ROUNDUP360

Knee

Genetic determinants of ACL strength

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It is well established that women have a higher incidence of anterior cruciate ligament (ACL) injury when performing the same sporting activity as men, and a range of 'pre-hab' interventions have become widely accepted such as landing training in running athletes and quads/hamstrings proprioceptive training. This has been demonstrated to reduce the incidence of ACL rupture and led to the belief that, at least in part, the difference in rupture rates can be explained by differences in protective muscle activity. However, what it doesn't explain is the structural differences between male and female ligaments. In an interesting comparative anatomy and genomic study from **Ohio (USA)**, a research team took biopsies from ruptured ligaments in normal male and female subjects to establish the differences in anatomic, hormonal and neuromuscular factors.[1] Biopsies were performed in 14 athletes (seven male and seven female) and the samples were analysed by histological and microarray analysis in a subset of patients. Those genes that were potentially positive were further quantified by reverse transcription real-time polymerase chain reaction (RT-qPCR). Of the 32 candidate genes identified on microarray analysis, 14 were not linked to the X or Y chromosome. RT-qPCR identified significant differences in expression of three genes of interest across the population of 14 samples. These were genes involved in matrix regulation, with ACAN (aggrecan) and FMOD (fibromodulin) upregulated in females *versus* their male counterparts, and downregulation of WISP2 (WNT1 inducible signalling pathway protein 2). Interestingly, the histology did not yield any potential differences between groups. This work suggests that genetic differences in genes responsible for matrix and collagen regulation are at least partially responsible for the differences in ACL rupture rates between men and women.

TKA outcomes influenced by prosthesis

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Improving outcomes following total knee arthroplasty (TKA) is a challenge. Despite a range of randomised studies aimed at linking outcomes to factors as diverse as surgical approach, patellar resurfacing, post-operative analgesia and bearing surface mobility, there have been no clear winners and improving outcomes remains a difficult thing to achieve. Researchers in **Edinburgh (UK)** have published what may turn out to be one of the most important randomised trials this year.[2] The research team set out to establish if the design of the prosthesis really does affect functional outcomes after TKA. The trial team randomised 212 patients to either a Kinemax or Triathlon knee in a single-centre double-blind randomised controlled trial (RCT). Outcomes were assessed using the Oxford Knee Score at six weeks, six months, one and three years. Secondary outcomes including range of motion, pain, power output and satisfaction surveys were also collated. Interestingly, and for the first time in a large scale RCT, there were significant differences seen between the two prosthesis types. The Triathlon knee significantly outperformed the Kinemax in terms of range of motion and pain. The Oxford knee scores favoured the Triathlon, but this did not reach statistical significance. The satisfaction scores, however, were also significant in favour of the Triathlon. This study is interesting in two ways: it demonstrates that in terms of secondary outcome measures, the design of a prosthesis can determine outcomes, with consistent differences in a range of outcome scores. It also comprehensively illustrates differences in outcome scores and how the selection of a measure can affect the reported results. The Oxford Knee Score reported a non-significant difference between the prostheses, although satisfaction ratings (arguably a more blunt instrument) did demonstrate a difference. Given the number of RCTs that have significant differences in apparently relevant secondary outcomes (with no differences in primary outcome measures), perhaps it is time to re-examine the use of joint-specific patient-reported outcome measures as a primary outcome measure in this kind of study.

Single- or two-stage revision for infected TKA?

Revision of a prosthesis for infection is a complex topic – infected total joint arthroplasties can, in the worst scenario, result in amputation. Treating the infection (and infection-related outcomes) is clearly the most important outcome, however, maximising functional results without compromising 'cure rates' is of great interest to arthroplasty surgeons. The debate surrounding a single- or two-stage revision has been argued endlessly in the hip world[3], with most surgeons agreeing that, while the two-stage arthroplasty remains the gold standard for infection control, in many cases a single-stage revision offers similar cure rates and improved functional outcomes (with lower morbidity associated with a single procedure). There is little evidence to support the use of single-stage revision in the knee as opposed to the traditional two-stage approach. Surgeons in **London (UK)** have been practicing a highly selective single-stage revision approach for patients who were felt to be suitable. Their protocol recommends single-stage revision for patients with a known, sensitive organism, as well as no evidence of bone loss or immunocompromise. Over a five-year period they have undertaken 102 revisions for TKA infection, of whom 28 (27%) were treated with a single-stage procedure. Reporting a comparative prospective series to three years of follow-up, the authors aimed to establish the cure rate and functional outcomes in their own series. Patients treated with a single-stage approach had improved post-

operative functional outcomes (Knee Society Score 88 *versus* 76), while, incredibly, no patients had evidence of subsequent loosening at the final three-year follow-up. We would tend to agree with the authors, here at *360*, that while that paper ably shows that single-stage revision does have a place in the treatment of periprosthetic infection in the knee, this paper alone does not provide the whole picture. Ideally, a RCT would give the answer in the most credible and encompassing way.

Arthroscopic meniscectomy: a problem that just won't go away!

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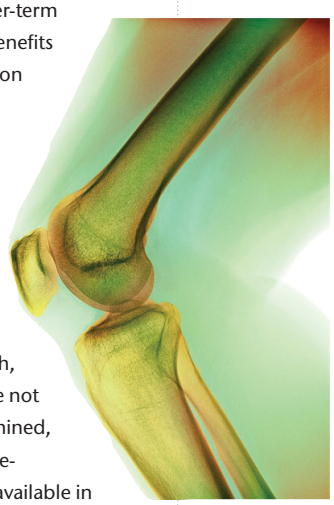
■ There have been a range of RCTs published in recent times which make for rather uncomfortable reading for arthroscopic surgeons of whatever subspecialist interest. With robust evidence to suggest that surgery as varied as ACL reconstruction, subacromial decompression and meniscectomy confers little benefit to the patient, in today's post 'credit crunch' healthcare economy it is rather difficult to see for how long these interventions are going to be funded. Although well designed and carried out, these studies have not sat well with surgeons, who intuitively believe the outcomes to be unrepresentative of general clinical practice. There is some solace to be taken in the most recent study from **Linköping (Sweden)**, taking a slightly different look at arthroscopic meniscectomy in middle-aged patients with meniscal symptoms.[4] While previous studies have focussed on patients with early osteoarthritic changes, this study focuses on patients with mechanical meniscal symptoms. The authors randomised 150 patients with meniscal symptoms but no osteoarthritis to either physiotherapy alone, or physiotherapy in combination with knee arthroscopy and meniscectomy of any significant meniscal pathology. Outcomes were assessed at 12 months using the Knee Injury and Osteoarthritis Outcome Score (KOOS pain) as the primary outcome measure. The trialists undertook both intention-to-treat and as-treated analyses with the same results. Pain at 12 months was significantly lower in the surgery group, as was the improvement in the KOOS pain score. It appears from this study that irrespective of the patient's age or symptom history, middle-aged patients with meniscal symptoms perform better at a year of follow-up post-surgery combined with physiotherapy, than physiotherapy alone. The current state of research would suggest that careful attention to the inclusion criteria of each study is needed.

Failure in arthroscopic anterior cruciate ligament (ACL) reconstruction

■ While the longer-term health economic benefits of ACL reconstruction have yet to be determined, there are few outcomes as definite as revision. The rates of revision surgery for ACL reconstruction are low and, as such, the risk factors have not been clearly determined, with only a few case-controlled studies available in the literature. This uncertainty changed abruptly with the publication from **Gothenburg (Sweden)** of a registry-based study of 16 930 patients who form the Swedish ligament register.[5] The research team queried the registry in an attempt to clearly define the outcomes of ACL surgery in terms of risk factors for revision surgery. The outcomes of revision surgery were assessed at two years of follow-up. The variables assessed as potential risk factors for revision surgery included patient demographics (age, sex, BMI), smoking status and activity levels including injury details. There was a revision rate of just 1.82% (n = 308) reported in this study. The research team identified increased risk of revision surgery associated with football play (relative risk 1.58) and an adolescent age (between 13 and 19 years: relative risk 2.67). There were, however, no differences seen in revision rates between men and women. There were no other demographic-related associations found in this registry analysis, which may in part be due to the limitations of such registry-based analyses but is more likely due to a genuine lack of differences.



ACL reconstruction in the over 50s?

■ Sticking with the topic of ACL reconstruction, investigators in **Santiago (Chile)** have tackled another highly controversial topic in their recent paper: how do older patients fare following ACL reconstruction?[6] They report their own prospective series of 50 older patients (aged 50 +) and their outcomes. The authors report a consecutive series of patients with outcomes assessed at a minimum of three years (mean of around four and a half years) using the Lysholm and International Knee Documenting Committee (IKDC) patient-reported outcome scores. Secondary outcomes of return to sports, further surgery and satisfaction rates were also reported in this interesting paper. The authors report a massive rate of 90% of patients having concomitant injuries, with 76% of patients suffering meniscal tears and around one third osteochondral injuries. Complication rates were low, with 6% suffering minor complications. We were surprised to find an 88% return to pre-injury sporting levels and a 96% satisfaction rate – as good or even better than those reported in the younger population. We would agree with the authors here at *360* that ACL reconstruction in the over 50s appears to be safe and offers excellent clinical results. What, of course, this paper doesn't document is what the outcomes are in patients who are treated conservatively – might they be similar or, perish the thought, even better?

Knee arthroplasty for early osteoarthritis

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■ One of the most widely-accepted and successful operations is total knee arthroplasty (TKA). While the results are not as universally reliable as total hip arthroplasty, around 95% of patients are expected to achieve an excellent result following modern TKA[3]. Picking out those one in 20 patients who will not get quite such a good result is key – and researchers in **Preston (UK)** have taken a fresh look at the indications for TKA.[7] Reasoning that patients undergo TKA when they have signs of osteoarthritis on their radiographs but the clinical reporting of symptoms is, for most surgeons, the chief indication for arthroplasty, they set out to see if the pre-operative radiographs had any bearing on reported post-operative outcomes. Using their own cohort of patients, the authors reviewed five years' worth (1708 patients) of consecutive patients. Radiographs taken pre-operatively were reviewed for the purposes of the study, and patients with a Kellgren–Lawrence score of two or less on their pre-operative radiograph were reported separately as the 'early osteoarthritis group'. The study cohort included 44 TKAs performed in the early arthritis group – all had undergone diagnostic arthroscopy to ensure a correct diagnosis. By final follow-up, the mean Oxford Knee Score was significantly poorer (by 6 points) in the early osteoarthritis group compared with the rest of the cohort. In addition, the rate of further surgery was 18% as compared with 1.6% in all patients. This study does not paint a rosy picture for TKA in early osteoarthritis. Even in the presence of significant disabling

symptoms, the message here appears to be that without radiographic changes, caution should be the watchword when offering TKA to these patients.

All-inside meniscal repair

In what is an extremely informative RCT, investigators in **Sandvika (Norway)** have attempted to establish if there are any differences between devices available for 'all-inside' meniscal repair.[8] They designed and completed a RCT comparing the Biofix arrows and FasT-Fix devices. Forty-six patients were randomised to either Biofix (n = 21) or FasT-Fix (n = 25) devices. The research team used functional outcomes (KOOS and Tegner activity levels) to assess for outcomes within two years. Unsurprisingly, around a quarter of patients were re-operated within two years of their initial surgery. There were significant differences between the two devices, with the risk of re-operation 3.6 times higher in the Biofix group when compared with the FasT-Fix group. However, both treatment groups had improvements in the KOOS subscales and there were no differences between the subgroups. As perhaps would be expected, the outcomes of meniscal repair are dominated by the failures – and the failure rates in this study were significantly higher in the Biofix arrows when compared with the FasT-Fix group.

Steroids, thrombogenic markers and TKA

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The sequelae of thromboembolic disease and the post-thrombotic limb following TKA are significant, as are the medico-legal consequences. Much space in this and other journals has been given to discussions surrounding the pros and cons of various types of thromboprophylaxis in addition to the limitations of the (for the most part) industry-funded studies investigating the benefits of thromboprophylaxis in this patient population. While we are familiar with the well-trodden arguments of bleeding complications *versus* the risks of thromboembolism, our interest was very much piqued by a small study from **New York (USA)** which set out to examine the effects of pro-inflammatory mediators and venous thromboembolism (VTE).[9] The researchers, arguing that VTE is predisposed by systemic inflammation and pro-inflammatory cytokines including IL-6, set out to see if thrombogenic markers could be modulated by steroids in the peri-operative period. They designed a double-blinded RCT involving 15 patients in each arm. Patients were randomised to either 100 mg IV hydrocortisone two hours pre-operatively, or placebo (normal saline). Outcomes assessed were thrombogenic markers (serum prothrombin fragment (PF1.2) and plasmin-alpha-2-antiplasmin complex (PAP)). These outcomes were assessed in blood samples pre-incision and four hours post-tourniquet removal. The results were really startling, with significantly lower levels of PF1.2 and PAP at four hours in the steroid group when compared with the control. While these are early basic science-derived results and do not relate directly to lower incidences of VTE, it is a tantalising thought to be able to modulate the immune response in such a way as to be able to reduce the incidence of post-operative VTE. A larger clinical trial would be needed here, and there are certainly a number of unanswered questions surrounding the potential implications for longer-term infection and wound breakdown rates, but we would be fascinated to see the results of a suitably-powered clinical study.

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