

a team based in **Seoul (South Korea)** investigated the contribution of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as biomarkers for predicting overall survival in patients treated with surgery and postoperative radiotherapy for soft-tissue sarcoma.<sup>6</sup> The team analyzed preoperative data from 99 patients presenting with limb soft-tissue sarcoma. Raised CRP was seen in 33 patients and raised ESR was seen in 44 patients; both were associated with subsequently reduced overall survival, disease-free survival, and distant-metastasis-free survival. Further analysis showed that elevated ESR is an independent prognostic factor for overall survival and distant-metastasis-free survival after controlling for other known factors. The authors undertook a receiver-operating characteristic curve analysis and established that a threshold of 0.14 mg/dl for CRP, 15 mm/h for ESR, and >1.95 for neutrophil:lymphocyte ratio were predictive of a poor outcome. This study lends weight to the established hypothesis that global inflammation plays a role in outcomes, and perhaps suggests a potential therapeutic target in the future, as well as helping to identify which patients are most likely to suffer from complications.

### C-reactive protein as an independent prognostic indicator for disease-specific survival in patients with soft-tissue sarcoma

■ This study from **Wuhan (China)** again looks at the value of systemic inflammatory markers in prognostication for soft-tissue sarcoma.<sup>7</sup> These authors, however, present an evidence synthesis investigating the role of C-reactive protein (CRP) as a prognostic indicator for disease-free survival in the same condition. A systematic literature search was carried out for studies that investigated the correlation between CRP, disease-free survival, recurrence, and clinical characteristics. The team found nine eligible articles reporting a total of 1655 patients, and carried out a random-effects analysis to show that raised CRP correlates to both poor disease-specific survival and poor disease-free survival. The authors excluded a single heterogeneous study and used a fixed-effects model to show that elevated CRP level was firmly correlated with poorer disease-specific survival (hazard ratio (HR) 2.36) and disease-free survival (HR 1.78). This is a useful study that helps to paint a picture of the factors influencing survival in this challenging condition.

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## Children's orthopaedics

### The value of the 'clicky hip' in selective screening for developmental dysplasia of the hip X-ref

■ There is some controversy and difference in opinion in the literature regarding the value of the 'clicky hip' when considering screening and investigation for developmental dysplasia of the hip (DDH). It is well recognized that DDH is a spectrum of pathology ranging from subtle dysplasia in a stable hip through to those that are dislocated. Early diagnosis is associated with improved outcomes, and missed dislocations have catastrophic consequences. While all children receive a hip examination as part of their baby checks in the United Kingdom, a selective screening programme is standard for access to ultrasound imaging. Patients with a history or examination of 'clicky hip' are not a universally accepted criterion for referral for paediatric screening. This excellent paper from **Nottingham (UK)** sought to use their large prospectively collected database to assess how many patients with a presentation of a 'clicky hip' and no further risk factors actually had a dysplastic hip on

their initial ultrasound scan, and also what proportion of the children treated for DDH were initially referred as a 'clicky hip'.<sup>1</sup> This was a single-centre study in a large teaching hospital including all referrals to the paediatric hip clinic over a four-year period; all patients received an ultrasound scan and were clinically examined by a consultant surgeon. Over that period, 5716 children were referred and 1754 (30%) had a 'clicky hip' but lacked additional risk factors for DDH. Overall, 7% of children with a 'clicky hip' had an abnormal ultrasound scan, including 1% or 16 children with Graf 2b, 2c, 3, or 4 dysplasia. When reviewing the 141 patients treated in a Pavlik harness during the study period, 16% had been referred with a 'clicky hip' in the absence of abnormal clinical examination or any other additional risk factor. Worryingly, this group included Graf 3 or 4 hips in six children. Given the terrible consequences of missed diagnoses and the relative difficulty in providing late treatment, here at 360, we would agree with the authors conclusion that this is an important indication for referral that should not be removed from the screening

pathway. The authors also make an important observation on how such pathways are applied and, with a diverse group of clinicians performing baby checks, any manoeuvre reducing the sensitivity of the pathway to detect pathology does seem unwise.

### Conscious sedation and fracture reduction X-ref

■ In many emergency departments there can be a strong reluctance to perform conscious sedation on paediatric patients who require manipulation of a displaced fracture. This is often due to an inability to provide the sedation safely, but there is also an argument that a further procedure is almost always required, leading to the reluctance to introduce what is seen as an unnecessary step. However, with inpatient beds and access to emergency operating space at a premium in many centres, any opportunity to safely and effectively intervene early would be welcome. This paper from **Boston, Massachusetts (USA)** examines the case mixture and outcomes in the children's emergency department

of a level I trauma centre over a one-year period.<sup>2</sup> Only patients presenting overnight were considered, where the treatment options were definitive manipulation under conscious sedation and discharge home, inpatient hospital admission, or discharge with a view to later admission at a satellite hospital. The authors identified 1298 fractures who were reviewed, and conscious sedation was undertaken on 386 patients, mainly including wrist fractures, both bone forearm fractures, and tib-fib fractures. All of these patients were then reviewed to establish instances where a change in plan was cast wedging or surgical procedures. The intervention rates for both bone forearm and wrist fractures were highest at 81% and 63%, respectively. At senior review, 3% of patients initially reduced required a change in management to surgical intervention. Overall, 53 fractures (14% of cases) lost alignment and required further intervention, with 33 requiring repeat surgery and 20 needing cast wedging. There were two cases that went on to malunion and five in which growth arrest occurred. This paper obviously does not tell us the degree of displacement of the initial injury and the manipulations were performed by a third-year orthopaedic resident, so it is not clear that all fractures required intervention at all. Furthermore, parent/guardian satisfaction was not recorded, but this is difficult to compare and value in relation to the alternative theoretical scenario of admission and operation. The argument that a procedure in the emergency department is distressing is surely outweighed by the distress of an inpatient admission and operating theatre attendance. However, given the low rates of reintervention that were required, conscious sedation and reduction in the emergency department does seem to be a worthwhile pursuit when considering the orthopaedic management alone and in appropriate centres where the procedure can be performed.

#### Lateral clavicle fractures in children and adolescents X-ref

■ It is tempting to extrapolate the treatment of adult injury patterns to the paediatric population, but in many cases this is inappropriate. Paediatric lateral clavicle fractures are one such case where the management in adults is frequently operative, but robust evidence for or against surgical intervention in the paediatric population is lacking. The matter becomes even less clear when the difficulties of growing bones, the scarcity of validated outcome measures, and the variation in professional opinion are considered. The studies that do exist often lack the number of cases required to draw firm conclusions. This group from **Bern**

(**Switzerland**) therefore sought to investigate and report on which treatment is best for these injuries by pooling their cases of lateral third paediatric fractures referred to their tertiary paediatric trauma centre.<sup>3</sup> The authors examined: the health-related quality-of-life outcomes of these patients, using the Paediatric Quality of Life Inventory (Peds-QL); whether the Peds-QL was associated with age at injury; and whether the fracture or its displacement had an effect on the Peds-QL. They were able to report on the outcomes of 69 patients over an 11-year period, all of whom were reviewed and sent a questionnaire including the Quick Disabilities of the Arm, Shoulder and Hand questionnaire (QuickDASH) and the Peds-QL. The minimum follow-up was two years and 56 patients responded, giving a follow-up rate of 81%. Only one case was treated operatively; in the conservatively treated cases, the mean QuickDASH was 1.2, the mean physical function score of the head to QLD was 97.8, and the mean psychosocial function score was 91.8. No statistically significant association could be identified between age at time of injury and outcome, nor between fracture pattern or displacement and outcome. There will obviously be a significant ceiling effects on the scores and the relatively low numbers involved increase the chance of a type II error. However, we would agree with the authors' conclusion that these cases invariably do well with conservative management, which should be the default. Strong evidence-based justification would be required to diverge from this position.

#### Anderson–Green growth-remaining graphs or White–Menelaus in the distal femoral and proximal tibial physes?

■ Ever since its introduction as a technique for managing leg-length discrepancies, the search has been on for the optimal method to determine the amount of growth remaining in the physes, therefore making the age of intervention or duration of treatment for physal fusion an essential factor. This paper from **Dallas, Texas (USA)** compared the accuracy of the Anderson–Green growth-remaining graphs, which are based on average growth per year  $\pm$  two standard deviations, and the White–Menelaus arithmetic method, which assumes a constant rate of growth per year until skeletal maturity, for the prediction of growth remaining.<sup>4</sup> The team retrospectively analyzed their own database of patients managed with epiphysodesis for lower leg-length discrepancy and included the healthy unoperated legs of all cases followed to skeletal maturity. They compared the observed and predicted growths using both methods for both skeletal and chronological ages.

Overall, 441 bones were included in 221 patients with an even male-female distribution and a range of ages from nine to 16.5 years at the time of surgery. Interestingly, the results showed no relationship between the length percentile of the segment at the time of the epiphysodesis, and the amount of growth that actually occurred. The growth in the distal femur and the proximal tibia was relatively constant, at 9 mm and 6 mm per year, respectively. The authors identified that for both methods, skeletal age was a better predictor of growth remaining than chronological age. Overall, the White–Menelaus method more accurately predicted the remaining growth than the Anderson–Green charts. The distribution of the growth resembled the Anderson–Green charts but the initial bone segment length was not predictive. This latter observation explains a possible source of error when using this method, and the findings of this study are certainly useful for those surgeons undertaking these procedures. In surgically induced growth arrest, timing is everything, and understanding what is likely to happen in the future is essential for establishing the best way forwards for each individual case.



#### Is percutaneous hamstring lengthening effective in children with cerebral palsy?

■ The treatment of crouch gait in cerebral palsy (CP) is a challenging field, and while extensive intervention is sometimes required, there is often an inherent advantage to percutaneous treatments that may allow for a more rapid rehabilitation and reduce the risks of loss of function and increased dependency. It is important to ensure, however,

that such treatments are not inferior to their traditional open counterparts. This paper from **Los Angeles, California (USA)** compared the clinical outcomes of 65 CP patients who underwent a traditional open hamstring lengthening surgery and 22 patients who underwent a percutaneous lengthening procedure.<sup>5</sup> Their work is strengthened from the usual comparative series, as patients underwent detailed gait lab kinematic analysis both pre- and postoperatively at a mean time of 30 months postsurgery, and this data was helpfully reported in the paper. The cases were performed over an 18-year period and the mean ages were similar between the groups at 8.5 and 8.3 years, respectively. A wide range of kinematic variables and static range of movement measurements were performed and compared between the groups. Both groups obtained a statistically significant decrease in knee flexion angle at initial contact, with a mean of 13° decrease in the open and 19° decrease in the percutaneous groups. A statistically significant increase in the maximum knee extension stance was also found for both groups, with a change of 8° in the open and 14° in the percutaneous groups. No significant differences were found between any of the kinematic variables and the postoperative changes in static range of movement were similar between the groups. No complications were observed in the percutaneous group, although the authors acknowledge that this is a risk inherent to this type of procedure. A 12% complication rate was seen in the open group. This study does suffer from being a retrospective single surgeon series where the older technique was performed earlier in the series and the newer more recently, where the learning curve would be flatter. Furthermore, the patients treated with the open procedure usually had a long leg cast for three to four weeks postoperatively, whereas the percutaneous release patients did not. Nevertheless, the potential utility of a percutaneous release is demonstrated, with further investigation being required to demonstrate superiority.

### **Emergency department closed reduction versus in situ splinting in the treatment of paediatric supracondylar humerus fractures**

■ Having reviewed one paper considering the closed manipulation of paediatric fractures in the emergency department, we continue the theme in this issue of 360 by including this paper on the treatment of Gartland type II or III supracondylar humeral fractures using this method. This team from **New York, New York (USA)** reviewed non-polytrauma patients, all less than ten years old and

presenting with a Gartland type II or III fracture.<sup>6</sup> All of the patients, as one might expect, had no vascular compromise. The series was drawn from a retrospective period and all presented to a single hospital over an eight-year period. Treatment varied, in that patients were treated either with or without reduction in the emergency department. For the first four years, these patients were treated with closed reduction and splinting under conscious sedation in the emergency department, and were then admitted for surgical management. In the second four-year period, the patients were splinted without reduction and admitted to hospital. In all, 157 patients were included and a subgroup of 89 were treated with reduction in the emergency department. Demographically, the patient groups were very similar, with a median age of 4.7 and 5.4 years, respectively. In the closed reduction group, 62% of injuries were Gartland III compared with 53% in the no closed reduction group. Surgical parameters, such as time to surgery and median theatre time, as well as median length of stay and the number of Kirschner wires used for closed pinning, were recorded. In the cohort of patients managed without emergency department reduction, there was a lower mean delay to surgery, presumably because their priority was relatively downgraded. They also had a shorter length of stay in hospital, at a mean of 34 versus 40 hours. No significant differences were found between the groups in terms of treatment or complications. In unstable injuries, which would still require surgical management regardless of the position achieved in the emergency department, there was no utility in emergency department manipulation, which adds risk and distress for no perceived benefit.

### **Curative-intent radiotherapy for paediatric osteosarcoma: the St. Jude experience X-ref**

■ Surgical resection and chemotherapy are the treatments of choice for osteosarcoma, but a number of factors may limit the applicability of resection, including difficult to access surgical sites, or those sites where a resection may create unacceptable levels of morbidity for the patient. Radiotherapy has traditionally had a low profile in the treatment of what are usually radioresistant lesions. However, there have been some reports suggesting that patients may benefit from improved survival rates for nonresectable tumours. In the context of an uncertain, but possibly limited, role for radiotherapy in osteosarcoma, this group from **Memphis, Tennessee (USA)** present their experience.<sup>7</sup> All patients were managed with curative-intent radiotherapy and the authors examined the outcomes of

the disease, failures and predictors of failure, and side-effect profiles. In all, 28 paediatric patients who were treated with curative-intent radiotherapy at a median dose of 60g and chemotherapy with or without operative resection, over a 27-year period, were retrospectively identified. Gray's method was used to estimate the cumulative incidence of local failure. Statistical methods, including Cox's proportional hazards and competing risk regression models, were used to determine the overall predictors of outcome. The median age of the patients was 13 years, with a slight preponderance of male patients. A median follow-up of 18 months for the entire cohort and 99 months in living patients was achieved. Nine patients (32%) developed local failure and eight of these presented with Stage IVa disease. Four of these patients received radiotherapy primarily and five were treated at the time of a recurrence of their disease, with eight developing distant metastases and subsequently dying. There were 16 potential radiotherapy-associated toxicities identified in 11 of the patients; two of these were significant grade 3 toxicities, including a sensorineural hearing loss and a growth arrest of the breast. Five-year survival was 42.6% for the entire cohort of patients. Although no clinicopathological features were identified to be associated with local failure, the authors did establish that a lack of chemotherapy or the presence of metastases at the time of radiotherapy was an independent predictor of decreased overall survival. In those patients treated at their initial presentation, the local failure of treatment and competing risk of death rate was 25%; the overall survival rate was 54.6%. Therefore, a local tumour control rate of 75% was achieved in patients with primary disease. This is important, as the results are comparable to studies of adult patients, which seems intuitive but is not always the case when attempting to extrapolate adult results. The final caveat is that 22 of the 28 patients also had surgery, which obviously will bias the efficacy of the radiotherapy; however, we would certainly acknowledge the difficulty in studying this rare disease and commend the authors on a well-written and worthwhile paper.

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## Research

**X-ref** For other Roundups in this issue that cross-reference with Research see: *Hip & Pelvis Roundup 6; Knee Roundup 8; Wrist & Hand Roundups 5 & 6.*

### Detection of total hip prostheses at airport security checkpoints X-ref

■ A common question that pervades all branches of orthopaedic surgery is whether implants will be detected by airport metal detectors. Although this often seems an irrelevant query, it is one of the more practical reminders that patients have of their surgery. To help give a straightforward answer, a team from **Tokyo (Japan)** sought to establish if implant detection rates varied between total hip arthroplasty implants and materials using airport metal detectors.<sup>1</sup> The group identified a retrospective unselected series of 1684 patients who had undergone hip arthroplasty, and questioned them as to their travel activities and security experiences at airports. Of the group, 671 had flown in the intervening period, with 346 reporting implant detection. Patients with unilateral arthroplasties on domestic flights had the lowest detection rate of 23%, whereas bilateral arthroplasty on international flights showed a detection rate of 86%. Subsequent logistic regression showed that cup size and implant material were the most relevant variables on domestic flights, and cup size alone was the most relevant variable for international flights. Although a convincing argument could be made that the detection rate is high in large implants and bilateral surgery cases, it is surprising that the detection rates differ between domestic and international flights, and it is possible that there is a sample size problem here.

### Saline solution lavage and reaspiration in infected total joints X-ref

■ Making the diagnosis of septic arthritis is critical, both in native and prosthetic joints. A plain blind aspirate is usually all that is required. However, particularly in the case of prosthetic joints, this is sometimes not enough. Many surgeons advocate increasing diagnostic accuracy,

particularly of those patients with a 'dry tap', through lavage of the joint. A volume of sterile saline is injected into the joint and reaspirated to get a sample for culture and sensitivity. Although increasingly commonly performed, data to support the practice are relatively scarce. In this study from **Beijing (China)**, the authors sought to evaluate the impact of the technique on diagnostic accuracy for joint infection in both prosthetic and native joints.<sup>2</sup> The authors based the findings of their study on previously collected data from 268 aspirations performed in a single unit by a single surgeon. If less than 1 ml was aspirated, then 10 ml of saline was infiltrated into the joint, which was then reaspirated. The fluid was subsequently placed into blood culture bottles and inoculated for 14 days. Saline lavage was required in 47 prosthetic and 35 native suspected joint infections, while aspiration alone was used in 99 prosthetic and 105 native joints in this series. Overall, 29% of suspected knee infections and 42% of suspected hip infections underwent lavage. The sensitivity, specificity, positive predictive value, and negative predictive value of culture were 0.795, 0.957, 0.951, and 0.817, respectively. For 'dry tap' cases necessitating lavage, the values were 0.851, 0.857, 0.889, and 0.811, respectively, suggesting that the overall diagnostic accuracy of saline lavage is comparable to a simple tap. Although the results seem impressive, this study utilized a blood culture system to improve the culture yield. While caution should be applied when using lavage to obtain a sample, since a cell count cannot be obtained, surgeons should consider using a blood culture system when attempting to culture a diluted aspirate from a prosthetic joint. It is not quite clear to us here at 360 how the eventual diagnosis of infection was reached and, although a modified version of the Musculoskeletal Infection Society criteria was utilized, the study's inclusion of the test being evaluated in the diagnostic criteria for the endpoint inflates the apparent diagnostic accuracy. This explains the specificity of 0.96 reported for positive culture from plain aspiration.

### Enhancement of the chondrogenic differentiation by ghrelin X-ref

■ One of the modern 'holy grails' of surgical practice is harnessing the power of biological regeneration and applying this to a large range of pathologies. *In vitro* cell lineages have been responsible for some of the most fundamental breakthroughs in modern surgical practice, but a current bar to their success is the difficulty in ensuring appropriate cellular differentiation from the stem cells. In an effort to further the research into these cell lines, a study group from **Beijing (China)** have conducted an investigation looking at improving chondrocytic differentiation of mesenchymal cells through enhancing the effect of transforming growth factor (TGF)- $\beta$  using ghrelin, measured using gene expression analysis, sulphated glycosaminoglycan and collagen assessment, and histological staining.<sup>3</sup> In this animal study, rats with cartilage injury were used as the *in vivo* models, with cultivated cell lines used *in vitro*. Following the administration of TGF- $\beta$  with ghrelin in the injured rats, chondrocytic regeneration was found to be much improved when compared with TGF- $\beta$  alone after mesenchymal stem cell implantation. When used on cell lines, ghrelin increased the expression of SOX9, aggrecan, and collagen type II, increased the synthesis of sulphated glycosaminoglycan and collagen, and enhanced the phosphorylation of DNA (cytosine-5)-methyltransferase 3A and extracellular signal-regulated kinases 1 and 2. Ghrelin seems likely to improve chondrocyte differentiation protocols and has laid the groundwork for an investigation of the multiple factors involved in chondrocyte differentiation. There is clearly quite a broad scope for improvement of the cellular quality on the 'benchtop' prior to use of these differentiated cell lines in surgical practice. We would also comment that there is potentially huge scope for use of ongoing biological support for cellular therapies after implantation rather than the current approach of simple carriers, such as a collagen fleece.