ROUNDUP360

Research

Blood supply to the femoral head after dislocation

Fracture dislocation of the femoral head often presents a complex problem, placing the blood supply to the femoral head in danger with the added complexities of open reduction and internal fixation (with or without an acetabular fracture). The femoral head is usually perfused by the medial femoral circumflex artery (MFCA) via the cruciate and trochanteric anastomoses. The forces and displacement involved at the time of posterior fracture dislocation will often tear retinacular vessels, placing the femoral head at risk of avascular necrosis. Surgical approaches and fixation methods are often chosen to maximise the chances of femoral head survival. However, it has not been made clear what the impact of injury and fixation methods is on patients in whom the femoral head has survived post-operatively. A research team in **Otowok (Poland)** built on previous research to establish the changes in blood supply following injury. They assembled a cohort of 35 patients who had suffered a fracture dislocation of the femoral head and compared them with a previous cohort of 16 anatomical specimens and 55 normal individuals in an inventive comparative case cohort. The researchers undertook CT angiograms taken on the 35 patients (mean age 37 years). By twelve months' follow-up, there were ten patients who had developed AVN of the femoral head. All of these patients had a delay to relocation of the femoral head. In all three groups there were three main arteries identified supplying the femoral head; the deep branch of the MFCA, the postero-inferior branch of the MFCA and the piriformis branch of the gluteal artery. In the majority of cases the deep branch of the MFCA was patent (over 90% of cases). At the time of dislocation the authors found that it was the deep branch that was occluded when the hip was dislocated, either at the bifurcation or up to 35 mm distal to this. The authors noted that, surprisingly, the MFCA was not absent or ruptured in those hips undergoing AVN and in fact had a larger diameter suggesting revascularisation. The authors argue that delay to relocation and preservation of the vascular supply with relative hyperaemia in the deep branch of the MCFA supports the hypothesis that AVN is caused by relative hypoperfusion and kinking of the nutrient arteries.[1] Expedient reduction and fixation seems the best strategy to avoid this potentially devastating complication.

Diabetes and hip replacement

Total hip replacement (THR) has previously been called the 'operation of the century', with an impressive safety profile and an effect size that dwarfs most interventions, however, the success of THR is both orthopaedics' best success story and its Achilles heel. Comparisons with other interventions are far from fair and the remarkable success of THR has set a bar which is so high it is difficult for other interventions to compete. However, despite this track record, THR is not without its problems. Complications, while rare, can be devastating for both surgeon and patient alike. Diabetes is becoming more common in the arthroplasty age group and is a risk factor for many adverse outcomes in THR (such as infection). Researchers in **Edinburgh (UK)** set out to establish what precisely the interaction between diabetes and poor outcomes in THR was. They conducted a systematic review and meta-analysis of the literature (Level II evidence) to establish the interaction between diabetes and complications associated with THR. The research team conducted a thorough literature search and included papers reporting the complications of interest (thromboembolic events, coronary events, UTI infections, respiratory tract or surgical site infections and revision arthroplasty). The research team used a slightly unusual Bland & Altman method to estimate odds ratios for the various outcomes and the incidence of relation to diabetes in each series. While the authors' Pubmed search yielded 193 articles, only ten articles met the inclusion criteria (although these ten articles did report the outcomes of nearly 592,000 patients), reporting an incidence of 5% of diabetes mellitus. The analysis of this impressive dataset suggests that diabetes is associated with an increased risk of surgical site infection (OR 2.04), urinary tract infection (OR 1.43) and lower respiratory tract infection (OR 1.95), all of which were significant. There was no association with other types of complication.[2] For a common complication, it is surprising how great the increased risk associated with diabetes is. This paper quantifies the risk associated with diabetes and joint replacement, and while there is an increased rate of infection, other complications such as myocardial infarction and failure of the prosthesis were not significantly greater. Increased complications inform risk management but given the satisfactory long-term results THR should not be rationed in patients with diabetes.

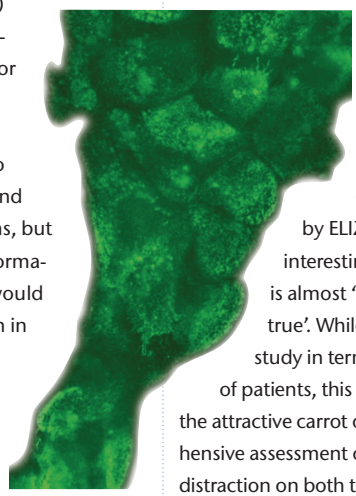
Bone remodelling over two decades following hip replacement

Much research has been performed on taper slip cemented and the various uncemented stems. However, despite the current fashions for other designs, there are large numbers of successful composite beam prostheses, either historical or contemporary. The natural history of the composite beam is that of stress shielding (particularly proximally) which results in cortical thinning despite the stem usually staying well fixed. Little is understood about the dynamics of cortical thinning. Researchers in **Lund (Sweden)** aimed to examine the dynamics of cortical thinning around well-fixed cemented Muller straight stems. They designed a study involving the hips with a minimum of 15 years' follow-up and no radiological signs of osteolysis. Radiological measures of cortical thinning were undertaken

in the 20 hips in the study who were followed for a mean of 20 years. Measures were taken medially and laterally at regular intervals to characterise the rate and type of cortical thinning. A total of 60% of the observed cortical thinning occurred during the first five years of the study and was more evident proximally. Given the rate of slowdown and the lack of loosening of the straight stems over the period of the study, the authors concluded that this is a non-pathological process mainly related to the composite beam type of stems and should not necessarily be viewed as a pathological process.[3]

Sham surgery as good as arthroscopic meniscectomy

Arthroscopic meniscectomy is one of the most commonly performed procedures worldwide for a range of indications. While few surgeons would argue about the indications for arthroscopic surgery in the locked bucket handle tear of the knee, many other indications are slightly less accepted. Millions of procedures are performed worldwide each year for patients with degenerative tears, osteochondral defects and for ACL reconstruction where the evidence is slightly poorer. Researchers in **Helsinki (Finland)** have attempted to shine a light on arthroscopic meniscectomy for degenerative medial meniscal tears in the absence of arthritis. They designed one of the few studies able to elucidate the effects of surgical intervention at all – the sham surgery study. Their multicentre randomised sham controlled study (Level I evidence) investigated the outcomes of 146 patients (aged 35 to 65). Inclusion criteria were symptoms consistent with a degenerative medial meniscus tear in the absence of radiological signs of osteoarthritis. Outcomes were assessed using outcome scores including clinical (Lysholm and Western Ontario Meniscal Evaluation Tool (WOMET) scores) and a VAS for knee pain after exercise. Follow-up was to 12 months and the patients were treated on an intention-to-treat basis. Amazingly, at the 12-month follow-up the investigators were unable to report any significant differences between the groups in any outcome measure. There were no significant differences between the two groups in the primary outcome measures, with improvements in the Lysholm score of 21.7 and 23.3 points in the meniscectomy and sham surgery group, respectively. Similarly, the WOMET score suggested slightly (but not significantly) better outcomes in the sham surgery group with improvements of 27.1 (sham) and 24.6 (arthroscopy). Again there were no differences between groups with respect to the need for subsequent knee surgery and serious adverse events.[4] In perhaps one of the most important studies undertaken in orthopaedics this year, the Finnish group have firmly reopened (and possibly closed) the debate on arthroscopic intervention for degenerate meniscal tears. Sham surgery studies are difficult to arrange, expensive and raise ethical questions, but provide essential information like this which would be impossible to gain in any other way.



Distraction in knee osteoarthritis

The treatment of patients with early onset osteoarthritis (OA) is difficult. With poor outcomes from arthroplasty (in terms of longevity and function), surgeons have reached for other options such as osteotomy, medical therapies and even joint distraction. Surgeons in **Utrecht (the Netherlands)** have presented a prospective series of patients treated with distraction for early onset osteoarthritis of the knee. The study team included 20 patients under the age of 60, all of whom had a VAS score of > 60 mm. Patients included in this study presented with end-stage knee OA and an indication for total knee replacement (TKR). They underwent two months of knee joint distraction (KJD) and their outcomes were assessed using serial VAS pain scores and the WOMAC questionnaire. This comprehensive study also included assessment of cartilage structure and function. KJD was applied for a mean of two months (54 to 64 days) and clinical parameters assessed using the WOMAC questionnaire and VAS pain score. Changes in cartilage structure were measured using quantitative MRI, radiography, and biochemical analyses of collagen type II turnover (ELISA). Follow-up was to just over two years on average and patients experienced a sustained clinical improvement, with improvements in WOMAC scores by 74% and VAS pain scores by 61%. Remarkably, the investigators also report increases in cartilage thickness (from 2.35 mm to 2.78 mm) and sustained decreases in the ratio of collagen breakdown to synthesis (as determined by ELIZA).[5] This is an interesting paper which is almost 'too good to be true'. While not a definitive study in terms of numbers of patients, this study dangles the attractive carrot of a comprehensive assessment of the effects of distraction on both the symptoms and biology of early osteoarthritis of the knee.

Does joint replacement prevent cardiac events?

Here at 360 we need no convincing as to the benefits of total joint replacement, representing one of the most successful medical interventions there is in terms of both health economic and functional outcomes. However, we would not have thought of joint replacement as good for your heart. Surgeons in **Toronto (Canada)** have set out to establish just that. They constructed a long-term cohort study of 2200 patients with hip or knee osteoarthritis to establish the effect that joint replacement had on their incidence of serious cardiovascular events using a propensity score analysis methodology. The study group were followed up over a 12-year period to either death or the end of the study. The rates of serious cardiovascular events for patients receiving primary total joint replacement compared with those who did not were calculated. The propensity score-matched cohort was constructed from 153 matched pairs of participants, all of whom had moderate to severe arthritis and had an exposure time of at least three years and a median follow-up of seven years. Those matched participants who underwent total joint replacement were significantly less likely to suffer a cardiovascular event during the period of the study. There was a remarkably favourable hazards ratio of 0.56 (95% CI 0.43 to 0.74). Patients in the seven-year exposure period had an absolute risk reduction of 12.4% and the number needed to treat calculation was eight.[6] The findings of this study are certainly unexpected and given the rigorous methodology this is likely a genuine finding.

Tranexamic acid leads the pack in knee replacement haemostasis

There is much poor quality evidence surrounding the use of both tranexamic acid and fibrin glues in reducing post-operative bleeding following total knee and hip replacement. Given the large number of studies with poor methodology and the suitability of the question to evaluation by a randomised controlled trial, we are surprised that it has taken so long for such a study to emerge. Researchers in **Barcelona (Spain)** have a done a grand job of evaluating all of the currently available options for intraoperative haemostasis during total knee replacement. They designed a randomised parallel group open clinical trial to compare fibrin glue, Tissucol (fibrinogen and thrombin) and intravenous tranexamic acid

with a routine haemostasis control group. Outcomes were assessed primarily by measuring total blood loss collected in drains after surgery. The investigators also evaluated the secondary outcome measures of hidden blood loss, transfusion rate, pre- and post-operative haemoglobin, units transfused, adverse events, and mortality. The trial included 172 patients randomised to the four groups. With regards to the primary outcome measure there was significantly less blood loss in the tranexamic acid group (244.1 mL ± 223.4 mL) when compared with all the other groups, fibrin glue (553.9 mL ± 321.5 mL), Tissucol (567.8 mL ± 299.3mL) and control (563.5 mL ± 269.7 mL). There was a relatively high rate of transfusion across all the groups at 21.1%. There were no clinically relevant differences between the intervention groups although there was a significantly higher transfusion rate in control *versus* tranexamic acid group (2 *versus* 12 patients).[7] There is yet more evidence presented in this study of the efficacy of tranexamic acid in preventing and reducing post-operative haemorrhage after total knee replacement. What this study is unable to tell us about is the incidence of untoward events. This is a rather small study powered to investigate bleeding rather than prothrombotic events.

Tranexamic acid safe and efficacious according to the literature

■ Researchers in **Shijiazhuang (China)**, almost as if on cue, published a comprehensive meta-analysis investigating the safety and efficacy of tranexamic acid in the published literature. They conducted a comprehensive meta-analysis of randomised controlled trials evaluating both intra-articular and systemic application of tranexamic acid in total knee replacement (TKR) patients. The authors conducted an extensive literature review for their meta-analysis, using all of the major indexing services including PubMed, EmBase, Cochrane library and Science direct. The standard 'Cochrane' style methodology was used, with two independent reviewers to assess the study quality, risk of bias and perform the data extraction. The researchers were able to include six studies in their analysis and performed meta-analysis on 647 patients. There were no increases in the rates of adverse events including DVT and PE in either the treatment or control groups across these studies. However, the use of tranexamic acid (either topical or intravenous) reduced observed total blood loss and the proportion of patients requiring blood transfusions (RR 0.28). The investigators noticed a mild dose response effect in tranexamic acid use and recommend higher doses (> 30 mg/ml).[8] When taken together, this meta-analysis and the RCT contribute significantly to our understanding of tranexamic acid in TKR here at *360*. While there are still relatively small numbers of patients evaluated in clinical studies, the efficacy of TXA has been demonstrated both as a single agent and against two types of tissue glue. Taken together with the safety data presented in the meta-analysis and allowing for the small numbers of patients in both studies, we cannot see why tranexamic acid infusions shouldn't become standard practice in primary total knee replacement.

Cartilage colonisation in bipolar ankle grafts

■ One of the more left-field options for ankle arthritis is the use of bulk bipolar allografts. Popular in some centres in the US and Europe for osteoarthritis, similar matched bulk allografts have found application in limb preserving tumour surgery, either where a prosthesis is contraindicated, or in some centres where these are used as first line treatments. However, opinion is divided on their use and likely long-term outcomes. There is plenty of data to support their short-term use, but the few long-term studies show increasing failure rates and relatively poor functional scores. One of the main objections that detractors have against allograft use is the perception that they remain an inert graft and that very little biological activity occurs, leading to an inevitable failure of a large dead bone graft. One of the surgical teams with much experience of this sort of grafting is from **Bologna (Italy)**, who have previously reported outcomes for bipolar grafting for both osteoarthritis and tumour applications. They set out to establish what actually happens at a biological level in patients treated with bulk bipolar ankle allograft for osteoarthritis. The research team used a series of 17 patients who had undergone bulk allografting. They retrieved a DNA sample from 15 cases and compared it with donor and host DNA in order to establish the host or graft match, thus giving an indication of any new host biological activity. In addition, in a subgroup of six patients, gene expression was assessed using six allograft cartilage samples and a qtPCR method. Further histology and immunohistochemistry (in-situ hybridisation) was used to confirm the PCR results and localise expression. Not surprisingly, the researchers found a mixture of results. From a geneotyping viewpoint, ten patients matched host DNA, three matched the graft DNA and two were a mixed picture. The local gene expression analysis (PCR) demonstrated that cartilage expression was occurring and that the graft was making new cartilage.[9] This paper is extremely interesting and shows for the first time that migration of host cells from the subchondral bone can be expected in the majority of cases and that those cells can be expected, given time, to engage in cartilage manufacture. In other words this represents some (and by no means conclusive) evidence that, given time, bipolar ankle grafts can act like a scaffold and support the ingrowth of host-tissue-specific cells.

CTs and proof of fusion

■ The advent of 3D imaging has revolutionised visualisation in post-operative patients, and particularly in patients with fractures waiting to heal or fuse. One of the difficulties with widespread adoption of a new technology is that sometimes the clinical relevance has yet to be assessed. Researchers in **Halifax (Canada)** have used the model of post-operative ankle fusion in an attempt to answer the question 'how fused is fused'. The research team assessed clinical outcomes using quality of life (SF-12) and clinical outcome scores (Foot Function Index (FFI), and American Orthopaedic Foot & Ankle Society (AOFAS) scores) administered at a 24-week review. At the same time a CT scan was arranged with the aim of determining the extent of osseous bridging callus. Impressively, the research team were able to assemble a cohort of 275 patients, all of whom had isolated joint fusion. They quantified the bridging callus into four broad categories; absent (0% to 24%), minimal (25% to 49%) moderate (50% to 74%), or complete (75% to 100%) and then investigated how dependent the outcome variables were on this volume of bridging callus. The authors were able to establish that the 'threshold' in their study was the minimal osseous bridging group. Patients with between 25% and 49% bony bridging were found to have a minimally clinically important change in all three outcome measures, while those in the absent callus group did not.[10] This study is one of the first to quantify the relationship between bony bridging and clinical symptoms, one that is intuitively there, but has not been previously investigated. We were delighted to read such an innovative article here at *360* but then disappointed by the anything but innovative statistical methods. This paper suffers like many others from artificially transforming continuous data (bony bridging) into ordinal data. A more comprehensive statistical analysis would have enabled the relationship between bony bridging and symptoms to have been explored further.

Atorvastatin is beneficial for muscle re-innervation after sciatic nerve transection

Neurological regeneration and re-innervation is not always guaranteed, even in the case of traction injury, let alone neurotemetic lesion. There is some evidence to suggest that Atorvastatin is neuroprotective after transient ischaemic insult, but there is no evidence of the role (if any) of atorvastatin in peripheral neurotemetic lesions following surgical re-innervation. Researchers in **Québec (Canada)** tested the potential efficacy of atorvastatin in 16 female Sprague-Dawley rats. A surgical model of sciatic nerve transection and re-innervation was completed with sutures and fibrin glue following sciatic nerve section and end-to-end microanastamosis. Rats were randomised to surgical repair plus saline, surgical repair plus atorvastatin and uninjured nerve. At five months following repair, the sciatic nerve and the gastrocnemius muscle were isolated and *in vivo* electrophysiological measurements performed.[11] The rats in the atorvastatin group demonstrated better kinematics with a markedly larger excursion of the hip-ankle-toe angle during walking and preservation of electromyographic activity (2.91 mV *versus* 0.77 mV) and maximal muscle force (85.1 g *versus* 28.6 g). Systemic administration of atorvastatin (in rats at least) over a 14-day peri-operative period apparently resulted in much improved function following peripheral nerve repair, and was associated with improving locomotion and the re-establishment of muscle strength and EMG activity. Certainly to our minds here at *360*, a candidate for surgical repair.

Microfracture relieves short-term pain in cuff repair

Microfracture is fashionable at the moment. It is a safe, cheap, reliable (and often efficacious) method of biological augment, most commonly used in the treatment of osteochondral defects. Reasoning that microfracture at the footprint of a rotator cuff repair may provide a biological augment and help in the tendon healing at the bone-tendon junction when arthroscopic cuff repair is undertaken, surgeons in **Modena (Italy)** set out to establish if there was any noticeable benefit in a randomised controlled trial (Level I evidence). The study recruited 57 patients who underwent shoulder arthroscopy for repair of complete rotator cuff tears and these were randomly allocated to two groups using a block randomisation method. The surgeon undertook microfracture at the footprint of the cuff repair in the treatment group, but not in the control group. There was no apparent baseline variation between the two groups, and both groups demonstrated improvement at final two-year follow-up in all measured outcomes (VAS, range of movement (ROM) and University of California at Los Angeles (UCLA) and Constant scores). While all of these outcomes were significantly in favour of the intervention group at the three-month follow-up, there were no differences to be seen by two years where both groups had significantly improved and were indistinguishable from each other. There were no adverse events noted.[12] Conclusions in these kinds of studies can be difficult to reach. When there is a short-term benefit from an intervention, on the one hand microfracture could be said to make no difference; on the other, it could be said to improve a patient's outcomes more rapidly and potentially have a health economic benefit. It would be interesting to see a full health economic utility analysis, but until then, here at *360*, we are inclined to agree with the authors. As a sustained, albeit short-term, benefit appears to occur, and microfracture itself is inexpensive, for now it looks to be a beneficial intervention.

Promising early results from L-PRF augmented cuff repairs

Sticking with the theme of biologically augmented rotator cuff repairs, researchers based in **Nice (France)** have this month published the pilot results from their randomised controlled trial aimed at establishing the safety and potential efficacy of leukocyte- and platelet-rich fibrin (L-PRF) in arthroscopic cuff repair. The study team hypothesised that use of L-PRF was not only technically feasible and safe, but that it results in higher neovascularisation rates and the incidence of early watertight rotator cuff healing. In this pilot study 20 patients, all presenting with chronic rotator cuff tears were randomised to either L-PRF augmented rotator cuff repair or standardised treatment. The research team used a standardised surgical approach with a double-row tension band repair. Outcomes were assessed with clinical examination, outcome scores (VAS, Constant score, Simple Shoulder Test), as well as Doppler ultrasonography, to assess the vascularisation. Outcomes were assessed at six and 12 weeks. While there were no clinically significant differences in the scores between the two groups (which would not be expected), the mean vascularisation index at the tendon-to-bone insertions was higher in the L-PRF group than in the healthy shoulder group.[13] This pilot study looks promising for the potential benefit of a different type of biological augmented rotator cuff repair. Higher neo-vascularisation rates would suggest a lower eventual failure rate, although all that can be concluded from a pilot study such as this is the safety profile of the intervention and it can be used to inform a power calculation.

Fatty degeneration in a rodent model

Degenerative cuff arthropathy and associated cuff tears is one of the most debilitating of upper limb conditions. Patients can be left with little in the way of function. Particularly challenging to treat can be the chronic cuff tear associated with 'fatty degeneration'. While clearly visible on the MRI scan and seen arthroscopically as muscle atrophy and an infiltration of fat into the area, little is known about the pathophysiology. Researchers at **Ann Arbor (USA)** aimed to improve understanding of the changes in the contractile properties of muscle fibres and the mechanism behind fatty degeneration. The research team used a massive cuff tear model in elderly rats. Following development of the tear, fibre contractility and type distribution were assessed 30 days after the tear and interpreted along with measured expression of messenger RNA and micro-RNA transcripts specific for muscle atrophy, lipid accumulation, and matrix synthesis. A month following the tear the research team identified a reduction in contractile force coupled with induction of RNA molecules regulating atrophy, fibrosis, lipid accumulation, inflammation, and macrophage recruitment. Histologically, areas of fat accumulation were observed and associated with accretion of macrophages.[14] The extent of degenerative changes in this model was greater than that usually seen in humans, making this potentially an ideal disease model to study. This may well be due to the single insult nature of the massive cuff tear in this model, where in humans it is often a more gradual process with accumulation of small tears. Aside from confirming changes in muscle strength and contractility, the research team established that, contrary to previous belief, activation of canonical intramyocellular lipid storage and synthesis pathways are not responsible for fatty degeneration associated with chronic arthropathy, but it is more likely an inflammatory process.

Octogenarian RTCs: not as bad for you as you might think

As of 2008, more than seven million automobile drivers in the US were aged 80 years and older, and surprisingly in this age group motor vehicle collisions (MVC) are the second most common mechanism of injury, following falls. Researchers in **Wichita (USA)** set about evaluating the one year post-discharge mortality in octogenarians involved in a MVC. The research team established the cause of death and risk factors predictive of mortality. This careful

ten-year retrospective review (Level IV evidence) set out to establish patient demographics, injury severity and patterns, hospitalisation details, and post-trauma outcomes predictive of one year mortality. Like many such studies, determining the exact cause of death for patients who died within 12 months of hospital discharge can be tricky, and relies on state death databases and hospital records, when patients did not necessarily have a post mortem examination. The authors aimed to determine if there was a relationship between injury severity and pattern to the one year post-discharge mortality. Impressively, the authors were able to include a total of 199 patients in this study, with a mean age of 84.2 and Injury Severity Score (ISS) of 9.3. Unsurprisingly in this age group, the one year mortality was quite high at 11.1% (22 patients). In around half of these the cause of death was directly related to trauma (n = 9) and likely related in a further third (n = 7). The remaining six patients died of unrelated causes. Patients who were more severely injured (ISS > 15, p = 0.004) and those admitted to the intensive care unit (ICU) (p = 0.0051) were more likely to die within one year of hospital discharge and although not significant, the authors note a trend towards a higher mortality in patients with pneumonia. However, rib, hip, and pelvic fractures, spinal cord injuries, intubation upon hospital arrival, and need for mechanical ventilation were not associated with a higher post-discharge mortality rate.[15] The results of this study show that although many believe that the majority of octogenarians involved in a MVC die within one year of discharge, this is untrue. The only predictors of mortality within one year of discharge are injury severity, ICU admission, and ICU length of stay.

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