good, however, with a five-year disease-specific survival (97.4%) and local recurrence rates (91%) similar to those with primary soft-tissue sarcomas reported in most contemporary series. Unsurprisingly, those patients who had had an inadvertent incomplete excision did significantly worse than

those who had no tumour cells visible at revision excision.

Improved survival in sarcoma patients using specialized multidisciplinary board

■ Few would dispute that multidisciplinary team (MDT) meetings, now commonly seen across a broad range of surgical and nonsurgical specialties, add a significant dimension to the process surrounding diagnosis and treatment, as decision-making is tailored to the individual needs and circumstances of the patient. Although there is precious little evidence to suggest that MDT meetings prolong life, we all intrinsically feel they ought to. This current paper from **Lyon (France)** is one of the few with a sufficient number of patients presenting and being treated to allow us to draw some useful inferences about their treatment.⁵ The authors undertook an impressive nationwide study over a period of five years, with the intention of determining whether a pretreatment multidisciplinary tumour board (MDTb) presentation at 26 reference sarcoma centres had any impact over a five-year period. In one of the most impressive and extensive studies of soft-tissue sarcoma, the authors report the outcomes of 12 528 patients with a primary diagnosis of soft-tissue and visceral sarcoma. Of these, 5281 (42.2%) had discussion at the MDTb prior to treatment, and 7247 (57.8%) after initial treatment commenced. In one of the few papers to study joint decision-making effectively, we were delighted to see the thoroughness with which these authors presented

and discussed their results. They established that early presentation to a MDTB was associated with better compliance with national clinical practice guidelines, and specifically adherence to recognized tumour care pathways (biopsy and imaging prior to surgery). They also established that those patients with a preoperative discussion had a higher quality of initial surgery, and fewer reoperations. This also translated to better outcomes, with local relapse-free survival and overall relapse-free survival reported as being significantly better in patients presented to a MDTB before initiation of treatment. The authors also undertook a multivariate analysis to check for confounders and established that these factors remained significant. The results here really do speak for themselves. Presentation to, and discussion with, the MDT prior to embarking on significant tumour surgery is an essential part of achieving a good result.

The top research priorities in orthopaedic oncology

■ Champions of evidence-based medicine, this group from **Hamilton (Canada)** have published a really useful consensus document targeting priorities for research achieved using a modified Delphi approach.⁶ The aim was to achieve a priority-setting exercise to allow the limited financial and clinical resources available to orthopaedic oncologists to direct researchers

effectively towards the most clinically relevant questions. The priority setting exercise used a formal consensus-based approach involving clinician-scientists and stakeholders to identify the top priority research questions using a three-step modified Delphi process. The process involved the full range of stakeholders including orthopaedic oncologists, researchers, and funding agency and patient representation. Clinically relevant research questions were elicited from the 114 participants (61 of whom returned them). These questions were then rated using a Likert scale and those that reached the *a priori* consensus thresholds progressed for consideration at an in-person consensus meeting. At this meeting, four priority questions were agreed upon: 1) Does less intensive surveillance of patients with sarcoma affect survival?; 2) What are the survival outcomes over time for orthopaedic oncology implants?; 3) Does resection *versus* stabilization improve oncologic and functional outcomes in oligometastatic bone disease?; and 4) What is the natural history of untreated fibromatosis? We applaud the authors for their attention to detail and for publishing this useful paper.

Immune surveillance plays a role in locally aggressive giant cell lesions of bone

■ Could immune surveillance be a start to molecular basis for

follow-up? This paper from **Boston, Massachusetts (USA)** may be the answer to the consensus document above.⁷ The giant cell lesion of bone, although thought to be only locally aggressive, is able to form metastasis. These lesions carry with them a relatively low yield for long-term surveillance, but do at times metastasize. Patients therefore often carry a long-term follow-up burden. This paper concerns the potential for immune surveillance that may offer a route to a molecular test for recurrence. In this basic science paper, the authors aimed to characterize the expression of the human leucocyte antigen (HLA) class I and class II antigens and tumour-infiltrating lymphocytes. They then went on to try to identify the role of B7-H3, an immune modulating surface antigen. The candidates for this study were 93 patients previously treated at the Massachusetts General Hospital, all with tissue core biopsy. The research team then went back to look at the lymphocytes in these historic samples. The authors identified lymphocytes in all tumour biopsies with a lower mean number of CD8+ T cells in aggressive tumours (median 4.8 vs 15.8). In keeping with this, HLA I was highly expressed by multinucleated giant cells in all tumours, but was low in expression in mononuclear stromal cells in patients with aggressive tumours. Overall, low HLA class I expression combined with low CD8+ T cell infiltration was most highly associated with tumour

aggressiveness (OR7.81). So, there is the potential here for both a biological marker of giant cell aggressiveness, and perhaps even a marker of activity that would eventually transform follow-up for giant cell tumours into an annual blood test rather than regular imaging and clinical reviews.

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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 8**

Scoliosis management in patients with Duchenne's

X-ref

■ In this valuable look back from **San Diego, California (USA)**, the authors present 30 years of a single

institution's experience in treating spinal deformities in children with Duchenne muscular dystrophy (DMD).¹ The complexities of treating scoliosis in patients with muscular dystrophy are well known; however, there are few long-term series on which to inform clinical practice, particularly when contemplating surgery. In this 30-year retrospective series, the authors were able to

identify 60 patients, all with DMD, treated operatively for their scoliosis. There was a mixture of operative techniques, as one would expect with such a long-term follow-up series. Of the 60 reported patients, 47 were treated using the Luque wire constructs and the remaining 13 were treated using a posterior pedicle screw construct. In the Luque group, there was a high rate

of intraoperative and postoperative complications, with an overall complication rate of 68% (n=31/47). A total of 12 patients (26%) had implant-related complications and an overall 4% infection rate was found. In contrast, the pedicle screw group (although much smaller) reported an overall 54% complication rate (n=6/13), with only a single (8%) implant-related complication