X-ref ***For other Roundups in this issue that cross-reference with Knee see: Hip & Pelvis Roundups 1 & 2; Sports Roundups 1 & 3; Foot & Ankle Roundup 6; Research Roundup 6.***

Prosthetic joint infection in total knee arthroplasty

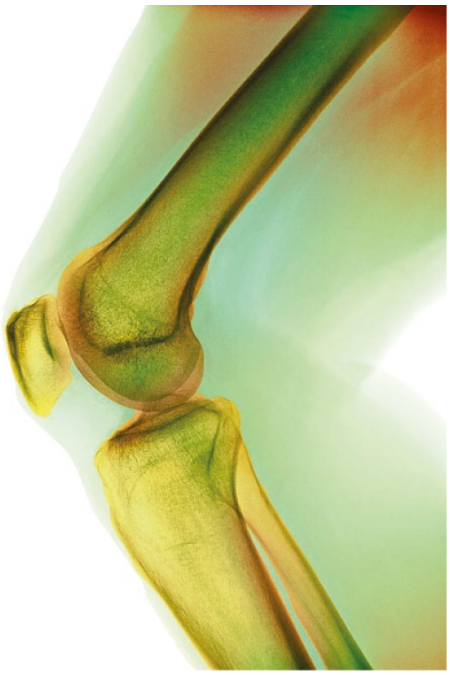
As the treatment for prosthetic joint infections (PJIs) evolves, one-stage exchange arthroplasty, which used to be more common in Europe, has gained popularity on the other side of the pond. There is still a lot of discussion about the best way to deal with infected arthroplasties, with a number of competing strategies regularly receiving column inches in the orthopaedic literature. In an interesting paper from **Detroit, Michigan (USA),** the authors used a modelling study approach to re-evaluate the decision-making process associated with one and two stage revision arthroplasty for infected total knee arthroplasties (TKA).[1] The surgical team note that, while two-stage revision is considered the benchmark for treatment of infection, a single-stage revision has lower costs, lower mortality, and better quality of life. The authors designed a decision analysis to determine the optimal decision for the management of PJI following TKA, to establish what the best current treatment strategies are for treatment of infected TKA. The study focused on two decision trees that were constructed based on currently reported outcomes in the literature. The expected-value decision tree, using a Monte Carlo simulation, was set up to estimate the quality-adjusted life-years and costs associated with one-stage and two-stage revision for all pathogens, and also for difficult-to-treat infections such as methicillin-resistant *Staphylococcus aureus* (MRSA). The outcomes essentially favoured one-stage revision in 85% and 69% of the trials for the two decision trees. A further sensitivity analysis established that the outcomes of the decision tree were driven by reinfection and one-year mortality rates. While two-stage revision remains the benchmark treatment, this paper (and others) suggest that surgeons really should consider implementing one-stage exchange arthroplasty in PJI treatment in and around the knee, particularly in non-resistant bacteria scenarios.

Full-thickness cartilage defects and total knee arthroplasty

The indications for performing total knee arthroplasty (TKA) when seeing patients in clinics are generally driven not by investigation, but by quality-of-life metrics (including activities of daily living), exhaustion of conservative therapy, and radiographs indicating end-stage degenerative joint disease. However, despite clinicians' almost-universal functional approach, patients do present to clinic with full-thickness cartilage defects as detected by MRI. In the absence of symptoms, these patients are usually (and quite sensibly) told to wait for the symptoms to worsen, prior to any form of arthroplasty intervention. The question asked by these authors from **Columbus, Ohio (USA)** is: what is the significance of full-thickness cartilage defects in an otherwise 'coping' individual who is functionally independent?[2] The authors based their findings on a large cohort of 1319 adults, all of whom were taking part in the 'Osteoarthritis Initiative', a prospective multicentre study with median nine-year follow-up data. Those with severe osteoarthritis (OA) (Kellgren-Lawrence grade 4) were excluded. The overall risks of conversion to TKA due to defect presence and size, as well as OA grade, was determined with Cox proportional-hazards modelling. Potential confounders that were controlled for included age, sex, race, weight, knee alignment, symptom severity, quality-of-life scores, and activity level. Within the main cohort, 37.6% of patients (n = 496) presented with full-thickness defects in the knee. In terms of year-on-year incidence, there was a 2.15% annual rate of conversion for those with full-thickness defects, compared with 0.57% for those without. The adjusted analysis suggests that the presence of a full-thickness defect increased the risk of TKA, regardless of OA grade, with ⩾ 2 cm defects having a hazard ratio (HR) of 5.27, and a HR of 2.65 for smaller defects. While these findings do not support the idea that patients with full-thickness defects should have a TKA, even if they are asymptomatic, patients with large defects should be kept under a watchful eye, rather than simply discharged.

Is duloxetine the answer for central sensitization

In the age of the opioid crisis, utilizing other medications for pain relief can be beneficial for our patients, and evaluating alternative treatment strategies is central to achieving a 'good result' following total knee arthroplasty (TKA). There is ample evidence that patients have a poorer clinical result when they are faced with ongoing pain. Estimates of pain post-TKA vary; however, there is plenty of evidence in the literature suggesting ongoing pain in between 10% and 20% of patients following TKA. At least some of this pain is due to central sensitization and abnormal pain pathways. Treatment strategies are remarkably rudimentary in many institutions, and patients are simply given ever-increasing opioid dosages, which sadly often results in addiction and no improvement in quality of life. One potential approach is to deal with the central sensitization, and there is a small volume of evidence that duloxetine (Cymbalta), which has historically been used for psychiatric patients, may be beneficial for patients with aberrant central pain pathways, including those TKA patients with central sensitization. Duloxetine is a selective serotonin norepinephrine reuptake inhibitor (SNRI) that has been shown to be able to ameliorate the pain associated with central sensitization. This drug may become useful in our multimodal pain regimens, although we have to be concerned with combining duloxetine and gabapentin. Researchers from **Seoul (South Korea)** report their own prospective randomized trial investigating the potential benefits of duloxetine as an intervention to treat those patients suffering with central sensitization and abnormal pain sensations following TKA.[3] This was a relatively small study, with 464 patients screened and 80 included as patients with signs and symptoms of central sensitization. Patients were randomly allocated either to receive duloxetine (30 mg, one day before surgery and for six weeks after surgery) or to the control group (no duloxetine). The outcomes were assessed during the 12-week postoperative period. The reported outcome measures include the Brief Pain Inventory, the 36-Item Short-Form Health Survey questionnaire, the Measure of Intermittent and Constant Osteoarthritis Pain, and the Hamilton Depression Scale. The usual secondary outcome measures, including adverse events, were also assessed. There were significantly better outcomes in terms of pain levels at all timepoints between two and 12 weeks favouring the duloxetine group; this was also reflected in superior emotional and physical function scores. This finding is clearly in need of further investigation. Pain relief following TKA is crucial to getting a good outcome, which is notoriously difficult to achieve in sensitized patients. The authors of this study have dangled the attractive proposition of some better pain control.



Platelet-rich plasma *versus* hyaluronic acid injections for knee arthritis

There has been considerable interest in using platelet-derived growth factors and other blood-derived factors to delay the progression of degenerative diseases, including osteoarthritis. The advocates for such an intervention argue that platelet-rich plasma (PRP) is able to modulate the intra-articular environment to reduce inflammation and stimulate the regeneration of cartilage, synovium, and menisci. There have been some supportive studies of this technique, which has led to it becoming a relatively common procedure in the outpatient setting as an alternative to more traditional outpatient interventions, such as hyaluronic acid (HA) and corticosteroids. While there have been previous randomized controlled trials comparing PRP with HA, these have all had a relatively short follow-up. The authors of this study from **Bologna (Italy)** argued that a longer evaluation might suggest a difference between HA and PRP.[4] A total of 192 patients were randomized either into a group that received three-weekly intra-articular injections of leucocyte-rich PRP, or into a group that received three-weekly injections of high-molecular-weight HA. To ensure that the study was blinded, all patients underwent blood sampling to obtain autologous PRP, which was then only used in the PRP group. The syringe was then covered to prevent the patients from identifying what substance was being injected into their knee. The International Knee Documentation Committee (IKDC) score, EuroQol visual analogue scale (EQ-VAS) score, and sport activity level assessed by the Tegener score were measured. All of these measures significantly improved and remained stable for up to 24 months post-injection in the PRP group, with a subsequent tail-off. Of note, the patients in the PRP group were significantly younger on average than those in the HA group. The HA group also saw a statistically significant increase in the IKDC score and the Tegener score over 24 months before it started to reduce. However, there was no improvement in the EQ-VAS score up to 24 months following injection, and this reduced to lower values than the preoperative baseline score. While both treatments were effective in improving patients' symptoms, the authors could not find any benefit of one treatment over the other. Both had very similar effects. The median duration of beneficial effect was 12 months for the PRP group and nine months for the HA group, but this was not statistically significant. The HA group did see a higher rate of reintervention, with either a new injection or a surgical intervention within 24 months of the injection, which was statistically significant. Some have suggested that utilizing more of a biological approach, such as PRP, may yield longer-term benefits, thus justifying its significantly higher cost. However, the findings of this study did not suggest that PRP had any significant clinical advantage (based on clinical outcome scores) over HA, which attempts to provide benefit by viscosupplementation. A slightly concerning feature was that patients in the PRP group were significantly younger than the HA group, despite randomization. This may explain why more patients in the HA group had a further intervention following injection, as a younger patient may elect to soldier on, rather than having a further procedure such as surgery. In addition, the blinding was lost at one year, which may have inadvertently affected the results at subsequent follow-ups. Readers should be aware of this study, as we suspect it may be quoted by those who support the use of PRP and those who do not. While there may be no superiority with using PRP compared with HA, it is, at the very least, comparable. However, be wary if others argue that it reduces the risk of reintervention, as the two groups were probably not comparable, as suggested by the statistically significant difference in age between the two groups. Given that the comparison here is with HA, which itself is a contentious treatment, and is likely to have little benefit over physiotherapy alone, there is definitely some thought needed regarding how to properly contextualize these findings within the rest of the literature. More long-term randomized controlled trials are needed to definitively solve this issue.

High tibial osteotomy: not so good in older females?

Over the past 50 years, high tibial osteotomy (HTO) has waxed and waned in popularity, but recently, with increasing interest in joint-preserving techniques, it is undergoing somewhat of a renaissance. HTO is traditionally thought to benefit younger, more active patients with a symptomatic medial compartment osteoarthritis and a varus malalignment. In these patients, the aim of the HTO is to restore – or even slightly overcorrect – the coronal alignment, in order to redistribute the mechanical axis of the lower limb through the knee to the centre or lateral compartment. HTO may delay the need for an arthroplasty, which has shown disappointing outcomes in younger patients. The difficulty is in deciding which patients will benefit, as enthusiasm for this technique currently outweighs the evidence in the literature. It is for this reason that, here at *360*, we were so pleased to see this series from **Edinburgh (UK),** which goes some way to filling this evidence gap.[5] In their series, a total of 111 patients with a mean age of 45 years (18 to 68) underwent an opening HTO for isolated medial compartment osteoarthritis with an overall mean follow-up of 12 years (6 to 21). A total of 40 patients (36%) were converted to a TKA at a mean follow-up of 6.3 years. There was a five-year survival rate of 84%, a ten-year survival rate of 65%, and a 15-year survival rate of 55%. These rates are in line with both accepted practice and those published elsewhere. Independent risk factors for failure were found to be older patients and female sex. Patients older than or equal to 47 years old were associated with a statistically significant increase in risk for failure. For each additional year, there was a 7% increased risk for failure, and women were more than twice as likely to undergo conversion a TKA. The conclusions drawn from this large study can help inform discussions regarding the clinical management of isolated medial compartment in the younger patient. Much has been published on the outcomes of TKA in the younger patient, with high revision rates and failure to meet the high expectations of the younger patient population of particular importance. HTO can be a viable and useful option in managing this particular patient group, and is best performed in centres with the necessary surgical expertise, but also in those centres that are experienced in careful patient selection.

Prosthesis, polyethylene, and 336 997 prostheses

A major focus in commercial research and innovation is the development and refinement

of implants. There are few procedures as successful in terms of improving patients' lives, and with such a great health-economic profile, as total hip and knee arthroplasties. However, all of these prostheses have a limited life expectancy and there is a rising and ever-present revision burden. As the joint registries are starting to come of age, reporting patients in their hundreds of thousands with longer and longer follow-up, there is more and more that can be done with the data in terms of unpicking what is, and what is not, successful. This registry review from **Adelaide (Australia)** is typical of the more subtle analyses that are now available as a result of this increase in data.[6] The authors of this study reviewed the outcomes from the Australian Joint Registry (AJR) with the aim of establishing the overall effect of prosthetic design features on the revision risk for infection in total knee arthroplasty. There is little known about joint arthroplasty design and polyethylene type with relation to infection, despite the public health burden of infection in joint arthroplasty. The authors queried the AJR and set out to establish the overall infection rate when knee arthroplasty designs were grouped into four different cohorts based on component design: minimally stabilized total knee prostheses with crosslinked polyethylene (XLPE); minimally stabilized total knee prostheses with non-crosslinked polyethylene (NXLPE); posterior-stabilized total knee prostheses with XLPE; and posterior-stabilized total knee prostheses with NXLPE. The authors excluded early infection (within six months) with the rationale being that this would help to reduce potential confounders. The authors also adjusted for age, sex, and antibiotic cement, but did not adjust for patient comorbidities. Overall, 336 997 primary total knee prostheses were included, of which 1651 (0.49%) underwent revision for prosthetic joint infection. The results reported here are a little confusing. The authors established that the lowest rate of infection was for minimally stabilized total knee prostheses with XLPE bearing surfaces. When NXPLE was used with the same implant types, the revision risk for infection was 25% higher. With regard to implant type, the revision rate was 89% higher for posterior-stabilized total knee prostheses with XLPE *versus* the minimally stabilized total knee prostheses with XLPE bearing surfaces. This jumps again to 102% higher for posterior-stabilized total knee prostheses with NXLPE. The authors went on to examine the effects of XPLE on posterior-stabilized total knee prostheses and found that the revision risk for infection was not significantly different between the two. While the headline result seems reasonable – that minimally stabilized total knee prostheses in this observational registry series had the lowest infection rate – it is somewhat difficult to draw any firm conclusions about causation, as there are conflicting observations presented here.

Metal allergy and unicondylar knee arthroplasty

There are significant difficulties associated with allergies and intolerances. Some patients may report a drug allergy when they are actually referring to recognized side effects, may misidentify allergies (many self-reported latex allergy sufferers are actually allergic to the talcum powder used in rubber gloves), or may describe contact dermatitis as allergies. This can cause confusion when, for example, considering the use of metallic implants for those who suffer from nickel-contact allergy. The authors of this non-designer study from **Heidelberg (Germany)** evaluated the clinical outcome and survival rates of unicondylar knee arthroplasty (UKA) using a standard cobalt-chromium (CoCr) alloy in a cohort of patients reporting signs of a hypersensitivity to metal.[7] The authors identified a cohort or 82 patients from a population of 1737 patients, all of whom were suitable for this study by virtue of reporting a cutaneous metal hypersensitivity to one or more of cobalt, chromium, or nickel. The outcomes that were reported by the authors of this study include possible signs of hypersensitivity and short-term implant survival at a minimum follow-up of 1.5 years. The outcomes were available to an average follow-up of three years. There were no reports of systemic symptoms or hypersensitivity to the standard CoCr implants in that follow-up period. There was only a single revision due to a periprosthetic fracture, which was not attributed to any form of sensitivity response. This paper is important, as it is one of the only papers to establish the risk of revision with standard CoCr prosthesis implanted into individuals with a self-reported sensitivity. It would appear, based on these results (and given the usual caveats for small case series), that it is safe to continue to use standard prosthesis in those patients with self-reported allergies.

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