ROUNDUP360

Knee

For other Roundups in this issue that cross-reference with Knee see: Hip & Pelvis Roundup 8; Trauma Roundup 10; Oncology Roundup 2; and Research Roundups 2, 5 and 6.

National guidance on arthroplasty thromboprophylaxis is effective

x-ref Hip & Pelvis

Reaching consensus on the simple matter of who should receive thromboprophylaxis, for how long, and in what form, has occupied the executive committees of national orthopaedic societies and specialist hip and knee surgery professional bodies for the best part of the past decade. Thromboembolic disease is a common occurrence following total joint replacement, and so prophylaxis is recommended by most professional societies in an attempt to reduce the morbidity and mortality associated with venous thromboembolic events (VTE). The North Americans reached their first consensus statement in 2009, with the AAOS publishing guidelines for VTE prophylaxis in patients undergoing total hip or total knee replacement. This guidance differed slightly from the previously widely adopted American College of Chest Physicians guidelines (ACCP), however, both were aimed fairly and squarely at reducing the incidence of post-operative pulmonary embolism. Guidelines are a synthesis of current research and usually adopted in a blanket manner once published, so it is refreshing to see researchers from **Farmington (USA)** aiming to assess the efficacy of the first-generation AAOS guidelines in the prevention of VTE.[1] The researchers focused on the incidence of clinically relevant VTE events in their single institution cohort of 3289 consecutive patients. Their prospective cohort study included all patients who underwent either a total knee or total hip replacement and were prescribed prophylaxis according to the first-generation AAOS guidelines. All patients were mobilised on post-operative day one and the clinical teams used pneumatic foot-pump compression devices throughout their hospital stay. In this cohort, the surgical teams observed 36 VTE events, all of which were diagnosed by Doppler ultrasound or CT angiography within 90 days post-operatively. In terms of risk factors, a history of DVT and long-term warfarin use were significantly associated with post-operative complications. An increased risk of VTE was also observed in patients undergoing total hip replacement when compared with total knee replacement (1.56% vs 0.46%). The authors observed that implementation of the first-generation AAOS guidelines resulted in a 90-day incidence of VTE of 1.1% at their institution. This is an important benchmark paper. It is impossible to reduce the incidence of VTE to 0%, and any thromboprophylaxis regime needs to be implemented as a balance of risks and benefits. This paper provides a helpful yardstick for future revisions to the AAOS guidance and as a tool against which alternate regimes can be measured.

Unicompartmental knee replacement has the edge in terms of short-term complications

The longevity of unicompartmental knee replacements (UKRs) has been called into question recently, with a number of reports from the major joint replacement registries making the argument that with significantly poorer long-term outcomes (in terms of revision) in patients undergoing arthroplasty, there is an increasingly narrow range of indications for unicompartmental joint replacements. The counter-argument is equally forcefully made that longevity is only one marker of success in arthroplasty, and that with the potential for higher satisfaction rates, functional scores and lower complications, there is still very much a broad window of indications for UKR. There is a large number of studies investigating the use of UKR as an alternative treatment for knee osteoarthritis in a selected group of patients. While some studies report improved range of movement and quicker recovery with a UKR, the short-term complication rates have not been well described when compared with the benchmark of total knee replacement (TKR). Researchers in **Iowa City (USA)** focused on complications for their study rather than the more usually evaluated implant longevity or clinical outcomes. Using a benchmark of complications occurring within 30 days of surgery, their study utilised the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database to address the question, 'which arthroplasty method has a lower short-term complication rate?'[2] Large database studies such as this require clever statistical methodology, and the team used a propensity score-matching method to allow comparison between patients to compensate for the selection bias associated with such database studies. The ACS NSQIP dataset included 29 333 patients who were identified by CPT code (consisting of 27 745 TKRs and 1588 UKRs). Using validated UKR patients, these were matched with a subset of TKR patients. After adequate matching, the overall complication rate did not differ significantly between TKRs (5.29%) and UKRs (4.16%); however, patients undergoing a TKR had a significantly higher rate of thromboembolic events, operative time, and increased length of hospital stay. In short, although the short-term 30-day complication rate was similar, the UKR group did have a slight edge.

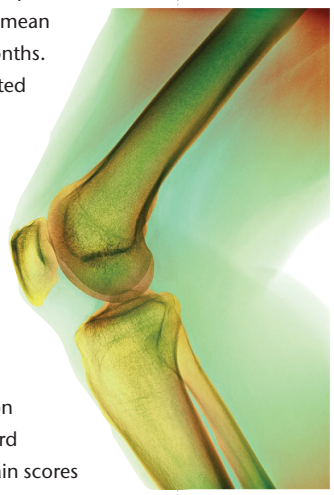
Stiff knees, timing and manipulation

Stiffness following a total knee replacement (TKR) can result in poorer than expected functional outcomes and patient satisfaction levels. When sufficiently restricted to affect function (normally taken to be flexion of less than 90°), patients are usually offered manipulation under anaesthesia (MUA) as an initial intervention. A number of previous studies have examined the functional

results after an MUA, however, the optimal timing is still very much debated and likely to have a significant effect on functional outcomes. This study from **Baltimore (USA)** aimed to answer some of the unresolved questions concerning the optimal timing of MUA following TKR.[3] The authors designed and conducted a retrospective review of 2128 TKRs performed at their institution, of which 144 required MUAs between 2005 and 2011. This study compares the outcomes of patients who had MUAs early (less than 12 weeks after TKR) and late (greater than 12 weeks after TKR). Although an arbitrary cutoff (the cynic in us, here at *360*, wonders if authors in these types of dichotomous outcome studies select their outcome thresholds to 'optimise' their results), the authors did establish that patients who underwent an MUA in the first 12 weeks following a TKR had significantly better flexion, overall range of motion, and Knee Society Scores than those that underwent an MUA 12 weeks, or more, post-operatively. The research team advise that in light of these findings, knee surgeons should have a low threshold to perform manipulations in the first 12 weeks post-operatively to maximise range of movement (ROM) and clinical outcomes. To strengthen their conclusions, the authors point out that in their series, at least, performing an MUA greater than 26 weeks post-operatively resulted in the poorest eventual ROM. Thus, the authors suggest performing an MUA six to 12 weeks post-operatively to maximise ROM and clinical outcomes. Patients should be counselled that an MUA is a time-sensitive decision and outcomes worsen after 12 weeks after surgery.

Neuropathic pain and total knee replacement

■ Approximately 20% of patients are dissatisfied after total knee replacement (TKR), and frequently persistent pain is a contributing factor to patient dissatisfaction. Neuropathic pain is a real, but arguably underappreciated, source of pain after TKR. Researchers from the knee unit in **Exeter (UK)** set out to establish what the incidence of neuropathic pain is, and, most crucially from our perspective here at *360*, what the longitudinal natural history of neuropathic pain is.[4] The research team designed this study with the aim of assessing pain levels post-operatively after TKR and at specific time intervals to determine if risk factors exist for the development of neuropathic pain. In a carefully designed and followed-up prospective study, the research team identified a cohort of 96 patients who underwent a primary TKR at a single institution and evaluated their pain levels at eight specific time points post-operatively. Follow-up was continued out to a mean follow-up of 46 months. As would be expected with a study of this nature, the mean pre-operative VAS score improved significantly at all time periods following surgery. Outcomes were established using a combination of functional (Oxford Knee Score) and pain scores (VAS for pain; painDETECT score for neuropathic pain), and depressive indices (Hospital Anxiety and Depression score). At the initial six-week evaluation, around one in four (n = 23/85, 27%) experienced possible symptoms of neuropathic pain and 8% were likely to have neuropathic pain. The incidence of neuropathic pain had fallen by three months to 17% with possible neuropathic pain (n = 16/82) and just two patients with likely neuropathic pain. The surgical team undertook a secondary clinical review and none of their patients with persistent pain had an obvious cause for this (such as malalignment or incorrect sizing). While the authors established a significant decrease in pain after TKR, some of their patients experienced persistent post-operative pain that cannot be predicted by pre-operative risk factors. This study is consistent with others in the literature in identifing a subset of patients (20% to 30%) who experience persistent post-operative pain. What is new is the characterisation of this as neuropathic pain, and the finding that this can be expected to peak between six weeks and three months post-operatively.



Synovial fluid α-defensin and CRP: a new gold standard in joint infection diagnosis?

x-ref Hip & Pelvis

■ The holy grail of arthroplasty diagnostics is the search for a reliable, repeatable, sensitive and specific test for periprosthetic joint infection (PJI). Current diagnostic tests are either highly sensitive but not very specific (biochemical markers e.g. CRP, ESR and PCR of aspirates), or highly specific but not very sensitive (e.g. culture of intra-operative samples and frozen sections). This can often result in a diagnostic conundrum, and the addition of imaging rarely helps with nuclear medicine techniques often 'hot' for years post-operatively in normal joints, and scatter, making MRI or CT almost useless. Researchers in **Philadelphia (USA)** have examined the use of a combination technique using both CRP and a newly emerging marker, that of synovial fluid α-defensin.[5] The α-defensin group of peptides is synthesised in response to most microbes, including bacteria, funghi and enveloped viruses. Also known as human neutrophil peptides, they have become the target of much research as a potential marker for a range of diseases. Synovial fluid α-defensin has emerged as a new biomarker for infection, but its use for accurately diagnosing a PJI, both alone and in combination with other tests, has not been studied. The authors of this prospective study included 149 synovial aspirates; 112 from patients with an aseptic cause of pain and 37 patients with established infection. The study was designed to establish the diagnostic accuracy of α-defensin in combination with CRP. The combination of synovial fluid α-defensin and CRP tests demonstrated a sensitivity of 97% and a specificity of 100% for diagnosing joint infection, while the synovial α-defensin test alone was 97% sensitive and 96% specific. One of the strengths of this paper is the heterogeneity of the cohort, including patients with wear, instability, and metallosis. The population included 23% of patients with a documented history of systemic inflammatory disease and 9% were taking immunomodulatory drugs and/or corticosteroids. In the infection subgroup, 27% were on antibiotic treatment at the time of the aspiration. Taking this into consideration, the sensitivity and specificity of α-defensin on its own is impressive. In combination with a CRP test the false positives yielded with α-defensin were reversed, leaving a highly reliable test for the diagnosis of infection that really should be considered for all patients where there is any shred of doubt about periprosthetic infection. We would inject a small amount of *360* caution into this study, as there is some conflict of interest - the authors are the owners of the company who perform the test. However, the reported combination of synovial fluid α-defensin and CRP tests represents an impressively accurate way to diagnose (or rule out) joint infection in all patients, including those patients with systemic inflammatory disease and patients on antibiotics.

How to assess anterior knee pain?

While the goal of total knee replacement (TKR) is essentially to decrease pain, thereby maintaining function, a well described subgroup of patients do not have the desired resolution of symptoms after TKR and report ongoing and persistent pain. While the Knee Injury and Osteoarthritis Outcome Score (KOOS) and Visual Analogue Score (VAS) are commonly used instruments for patient-reported pain levels, the difficulty is that these scores were not designed nor validated for assessing persistent post-operative pain. It is therefore reasonable to suppose that the instrument used for measurement may bias the reporting of results. In this retrospective study, authors from **Lund (Sweden)** undertook a review of patients from the Swedish Arthroplasty Register with the aim of comparing the KOOS and VAS outcome instruments from the point of view of post-operative pain.[6] Their study included the results of 2123 patients who underwent a primary TKR for arthritis, all of whom reported no requirement for pain relief or worse pain one year post-operatively. Pain levels were patient-reported by the VAS and KOOS pre-operatively and one year post-operatively. At one year post-operatively, 105 (4.9%) and 165 (7.8%) patients reported worse or no change in pain on the KOOS and VAS, respectively. Of the 220 patients who reported their global symptoms had increased or were unchanged in terms of pain, 50 (23%) reported increased or unchanged pain on both the VAS and KOOS. The authors found that patients who experienced no pain relief on either pain scale tended to have high anxiety/depression scores pre-operatively. In addition, patients classified as a Charnley category C were at an increased risk for poor pain relief outcomes according to VAS. In this cohort, using the VAS to assess pain resulted in twice the number of poor pain outcomes when compared with using the KOOS to assess pain (55 vs 115 patients, respectively). The authors suggest that when considering pain assessment following TKR, the level of pre-operative pain should be taken into account and pain relief recorded may vary depending on the instrument used to measure pain. Comparing pain relief post-operatively is highly subject to pre-operative pain levels; in fact, the authors found that patients who reported no pain relief requirement post-operatively tended to have low pain levels pre-operatively. This represents an important consideration when designing, reading and reporting studies.

Where is the evidence? Five new implants under the spotlight

x-ref Hip & Pelvis

History, like surgery, is said to repeat itself, and particularly with regards to its mistakes. The use of exciting shiny new implants can be extremely tempting to the orthopaedic surgeon, but the pages of journals past are littered with examples of the finest intent, but poorest outcomes from new implants. The most recent high profile examples would surely include the Capitol hip and ASR, both of which have met the orthopaedic and general mainstream press with unacceptably high failure rates in the last ten years. It was therefore somewhat disappointing for us, here at *360*, to read a recent article in the BMJ from surgeons in **Leiden (The Netherlands)** evaluating the evidence for both safety and efficacy of five recent new joint replacements.[7] The surgical teams undertook a review of the major available data sources and registries to evaluate the available public data for three innovations in total hip replacement (ceramic-on-ceramic bearings, modular femoral necks, and uncemented monoblock cups) and two in total knee replacement (high flexion knee replacement and gender-specific knee replacement). The review teams' comprehensive search yielded 10 557 search hits, of which 118 studies met their inclusion criteria. This rather large review covered the results of over 15 000 implants in around 13 000 patients. However, surprisingly, despite the large number of studies, there was relatively poor evidence to support these major innovations in orthopaedic practice. There was varying evidence to support the use of each device, with just four low-quality studies examining modular femoral necks, but 56 studies informing the use of high flexion knee replacement (of which seven were high quality). There was no evidence, however, that any of these innovations improved patient-reported outcomes. The picture was just as bleak with the national registries; although there were data reported over 12 years with 200 000 implants (and comparison with over 1 200 00 'traditional' designs), there was no evidence to support improved survival. The counter was in fact true, with higher incidences of revision with modular femoral necks (hazard ratio 1.9), ceramic-on-ceramic bearings (hazard ratio 1.0 to 1.6) and high flexion knee implants (hazard ratio 1.0 to 1.8). Perhaps it is time the orthopaedic community took a long, hard look in the mirror. Although we strive for excellence with our patients and every surgeon is trying to achieve the best possible outcomes, it seems that again and again innovation and novelty value are placed ahead of hard evidence when selecting our patient implants. It seems likely that innovations like the 'Beyond Compliance' system recently implemented in the UK in an attempt to control the introduction of new devices is needed now more than ever.

A fresh look at ACL reconstruction

The ACL is perhaps the most studied ligament in the body. There have been seemingly endless papers examining indications for surgery, orientation of bundles and types of surgery amongst many others. Perhaps unsurprisingly, given the ethical issues with re-operation, there are precious little long-term data regarding second-look procedures, so all outcomes are essentially based on clinical, imaging and PROMS data. We were delighted to see this paper from **Hiroshima (Japan)** which, amazingly, reported the clinical outcomes and requirement for second-look arthroscopy in a series of over 200 patients.[8] The surgical team used a mixture of augmentation and reconstruction to treat the ACLs of 216 patients (mean age 25 years) with 73 single-bundle ACL augmentations, 82 double-bundle ACL reconstructions and 61 single-bundle ACL reconstructions. Of the 216 patients in the series, 94 underwent proprioceptive testing (using threshold testing to passive motion). The arthroscopies yielded more improved synovial coverage in the augmentation group than in the other groups, along with better anterior draw testing (KT-2000 arthrometer 0.4 mm vs 0.9 mm double-bundle group and 1.3 mm single-bundle). These differences, however, were not translated into improved outcomes in the Lysholm scores or pivot-shift test. This is a powerful paper presenting clinical, surgical, PROMS and functional data surrounding a disparate group of patients treated for ACL rupture. We would agree wholeheartedly with the authors that their paper supports the use of ACL augmentation as a reasonable treatment option for patients with ACL remnants.

Unicompartmental knees – risks and benefits?

The attractive option of a unicompartmental knee replacement (UKR) offers patients and surgeons a smaller operation with less co-morbidity and potentially improved functional outcomes. Although longevity is widely known to be poorer than a total knee replacement (TKR) in the correct hands and the correct patient the arguments of better functional outcomes and lower complication rates may outweigh the poorer longevity. This kind of large 'population medicine' question can

be effectively answered by joint registries, and the team at the **National Joint Registry (UK)** have used a matched cohort of 101 330 patients with UKR and TKR in an attempt to answer these questions and shed some light on the risk/benefit balance from a national perspective.[9] The study team used a propensity score technique to use the data available to match 25 334 UKRs to 75 996 TKRs recorded in the national joint registry. The data was linked to the National Health Service Hospital Episode Statistics database to adjust for available confounders and some complex regression modelling was used to compare outcomes for revision, reoperation, complications, mortality and length of index stay. Of course despite all of this statistical wizardry, the series still suffers from the issues associated with selection bias. There are few patients in whom a surgeon is in genuine equipoise when selecting between a TKR and UKR – this obviously should be taken into account when interpreting the findings. Nevertheless, in one of the few orthopaedic studies published in *The Lancet*, the study team estimated that based on their propensity score matching, the UKRs suffered from a considerably worse survival when measured for both revision (HR 2.12, 95% CI 1.99 to 2.26) and for reoperation (HR 1.38, 95% CI 1.31 to 1.44) over the eight year follow-up period of the study. That said, the mortality was significantly higher in the TKR group at all time points (30 day HR 0.23). This difference was also reflected in longer lengths of stay, complication rates and rate of readmission in patients undergoing TKR *versus* UKR. Despite the size, power and publication in a credible journal we can't help thinking that this paper is comparing apples and oranges. While we are sure there is no bias in the study team (although the senior authors is from the designing centre of the most widely used UKR) asking questions about mortality and complications is only valid if the groups are appropriately matched. There is no data collated about the medical co-morbidities of the patients, their medical histories and pre-operative radiographs are not known. It is not clear to us that the propensity score matching used here is accurate enough to eliminate those biases. In common orthopaedic practice in the UK, given the likelihood of eventual revision of the UKR they are mostly reserved for fitter patients with unicompartmental disease. This selection bias could explain all the findings of this paper.

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