

ROUNDUP³⁶⁰

Research

For other Roundups in this issue that cross-reference with Research see: [Hip & Pelvis Roundups 1 and 3](#); [Knee Roundup 8](#); [Foot & Ankle Roundup 6](#); [Wrist & Hand Roundup 7](#); [Shoulder & Elbow Roundup 4](#); [Spine Roundup 7](#); [Trauma Roundups 3 and 7](#); and [Oncology Roundup 3](#).

Unpicking syndesmotric injuries: CT scans evaluated x-ref Foot & Ankle, Trauma

■ One of the key pieces of pre-operative information required by the trauma surgeon to undertake effective pre-operative planning is to understand the stability pattern of the fracture. Two of the most commonly used classifications to help with this are the Denis classification and the more complex Lauge-Hansen classification. Researchers in [Kyungki \(South Korea\)](#), noting that even the Lauge-Hansen classification doesn't provide sufficiently accurate information on the competence of the syndesmosis in supination-external rotation (SER) injuries, aimed to use CT scan information to identify factors associated with syndesmotric injury.¹ An impressive 191 patients with consecutive ankle fractures (of whom over 100 were male) were included in this prospective diagnostic study. All patients had sustained an SER type injury and data including pre-operative radiographs, CTs and demographic data were collated as part of the study design. Patients were divided into those with and without a syndesmotric injury based

on the results of their intra-operative stress test. Radiographic and CT variables including fracture height, fracture length, medial joint space, extent of fracture, and bone attenuation were measured on radiographs and CT images. Around one in five of the patients included in the study were found at operation to have a clinically significantly unstable ankle fracture. The authors then undertook a logistic regression analysis to establish the factors that contributed to clinical instability. The study results suggested that suitable cutoff values for predicting unstable syndesmotric injuries include the fracture configuration on CT scan (height of > 3 mm; medial joint space of > 4.9 mm) and plain radiography (height of > 7 mm; medial joint space of > 4.5 mm). The use of overly complex classification systems with poor intra- and inter-observer reliability may be over; with improvements in diagnostic imaging, simple factors such as measurement of clear space and fracture height may well be as accurate. That said, only part of understanding the injury and planning surgery effectively is the residual function of the syndesmosis.

Surgical scrub suits and sterility in theatre

■ The 'theatre rules' are sacrosanct in almost every unit. Protocols surrounding footwear, masks, hats, scrub suits, gowns and even which doors can be used in theatres are universally and strictly enforced by fearsome theatre sisters, the difficulty of course being that the rules vary

from unit to unit and country to country. So are any of these rules all that important? Not able to tackle the whole question, researchers from [Singapore City \(Singapore\)](#) have picked out the question of theatre scrub suit attire and where is suitable in the hospital to roam in said scrub suits. They conducted a randomised controlled trial on a group of anaesthetists, allocated to one of three groups restricting their circulation in scrub suits.² The primary outcome measure of the study was the bacterial count from sample fabric pieces affixed at the chest, waist and hip of each scrub suit. Samples were taken every 150 minutes throughout the working day and each sample sent for microbiological analysis to establish the bacterial count on each sample (in terms of colony forming units (CFU)). The contamination of the scrub suits increased throughout the day, with highest counts at the hip and waist areas as opposed to the chest sample. Interestingly, the restriction of movement made no difference to the bacterial counts. There were no differences between anaesthetists who were restricted to theatre (mean CFU 25.2) and those allowed to visit the wards (18.5 CFU) and offices (17.9 CFU). While the authors of this paper have clearly demonstrated that circulation between different areas does not increase the bacterial load in scrub suits, we are not all that surprised, here at 360. The majority of these bacteria are likely to come from the anaesthetist, not the environment.

With our tongues pressed firmly in our cheeks we would venture that an alternate conclusion might be that anaesthetists need to change their scrubs regularly, wherever they have been!

Continuous passive motion and knee injuries

■ It is around 50 years since Dr Salter undertook his seminal studies looking at cartilage repair and nutrition using a lupine model. Early experiments gave rise to an explanation as to the function of cartilaginous sinusoids in nutrition of cartilage, and also the widespread use of continuous passive motion (CPM) to improve outcomes in post-operative and post-injury patients. Although not universal, there are ardent supporters of CPM as a useful modality to improve outcomes following treatment of intra-articular fractures, particularly around the knee. Researchers in [Austin \(USA\)](#) set out to establish the potential benefits of CPM on eventual knee range of movement after operative treatment of intra-articular fractures around the knee.³ They designed a randomised controlled trial to establish what the beneficial effects (if any) of CPM were with regards to a primary outcome measure of range of movement. Secondary outcome measures evaluated by the study included assessments of pain and lower limb function which were examined at regular intervals (two, six, 12, and 24 weeks). At the time of final follow-up, there was no difference between the outcome measure of knee extension, however,

knee flexion was improved early (at 48 hours) in the CPM group. Sadly, this flexion advantage was not significant at any other time point and did not persist until final follow-up. There were no significant differences in any of the other collated outcome measures. Patients did not tolerate early CPM well and in fact there were few advantages seen by the authors of this study who concluded that “the use of continuous passive motion in the immediate post-operative period following the treatment of intra-articular fractures offers no benefit”.

Pain at night melatonin-related?

x-ref Shoulder & Elbow

■ It is well recognised that pain perception can be relative and that many factors affect patients' perceptions of pain including their state of mind, background, psychological type, and trust in the surgeon, amongst a multitude of other factors. Surgeons and patients alike recognise that night pain is a particular difficulty, affecting patients' quality of life and mood particularly badly, however, the explanation and mechanism for enhanced pain perception overnight is not clear. Researchers in **Daegu (South Korea)**, using a cohort of patients, all with painful shoulders, investigated the potential for a hormonal influence on this experience of pain at night.⁴ The study involved a cohort of 63 patients with mixed shoulder pathologies (21 rotator cuff tear, 22 frozen shoulder and a control group of 20 with shoulder instability). The study team designed a basic science study using samples of joint capsule and bursa to establish expression of melatonin receptors (MTNR1A and MTNR1B) and of acid-sensing ion channel 3 (ASIC3). The study team used a tried and tested RNA expression methodology (RT-PCR) to establish the level of RNA expression and then measured the direct protein expression of ASIC3 using an immunoblot technique. The expression of all three factors measured was higher in the

rotator cuff tear and frozen shoulder groups, suggesting that melatonin plays a role in the pathophysiology of these shoulder diseases. Cell culture studies using a fibroblast model were then undertaken to establish the link (if any) directly to melatonin and inflammation. This study has effectively demonstrated that pro-inflammatory cytokines (Interleukin-1 β (IL-1 β) and tumour necrosis factor- α (TNF- α)) upregulate the expression of the melatonin receptors and that, in turn, melatonin induces the expression of ASIC3 expression and IL-6 production. To square the circle, the researchers finally conducted an antagonist study using luzindole which demonstrated reversal of the melatonin-stimulated ASIC3 and IL-6 production. This is a surprisingly complete basic science study that effectively establishes the role of melatonin in pain reception. Melatonin levels are known to change overnight and it is reasonable to suggest, as the authors have, that melatonin might be a potential target for pain modulation in these shoulder conditions.

Is blood flow the answer to night pain?

x-ref Shoulder & Elbow

■ The difficulty with hypothesis-driven science is that sometimes two equally likely explanations for an observation are well supported with potential evidence on both sides. Having firmly established in our reading of *JBJS [Am]* this month that in fact night pain in shoulder pathology may be due to hormonal changes mediated through melatonin receptors, we were somewhat dismayed to read a different but equally potentially valid paper from researchers in **Gifu (Japan)** in the *Journal of Orthopaedic Science*. These canny scientists hypothesised that given that there is a significant in-

crease in blood flow surrounding the rotator cuff and capsule of diseased shoulders, this may in fact have a role to play in the aetiology of night pain in the shoulder.⁵ They designed a basic science study to establish the relationship between blood flow and night pain in a cohort of patients with rotator cuff pathology. The research team used a pulsed Doppler ultrasonography method to evaluate 47 consecutive patients with established rotator cuff disease, then compared this with a control group of 20 normal controls with no known shoulder pathology. The research team established that while anterior humeral circumflex artery velocity and resistance was identical between sides in the control cohort and in patients without night pain, it did differ significantly in cohorts of patients with night pain between

the painful and normal shoulder. The research team suggest that “night pain, particularly involving aching, appears to be related to the haemodynamics”.

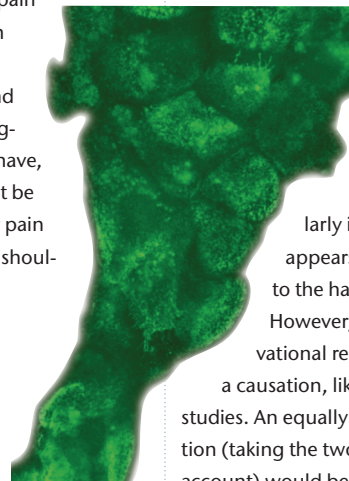
However, this is an observational relationship, not a causation, like in many other studies. An equally valid interpretation (taking the two studies into account) would be that melatonin mediates inflammation and the pain response in a diurnal manner, and this both affects blood flow (as a marker of inflammation) and pain perception in diseased shoulders. Both are equally valid explanations!

Venous thromboembolic disease following spinal surgery

x-ref Spine

■ One of the biggest challenges facing surgery today is minimising the risk of thromboembolic disease without encountering the inevitable complications associated with the various blood thinning agents available including wound

complications, bleeding and significant haemorrhage. Risk scoring is becoming an increasingly used tool in making appropriate patient decisions. The use of risk scores helps the clinician make a patient-by-patient decision rather than a population-based decision, however, they require large datasets to produce and validate. Researchers in **New York (USA)** set out to develop a risk score for judging the likelihood of post-operative venous thromboembolic events (VTEs) in spinal surgical patients.⁶ This population-based study looks at the incidence of post-operative adverse thromboembolic events using the Nationwide Inpatient Sample (NIS) over a nine-year period. Diagnoses were established using the ICD-9-CM diagnosis codes and covariates including patient demographics, hospital characteristics, and comorbidities. A huge sample of 710 154 spinal fusion procedures was analysed: there were 3777 recorded VTEs in 3525 (0.50%) procedures, of which, 2038 were deep venous thromboses (0.29%) and 1739 pulmonary emboli (0.24%). There were some obvious differences in baseline characteristics with VTE patients being older on average (57.63 vs 52.88 years), more often male (0.58% vs 0.42%), and black (0.78% vs 0.47%). There were also differences in hospital stay, with longer stays and higher total charges associated with the incidence of a VTE. The authors developed their own VTE Risk Index based on the demographic details they identified as increasing the risk of VTE. They suggest that their risk score would help in the decision making process surrounding clinical decision making. However, their score includes few covariates and only includes data that can be established from a ‘top down’ database, not those which should be included in a risk score intuitively; clotting disorders, aspirin use and blood transfusion, to name but a few, have been neither screened for nor included in this rather unsophisticated model.



Clots rare in lower limb plasters

■ The prevalence of thromboembolic disease is a key determinant to identifying the risk benefit of therapy with blood thinning agents. Taking a step back from the debate about who should receive thromboprophylaxis, researchers in **Toronto (Canada)** asked whether patients in a lower limb cast require thromboprophylaxis at all.⁷ The research team set out to establish what the event rates were for patients presenting with a lower-extremity injury requiring cast immobilisation or surgery in a prospective cohort study. Although there are venographic data available in the literature, there are no clinical follow-up studies to provide evidence as to clinical decision making. The research team set up a multi-centre prospective cohort aiming to define the prevalence of symptomatic DVT in patients with a lower limb fracture treated conservatively (tibial, fibular, or ankle fracture) or those treated with or without an operation (patellar or foot fracture). The study cohort included all patients treated at five centres in Ontario, Canada. Patients were treated according to the treating surgeon's preference, however, thromboprophylaxis was not used and all patients were immobilised in a plaster cast. The study included telephone follow-up at regular intervals to 12 weeks following injury. Over a three-year period, 1200 patients were enrolled in the study and 98% completed the three-week follow-up. However, not all patients were treated with a plaster cast – just 82% were immobilised. The event rate was low, with a 0.6% incidence of VTE (two proximal DVTs, three calf DVTs and two pulmonary emboli). The authors conclude that with no fatal events, and given that the clinically significant event rates associated with lower limb fractures stand at less than 1%, the rationale for recommending low-molecular-weight heparin and other prophylaxis should perhaps be called into question.

Immune-competent cells in Achilles tendinopathy

x-ref Trauma, Foot & Ankle

■ While it is well established that chronic Achilles tendinopathy is an inflammatory process which is probably driven by a combination of microtrauma and immune cell activation, the precise details remain somewhat opaque. In an ambitious study, researchers from **Silkeborg (Denmark)** designed a comparative case-controlled study in an attempt to fill some of the gaps in our understanding of where immune cells are implicated in chronic tendinopathy.⁸ The researchers obtained specimen biopsies from 50 patients with non-ruptured chronic Achilles tendinopathy and 15 healthy individuals with the aim of characterising and quantifying immune-competent cells in the tissue and establishing their influence on outcome. Tissue was obtained by biopsy at the time of ultrasound to confirm the diagnosis. The majority of the analysis was undertaken with immunohistochemistry assays to assess the presence of macrophages, haemosiderophages, T lymphocytes, B lymphocytes, NK cells, mast cells, Schwann cells and endothelial cells. A stereological technique was used to quantify their presence and a follow-up clinical examination undertaken at least four years after biopsy to establish the presence or absence of symptoms. As would be expected, the majority of patients had large numbers of macrophages, T lymphocytes, mast cells, and natural killer cells in the tendinopathy group. The quantitative analysis revealed that CD68-KP1+ macrophages and CD34+ endothelial cells were significantly more common in the tendinopathy group, while iron+ haemosiderophages were more commonly observed in those patients who were asymptomatic at final follow-up. This is an important study increasing our understanding the pathophysiology of Achilles tendinopathy. While

most clinicians have taken it as read that there is an inflammatory component to the disease process, the precise mechanisms for this have been unclear. This study illuminates the whole process. Not only have the researchers identified the likely role of macrophages and endothelial cells in tendinopathy, but also that iron+ haemosiderophages are associated with a good eventual prognosis. Here at 360 we would agree with the authors that they have shed new light on the role of immune-competent cells in chronic Achilles tendinopathy.

Infection in orthopaedics: perhaps more simple than first thought?

■ The incidence of post-operative infection in surgical patients has been falling in recent years with the use of decolonisation regimes, targeted antibiotics and novel technologies. It seems that with the reduction in infection rates, the typical pathogens have not changed, with an overwhelming number of infections being *Staphylococcus aureus*-based. What is, however, far from clear is why this is. Are these infections coming from the patients, surgeons or their environment? Researchers in **Lørenskog (Norway)** have devised some clever microbiological analysis looking at nasal carriers of *Staphylococcus aureus* who are known to have an increased risk of surgical infection.⁹ The research team investigated the carrier clones found in the nose of patients with deep surgical infection and those admitted for elective orthopaedic surgery using a genotyping method (multilocus sequence typing and staphylococcal protein A typing). The headline results of this study were that 85% of nasal carriers and 90% of surgical site infection isolates could be classified using the same four multilocus sequence typing clonal complexes. Interestingly, the risk of infection with *Staph. aureus* in nasal carriers compared with non-carriers was

5.8 times higher, and of the nasal carriers, 6.3% developed infection with, in all but one case, an isolate with an identical genotype. Surgical site infections were associated with nasal colonisation in this series, one of the most significant papers on microbiological infection in orthopaedics we have seen in a long time.

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