

PLENARIES

PL3

WHAT IS THE ACL?

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The Anterior Cruciate Ligament (ACL) plays a vital role in maintaining function and stability in the knee. Over the last several decades, much research has been focused on elucidating the anatomy, structural properties, biomechanics, pathology, and optimal treatments for the ACL. Through careful and objective study, the ACL can be understood to be a dynamic structure, rich in neurovascular supply. Although it is referred to as one ligament, it is comprised of two distinct bundles which function synergistically to facilitate normal knee kinematics. The bony morphology of the knee defines normal knee kinematics, as well as the nature of the soft-tissue structures about the knee. Characterized by individual uniqueness, bony morphology varies from patient to patient. The ACL, which is a reflection of each patient's unique bony morphology, is inherently subject to both anatomic and morphologic variation as well. Furthermore, the ACL is subject to physiologic aging, which can affect the anatomic and structural properties of the ligament over time. A successful anatomic ACL Reconstruction, which may be considered the functional restoration of the ACL to its native dimensions, collagen orientation, and insertion sites according to individual anatomy, considers all these principles. It is vital to respect the nature we observe, rather than to "create" nature to fit a one-size-fits-all surgery. Double bundle ACL Reconstruction may therefore be thought of more as a concept rather than a specific technique, one that respects the individual unique anatomy of each patient to provide a truly individualized, anatomic, and value-based ACL Reconstruction.

PL4

INNOVATION IN COMPLEX DEFORMITY CORRECTION IN ORTHOPAEDIC SURGERY

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Complex spinal deformities can cause pain, neurological symptoms and imbalance (sagittal and/or coronal), severely impairing patients' quality of life and causing disability. Their treatment has always represented a tough challenge: prior to the introduction of modern internal fixation systems, the only option was an arthrodesis to prevent worsening of the deformity. Then, the introduction of pedicle screws allowed the surgeons to perform powerful corrective manoeuvres, distributing forces over multiple levels, to which eventually associate osteotomies. In treating flexible coronal deformities, internal fixation and corrective manoeuvres may be sufficient: the combination of high density pedicle screws and direct vertebral rotation revolutionized surgical treatment of scoliosis.

However, spinal osteotomies are needed for correcting complex rigid deformities; the type of osteotomy must be chosen according to the aetiology, type and apex of the deformity. When dealing with large radius deformities, spread over multiple levels and without fusion, multiple posterior column osteotomies such as Smith-Petersen and Ponte (asymmetric, when treating scoliosis) can be performed, dissipating the correction over many levels. Conversely, the management of a sharp, angulated deformity that involves a few vertebral levels and/or with bony fusion, requires more aggressive 3 column osteotomies such as Pedicle Subtraction Osteotomies (PSO), Bone Disc Bone Osteotomies (BDBO) or Vertebral Column Resection (VCR). Sometimes the deformity is so severe that cannot be corrected with only one osteotomy: in this scenario, multilevel osteotomies can be performed.

PL5

TACKLING MUSCULOSKELETAL DISORDERS THROUGH INNOVATIVE TECHNOLOGIES: AN INTEGRATED APPROACH FROM PREVENTION TO RETURN TO WORK

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The future of work brings several challenges and opportunities for occupational health and safety on three major drivers: the rapid progress of technological innovation; demographic changes, in particular ageing of the workforce and migration; and changes in the labour market, especially owing to new ways of performing jobs. Innovation technologies are leading to an overall transformation of industrial processes that offer huge developmental perspectives in the world of work and opportunities for society. In the field of prevention of musculoskeletal disorders, relevant progresses have been made in the clinical setting and in the context of care, also in relation to the ageing society. In the near future, the adaptation of workstations and the implementation of sensors and enabling technologies (collaborative robots and exoskeletons) will offer, together with the innovations in the clinic and orthopaedic surgery, a significant contribution to the reduction of risks from biomechanical overload, as well as support interventions to increase work ability and reduce the impact of disability. However, the potential risk scenarios for health and safety in the workplace, along with the progress in occupational health research, lead to the need for creating an integrated system of skills and approaches to adopt a Prevention through Design perspective. This requires designing and conceiving processes taking into consideration occupational risk prevention and guaranteeing the return to work in a multidisciplinary and integrated perspective.

ORAL COMMUNICATIONS

OC01 FRACTURE HEALING

K1

SKELETAL SYSTEM BIOLOGY AND SMOKE DAMAGE: FROM BASIC SCIENCE TO MEDICAL CLINIC

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Cigarette smoking has a negative impact on the skeletal system by reducing bone mass and increasing the risk of fractures through its direct or indirect effects on bone remodeling. Recent evidence shows that smoking causes an imbalance in bone turnover, making bone vulnerable to osteoporosis and fragility fractures. In addition, cigarette smoking is known to have deleterious effects on fracture healing, as a positive correlation has been shown between the daily number of cigarettes smoked and years of exposure to smoking, although the underlying mechanisms are not fully understood. Smoking is also known to cause several medical and surgical complications responsible for longer hospital stays and a consequent increase in resource consumption. Smoking cessation is, therefore, highly advisable to prevent the onset of metabolic bone disease. However, some of the consequences appear to continue for decades. Based on this evidence, the aim of our work was to assess the impact of smoking on the skeletal system, particularly bone fractures, and to identify the pathophysiological mechanisms responsible for the impairment of fracture healing. Because smoking represents a major public health problem, understanding the association between cigarette smoking and the occurrence of bone disease is necessary in order to identify potential new targets for intervention.

OC01.1

META-ANALYSIS OF HEALING RATE OF NONUNION AND DELAYED UNION FOR LOW-INTENSITY PULSED ULTRASOUND (LIPUS)

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Introduction and Objective

Nonunion is incomplete healing of fracture and fracture that lacks potential to heal without further intervention. Nonunion commonly presents with persistent pain, swelling, or instability. Those symptoms affect patient quality of life. It is known that using low intensity pulsed ultrasound (LIPUS) for fresh fractures promotes healing. However, effectiveness of LIPUS for nonunion is still controversial. If LIPUS is prove to be effective for healing nonunion, it can potentially provide an alternative to surgery. In addition, we can reduce costs by treating nonunion with LIPUS than performing revision surgery.

Materials and Methods

The two authors carried out a systematic search of PubMed, Ovid MEDLINE, and the Cochrane Library. Meta-analysis of healing rate in nonunion and delayed union patients who underwent LIPUS was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) instruction method using a random effects model.

Results

The initial search identified 652 articles. Of these, 541 were excluded on the basis of the title because they were either a review paper or covered an unrelated topic. The abstracts of the remaining 111 articles were examined further. That review resulted in a sample of 12 articles. We performed a meta-analysis with a random effects model using Open Meta Analyst software. The result of pooled effect size of healing rate was 73.4% (95%CI: 65.3-81.6%). Due to the fact that nonunion lacks potential to heal without further intervention, we suggest that the therapeutic effect of 73.4% from LIPUS is sufficiently effective. As far as we know, there are no trials comparing the therapeutic effectiveness of surgery and LIPUS, so it cannot be said which is more advantageous. However, the healing rate of revision surgery was reported between 68-96%; therefore, our result is within that range. Thus, if surgery is difficult due to complications, we can recommend LIPUS.

Conclusions

Meta-analysis of healing rate of nonunion treated by low-intensity pulsed ultrasound is 73.4%, which suggests sufficient therapeutic effectiveness. Furthermore, we can say that LIPUS may provide an alternative treatment for nonunion patients who cannot tolerate revision surgery due to complications

OC01.2

A ROBUST TREATMENT ALGORITHM FOR PILON FRACTURES: OUR MANAGEMENT AND OUTCOMES

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Introduction and Objective

Despite the low incidence of pilon fractures among lower limb injuries, their high-impact nature presents difficulties in surgical management and recovery. Current literature includes a wide range of different management strategies, however there is no universal treatment algorithm. We aim to determine clinical outcomes in patients with open and closed pilon fractures, managed using a treatment algorithm that was applied consistently over the span of this study.

Materials and Methods

This retrospective study was conducted at a single institution, including 141 pilon fractures in 135 patients, from August 2014 to January 2021. AO/OTA classification was used to classify fractures. Among closed fractures, 12 had type 43A, 18 had type 43B, 61 had type 43C. Among open fractures, 11 had type 43A, 12 had type 43B, 27 had type 43C. Open fractures were further classified with Gustilo-Anderson (GA); type 1: n=8, type 2: n=10, type 3A: n=12, type 3B: n=20. Our treatment algorithm consisted of fine wire fixator (FWF) for severely comminuted closed fractures (AO/OTA type 43C3), or open fractures with severe soft tissue injury (GA type 3). Otherwise, open reduction internal fixation (ORIF) was performed. When required, minimally invasive osteosynthesis (MIO) was performed in combination with FWF to improve joint congruency. All open fractures, and closed fractures with severe soft tissue injury (skin contusion, fracture blister, severe oedema) were initially treated with temporary ankle-spanning external fixation. For all open fracture patients, surgical debridement, soft tissue cover with a free or pedicled flap were performed. For GA types 1 and 2, this was done with ORIF in the same operating session. Those with severe soft tissue injury (GA type 3) were treated with FWF four to six weeks after soft tissue management was completed. Primary outcome was AOFAS Ankle-Hindfoot score at 3, 6 and 12-months post-treatment. Secondary outcomes include time to partial weight-bear (PWB) and full weight-bear (FWB), bone union time. All complications were recorded.

Results

Mean AOFAS score 3, 6, and 12 months post-treatment for open and closed fracture patients were 44.12 and 53.99 (p=0.007), 62.38 and 67.68 (p=0.203), 78.44 and 84.06 (p=0.256), respectively. 119 of the 141 fractures healed without further intervention (84.4%). Average time to bone union was 51.46 and 36.48 weeks for open and closed fractures, respectively (p=0.019). Union took longer in closed fracture patients treated with FWF than ORIF (p=0.025). On average, open and closed fracture patients took 12.29 and 10.76 weeks to PWB (p=0.361); 24.04 and 20.31 weeks to FWB (p=0.235), respectively. Common complications for open fractures were non-union (24%), post-traumatic arthritis (16%); for closed fractures they were post-traumatic arthritis (25%), superficial infection (22%). Open fracture was a risk factor for non-union (p=0.042; OR=2.558, 95% CI 1.016-6.441), bone defect (p=0.001; OR=5.973, 95% CI 1.986-17.967), and superficial infection (p<0.001; OR=4.167, 95% CI 1.978-8.781).

Conclusions

The use of a two-staged approach involving temporary external fixation followed by definitive fixation, provides a stable milieu for soft tissue recovery. FWF combined with MIO, where required for severely

comminuted closed fractures, and FWF for open fractures with severe soft tissue injury, are safe methods achieving low complication rates and good functional recovery.

OC01.3

PLATELET-RELEASED FACTORS INDUCE AN IMMUNE REGULATORY SIGNATURE IN BONE MARROW MESENCHYMAL STROMAL CELLS

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Introduction and Objective

The early pro-inflammatory hematoma phase of bone healing is characterized by platelet activation followed by growth factor release. Bone marrow mesenchymal stromal cells (MSC) play a critical role in bone regeneration. However, the impact of the pro-inflammatory hematoma environment on the function of MSC is not fully understood. We here applied platelet-rich plasma (PRP) hydrogels to study how platelet-derived factors modulate functional properties of MSC in comparison to a non-inflammatory control environment simulated by fibrin (FBR) hydrogels.

Materials and Methods

MSC were isolated from acetabular bone marrow of patients undergoing hip arthroplasty. PRP was collected from pooled apheresis thrombocyte concentrates. The phenotype of MSC was analyzed after encapsulation in hydrogels or exposure with platelet-derived factors with regards to gene expression changes, cell viability, extracellular vesicle (EV) release and immunomodulatory effects utilizing cellular and molecular, flow cytometry, RT-PCR, western blot and immunofluorescence stainings.

Results

Our results showed that encapsulation of MSC in PRP induced changes in cell metabolism increasing lactate production and reducing mitochondria membrane potential. This was followed by significantly decreased mTOR phosphorylation and differential gene regulation. While PRP-released factors could support EV-biogenesis and immunoregulation-related gene expression, FBR hydrogel reduced CD63+ and CD81+ EV release by MSC. In co-cultures with mitogen stimulated PBMC, pre-exposure of MSC with PRP reduced the proliferation rate and frequency of peripheral blood CD4+ and favored the persistence of FOXP3+ regulatory T lymphocytes (32±4.7% compared to 9±2.3% in control co-cultures where MSC were exposed to FBR).

Conclusions

Our data indicate that exposure of MSC with a hematoma environment causes metabolic adaptation of MSC followed by increased immune regulatory functions, which in turn might contribute to resolution of inflammation required for successful bone healing.

OC01.4

IS POSTOPERATIVE NON-WEIGHT-BEARING NECESSARY? (INWN) A PRAGMATIC RANDOMISED MULTICENTRE TRIAL OF OPERATIVELY TREATED ANKLE FRACTURE

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Introduction and Objective

Ankle fractures are common and affect young adults as well as the elderly. An unstable ankle fracture treatment typically involves surgical fixation, immobilisation, and modified weight-bearing for six weeks. Non-weight bearing (NWB) cast immobilisation periods were used to protect the soft tissue envelope and osteosynthesis. This can have implications on patient function and may reduce independence, mobility and return to work. Newer trends in earlier mobilisation compete with traditional NWB doctrine, and weak consensus exists as to the best postoperative strategy. The purpose of this trial is to investigate the safety and efficacy of immediate weight-bearing (IWB) and range of motion (ROM) exercise regimes following ORIF of unstable ankle fractures with a particular focus on functional outcomes and complication rates.

Materials and Methods

A pragmatic randomised controlled multicentre trial, comparing IWB in a walking boot and ROM within 24 hours versus non-weight-bearing (NWB) and immobilisation in a cast for six weeks, following ORIF of all types of unstable adult ankle fractures (lateral malleolar, bimalleolar, trimalleolar with or without syndesmotic injury). The exclusion criteria are skeletal immaturity and tibial plafond fractures. The primary outcome measure is the functional Olerud-Molander Ankle Score (OMAS). Secondary outcomes include wound infection (deep and superficial), displacement of osteosynthesis, the full arc of ankle motion (plantar flexion and dorsal flexion), RAND-36 Item Short Form Survey (SF-36) scoring, time to return to work and postoperative hospital length of stay.

Results

We recruited 160 patients with an unstable ankle fracture. Participants' ages ranged from 15 to 94 years (M, 45.5 = SD, 17.2 = with 54% identified as female). The mean time from injury to surgical fixation was 1.3 days (0 to 17 days). Patients in the immediate weight-bearing group had a 9.5-point higher mean OMAS at six weeks postoperatively (95% CI 1.48, 17.52) P = 0.021. The complications rate was similar in both groups. The rate of surgical site infection was 4.3%. One patient had DVT, and another patient had a pulmonary embolism; both were randomised to NWB. Length of hospital stay (LOS) was 1(12, 0) 1.5 ± for the IWB group vs 1.5 ± 2.5 (0, 19) for the NWB group.

Conclusions

There is a paucity of quality evidence supporting the postoperative management regimes used most commonly in clinical practice. To our knowledge, immediate weight-bearing (IWB) following ORIF of all types of unstable ankle fractures has not been investigated in a controlled prospective manner in recent decades. In this large multicentre, randomised controlled trial, we investigated immediate weight-bearing following ORIF of all ankle fracture patterns in the usual care condition using standard fixation methods. Our result suggests that IWB following ankle fracture fixation is safe and resulted in a better functional outcome. Once anatomical reduction and stable internal fixation is achieved, we recommend IWB in all types of ankle fractures in a compliant patient.

OC02 BIOMATERIALS

K2

UNDERSTANDING THE REGENERATIVE RESPONSE INDUCED BY BIOMATERIALS SYSTEMS: INSIGHT INTO THE ROLE OF GLYCOSYLATION

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Biomaterials are no longer considered innate structures and using functionalisation and biofabrication strategies to modulate a desired response whether it is a host or implant is currently an important focus in current research paradigms. Fundamentally, a thorough understanding of the host response will enable us to design appropriate strategies. The input from the host response needs to be weighed in depending on the host disease condition. Our current inputs have been through a thorough understanding of glyco-proteomics based tools which we are developing in our laboratory. In addition, biomaterials themselves provide immense therapeutic benefits which needs to be accounted in the design paradigm. Using functionalisation strategies such as enzymatic and hyperbranched linking systems, we have been able to link biomolecules to different structural moieties. The programmed assembly of biomolecules into higher-order self-organized systems is central to innumerable biological processes and development of the next generation of scaffolds. Recent design efforts have utilized a glycobiology and developmental biology approach toward both understanding and engineering supramolecular protein and sugar assemblies.

OC02.1

UNDERSTANDING THE IMMUNOBIOLOGY OF ORTHOPAEDIC BIOMATERIALS

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Introduction and Objective

Total joint replacement (TJR) is indicated for patients with end-stage osteoarthritis (OA) where conservative treatment has failed. Approximately 1.3 million primary hip replacement surgeries have been recorded in the United Kingdom since 2003 and this number is set to rise due to an increase in obesity as well as an ageing population. Total hip replacement (THR) has a survival rate of 85% at 20 years; the most common reason for failure is aseptic loosening which often occurs secondary to osteolysis caused by immune-mediated inflammation responses to wear debris generated from the materials used in the THR implant. Therefore, by understanding the biological steps by which biomaterials cause immune-mediated reactions it should be possible to prevent them in the future thereby reducing the number of costly revision surgeries required.

Materials and Methods

The human osteoblast-like cell line (MG-63) was seeded at a density of 100,000 cell per well of a 6-well plate and treated with increasing doses (0.5, 5, and 50mm³ per cell) of cobalt-chromium (CoCr) particles generated on a six-station pin-on-plate wear generator or commercially available ceramic oxide nanopowders (Al₂O₃ and ZrO₂) for 24 hours. TNF-alpha was used as a positive control and untreated cells as a negative control. Cells were then analysed by transmission electron microscopy (TEM) to determine whether the osteoblasts were capable of phagocytosing these biomaterials. MG-63 cells were used in conjunction with trypan blue and the XTT Cell Proliferation II Kit to assess cytotoxicity of the biomaterials investigated. Cells supernatants were also collected and analysed by enzyme-linked immunosorbant assay (ELISA) to investigate changes in pro-inflammatory protein secretion. Protein extracted from lysed cells was used for western blotting analysis to investigate RANKL protein expression to determine changes to osteolytic activation. Lysed cells were also used for RNA extraction and subsequent cDNA synthesis for real-time quantitative polymerase chain reaction (RT-qPCR) in order to assess changes to pro-inflammatory gene expression.

Results

There was no significant change to cellular viability or proliferation in the osteoblasts treated with CoCr, Al₂O₃ or ZrO₂ when compared to the untreated negative control. TEM images showed clear and distinct intracellular vesicles within the cell cytoplasm which contained CoCr, Al₂O₃ and ZrO₂. RANKL expression increased at 5 and 50mm³ per cell CoCr and 50mm³ per cell Al₂O₃ and ZrO₂. Pro-inflammatory protein secretion of CXCL10, IL-8, and IL-6 all significantly increased at 50mm³ per cell CoCr, Al₂O₃, and ZrO₂. Similarly to the protein secretion, CXCL10, IL-8, and IL-6 gene expression was significantly upregulated at 50mm³ per cell CoCr, Al₂O₃, and ZrO₂.

Conclusions

Increased in vitro RANKL expression in response to CoCr, Al₂O₃, and ZrO₂ may result in disruption of bone metabolism and lead to osteolysis which can contribute to aseptic loosening in vivo. Significant increases in IL-6 are particularly important because as well as being a pro-inflammatory cytokine, IL-6 is also secreted by osteoblasts in order to stimulate mature osteoclast formation to mediate bone breakdown. CXCL10 and IL-8 are chemotactic cytokines and increased secretion in response to implant biomaterials can contribute to ongoing pro-inflammatory responses through the recruitment of monocytes and neutrophils respectively.

This is interesting as in vivo data demonstrates increased cellular infiltrate in patients experiencing responses to implant materials. Overall, these findings show clear immune activation as well as altered metabolism of MG-63 osteoblast cells in response to implant wear debris which is in agreement with in vivo clinical reports.

OC02.2

BRIDGE LOCAL CARTILAGE DEFECTS WITH A TITANIUM-FOAM-POLYMER COMPOUND?

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Introduction and Objective

Local cartilage defects in the knee are painful and mostly followed by arthritis. In order to avoid impaired mobility, the osteochondral defect might be bridged by a synthetic compound material: An osteoconductive titanium foam as an anchoring material in the subchondral bone and an infiltrated polymer as gliding material in contact with the surrounding natural cartilage.

Materials and Methods

Titanium foam cylinders (Ø38 mm) with porosities ranging from 57% to 77% were produced by powder metallurgy with two different grain sizes of the space holder (fine: $340 \pm 110 \mu\text{m}$, coarse: $530 \pm 160 \mu\text{m}$). The sintered titanium foam cylinders were infiltrated with UHMWPE powder on one end and UHMWPE bulk at the other end, at two different temperatures (160 °C, 200 °C), using a pressure of 20 MPa for 15 minutes. Smaller cylinders (Ø16 mm) were retrieved from the compound material by water jet cutting. The infiltration depths were determined by optical microscopy. The anchoring of the UHMWPE was measured by a shear test and the mechanical properties of the titanium foam were verified by a subsequent compression test. The tribological behaviour was investigated in protein containing liquid using fresh cartilage pins (Ø5 mm) sliding against a UHMWPE disc with or without a notch to simulate the gap between the implant and the surrounding cartilage. Friction coefficients were determined in a rotation tribometer and the cartilage wear in a multidirectional six-station tribometer from AMTI (load 10 - 50 N, sliding speed 20 mm/s, 37 °C).

Results

UHMWPE could be infiltrated into titanium foam by 1.1 - 1.3 mm with fine pores and by 1.5 - 1.8 mm with coarse pores. The infiltration was neither dependent on the type of UHMWPE (powder or bulk) nor on the temperature. The polymer was so well anchored inside the titanium foam pores that the shear forces for the compounds exceeded the shear strength obtained for a UHMWPE-cylinder. This effect was due to the increased stiffness of the compound plug. Uniaxial compression of the titanium foams after the shear-off of the polymer revealed yield strengths ranging from 50 - 88 MPa for porosities of 62 - 73%. The Ø16 mm samples yielded beyond physiological loads in the knee ($\geq 10x$ body weight) and behaved in a strain hardening and fully ductile manner, reaching deformations of at least 50 % of their initial height without the appearance of macroscopically visible cracks. For smaller plug diameters down to Ø8 mm, however, the lower porosity / higher strength foam should be used to limit elastic deformation of the compound to < 0.1 mm. Pore size did not significantly influence the strength and stiffness values. The elevated coefficient of friction between cartilage and UHMWPE of about 1 was not negatively affected by the presence of the gap. The height loss of the cartilage pin after 1 hour (respectively after 3600 reciprocating wear cycles) was 0.2 ± 0.1 mm using a flat disc. For discs with a 1 mm wide V-notch, the wear increased to 0.9 ± 0.3 mm.

Conclusions

The tested titanium foams are well suited to act as an anchoring material in the subchondral bone as mechanical properties can be tailored by choosing the adequate porosity and as bone ingrowth has previously been demonstrated for the used pore sizes. UHMWPE is not an ideal gliding partner against cartilage because the friction coefficients of frictions were high. The presence of a V-notched gap was detrimental for cartilage wear. More hydrophilic polymers like PCU should be tested as potential gliding materials.

OC02.3

THE EFFECT OF SIMVASTATIN ON COBALT-MEDIATED INFLAMMATORY CYTOKINE EXPRESSION

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Introduction and Objective

Total joint replacement is indicated for osteoarthritis where conservative treatment has failed, and in the UK the number of patients requiring hip and knee replacements is set to increase with an ageing population. Survival of total hip replacements is around 85% at 20 years with the most common reason for revision being aseptic loosening of the implant secondary to osteolysis, which is caused by immune-mediated reactions to implant debris. These debris can also cause pseudotumour formation. As revision surgery is associated with higher morbidity, mortality, infection rates, venous thromboembolism, resource demand and poorer subsequent function it is important to understand the mechanisms underlying the pro-inflammatory process to improve implant survival. Toll-like receptor 4 (TLR4), an innate immune receptor, has been demonstrated to mediate deleterious immune responses by the Tyson-Capper research group, including inflammatory cytokine interleukin-8 (IL-8) secretion. Statin use in epidemiological studies has been associated with reduced overall risk of revision surgery after hip replacement. In-vitro studies have demonstrated the potential for statins to reduce orthopaedic debris-induced immune responses which can lead to osteolysis and pseudotumour formation. As literature from cardiological investigations demonstrate that statins can reduce the expression and responsiveness of TLR4, this could be an exciting mechanism to exploit to reduce the host immune response to orthopaedic wear debris, thereby improving implant survival by reducing immune mediated osteolysis. This ongoing study investigates simvastatin's effect on cobalt ion-mediated changes in gene and protein expression of interleukin-8 and soluble-ICAM-1 (sICAM-1) which is an angiogenic factor implicated in pseudotumour formation.

Materials and Methods

TLR4-expressing human monocyte/macrophage THP-1 cells were pre-incubated with 50µM simvastatin for 2-hours or a vehicle control, before being exposed to 0.75mM cobalt chloride, in addition to a further 24-hour co-incubation with 50µM simvastatin or vehicle control. IL-8 protein and sICAM-1 secretion was measured by enzyme-linked immunosorbent assay (ELISA). Gene expression changes were quantified by TaqMan-based real time polymerase chain reaction.

Results

Pre-treatment with simvastatin significantly reduced cobalt-mediated IL-8 protein secretion (n=3) and sICAM-1 protein secretion (n=2) in THP-1 cells (p-value<0.0001). Work will be undertaken to determine changes in gene expression, the role of TLR4 in these responses and the effect of simvastatin on additional inflammatory markers.

Conclusions

Simvastatin significantly reduces cobalt-ion mediated IL-8 and sICAM-1 protein secretion in THP-1 cells. This in-vitro finding demonstrates the potential for simvastatin to reduce recruitment of leukocytes which mediate the deleterious inflammatory processes driving aseptic loosening and pseudotumour formation.

OC02.4

IN VITRO AND IN VIVO RESPONSE TO HYBRID FUNCTIONALIZED COLLAGEN MEMBRANE FOR DENTAL APPLICATIONS

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Introduction and Objective

Alveolar bone resorption following tooth extraction or periodontal disease compromises the bone volume required to ensure the stability of an implant. Guided bone regeneration (GBR) is one of the most attractive technique for restoring oral bone defects, where an occlusive membrane is positioned over the bone graft material, providing space maintenance required to seclude soft tissue infiltration and to promote bone regeneration. However, bone regeneration is in many cases impeded by a lack of an adequate tissue vascularization and/or by bacterial contamination. Using simultaneous spray coating of interacting species (SSCIS) process, a bone inspired coating made of calcium phosphate-chitosan-hyaluronic acid was built on one side of a nanofibrous GBR collagen membrane in order to improve its biological properties.

Materials and Methods

First, the physicochemical characterizations of the resulting hybrid coating were performed by scanning electron microscopy, X-ray photoelectron, infrared spectroscopies and high-resolution transmission electron microscopy. Then human mesenchymal stem cells (MSCs) and human monocytes were cultured on those membranes. Biocompatibility and bioactivity of the hybrid coated membrane were respectively evaluated through MSCs proliferation (WST-1 and DNA quantification) and visualization; and cytokine release by MSCs and monocytes (ELISA and endothelial cells recruitment). Antibacterial properties of the hybrid coating were then tested against *S. aureus* and *P. aeruginosa*, and through MSCs/bacteria interactions. Finally, a preclinical in vivo study was conducted on rat calvaria bone defect. The newly formed bone was characterized 8 weeks post implantation through μ CT reconstructions, histological characterizations (Masson's Trichrome and Von Kossa stain), immunohistochemistry analysis and second harmonic generation. Biomechanical features of newly formed bone were determined.

Results

The resulting hybrid coating of about 1 μ m in thickness is composed of amorphous calcium phosphate and carbonated poorly crystalline hydroxyapatite, wrapped within chitosan/hyaluronic acid polysaccharide complex. Hybrid coated membrane possesses excellent bioactivity and capability of inducing an overwhelmingly positive response of MSCs and monocytes in favor of bone regeneration. Furthermore, the antibacterial experiments showed that the hybrid coating provides contact-killing properties by disturbing the cell wall integrity of Gram-positive and Gram-negative bacteria. Its combination with MSCs, able to release antibacterial agents and mediators of the innate immune response, constitutes an excellent strategy for fighting bacteria. A preclinical in vivo study was therefore conducted in rat calvaria bone defect. μ CT reconstructions showed that hybrid coated membrane favored bone regeneration, as we observed a two-fold increase in bone volume / total volume ratios vs. uncoated membrane. The histological characterizations revealed the presence of mineralized collagen (Masson's Trichrome and Von Kossa stain), and immunohistochemistry analysis highlighted a bone vascularization at 8 weeks post-implantation. However, second harmonic generation analysis showed that the newly formed collagen was not fully organized. Despite a significant increase in the elastic modulus of the newly formed bone with

hybrid coated membrane (vs. uncoated membrane), the obtained values were lower than those for native bone (approximately 3 times less).

Conclusions

These significant data shed light on the regenerative potential of such bioinspired hybrid coating, providing a suitable environment for bone regeneration and vascularization, as well as an ideal strategy to prevent bone implant-associated infections.

OC03 ARTHROPLASTY

OC03.1

TRAUMA AND ACUTE ORTHOPAEDICS WORKLOAD DURING COVID-19 LOCKDOWN

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Introduction and Objective

In anticipation of reduced workload and need for minimisation of staff contact with infectious patients during the COVID-19 lockdown in 2020, Cairns Hospital reduced the junior orthopaedic staffing and absolved team structure.

Materials and Methods

We performed a retrospective audit of our department's workload during a predetermined three week period during the 2020 lockdown and in 2019.

Results

699 patient referrals from Emergency Department were captured; 358 in 2019 and 341 in 2020, a decrease of 4.7%. The same proportion were admitted (64.5%); similar numbers required operative intervention; 51.7% (2019) vs 50.1% (2020). There was a small reduction in spine and neck of femur fracture presentations (2% and 0.9% respectively). Common presentations such as supracondylar fractures and distal radius fractures remained nearly unchanged (increased 0.7% and 0.2% respectively). Overall, the referred patients' demographics were essentially unchanged. Department workforce was reduced by 45% (20 vs 11 doctors). Elective operating, excluding category 1, was suspended, resulting in an overall reduction of total admissions and operations by 29.7%. The average length of stay of inpatients increased by 25.3% (2.5 vs 3.16 days).

Conclusions

During lockdown, the acute orthopaedic burden remained almost unchanged. Despite a reduction in inpatient patient load, the average length of stay increased. This was multifactorial, including staffing reduction disproportional to workload, loss of team structure and continuity of care, and government enforced restrictions to the Cape York region. This can be used in future for planning the staffing allocation if further lockdowns are enforced during this, or future, pandemic.

OC03.2

RESIDUAL FUNCTIONAL IMPAIRMENT FOLLOWING HIP AND KNEE ARTHROPLASTY

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Introduction and Objective

An important subset of patients is dissatisfied after total joint arthroplasty (TJA) due to residual functional impairment. This study investigated the assessment of objectively measured step-up performance following TJA, to identify patients with poor functional improvement after surgery, and to predict residual functional impairment during early postoperative rehabilitation. Secondary, longitudinal changes of block step-up (BS) transfers were compared with functional changes of subjective patient reported outcome measures (PROMs) following TJA.

Materials and Methods

Patients with end stage hip or knee osteoarthritis (n = 76, m/f = 44/32; mean age = 64.4 standard deviation 9.4 years) were measured preoperatively and 3 and 12 months postoperatively. PROMs were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) function subscore. BS transfers were assessed by wearable-derived measures of time. In our cohort, subgroups were formed based on either 1) WOMAC function score or 2) BS performance, isolating the worst performing quartile (impaired) of each measure from the better performing others (non-impaired). Subgroup comparisons were performed with the Man-Whitney-U test and Wilcoxon Signed rank test resp. Responsiveness was calculated by the effect size, correlations with Pearson's correlation coefficient. A regression analysis was conducted to investigate predictors of poor functional outcome.

Results

WOMAC function scores were strongly correlated to WOMAC pain scores (Pearson's $r=0.67-0.84$) and moderately correlated to BS performance (Pearson's $r = 0.31-0.54$). Prior to surgery, no significant differences for WOMAC function scores and BS performance were found between the impaired and non-impaired subgroups. One year after TJA, our cohort performed significantly better at WOMAC and BS with largest effect size for the non-impaired subgroups (0.62 and 0.43 resp.) At 12 months postop, 56% of patients allocated to the impaired subgroup defined by WOMAC, represented the impaired subgroup defined by BS. Allocation to the impaired subgroup at 3 months postop, raised the odds for belonging to the impaired subgroup at 12 months for WOMAC with an odds ratio=19.14 (67%) and for BS with an odds ratio=4.41 (42%).

Conclusions

Assessment of BS performance following TJA reveals residual functional impairment that is not captured by pain-dominated PROMs. Its additional use may help to early identify those patients at risk for a poor outcome.

OC03.3

A RANDOMISED CONTROLLED TRIAL OF TOTAL HIP ARTHROPLASTY VERSUS PROGRESSIVE RESISTANCE TRAINING IN PATIENTS WITH SEVERE HIP OSTEOARTHRITIS: STUDY PROTOCOL FOR THE PROHIP TRIAL

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Introduction and Objective

Hip osteoarthritis (OA) is the leading cause for total hip arthroplasty (THA). Although, being considered as the surgery of the century up to 23% of the patients report long-term pain and deficits in physical function and muscle strength may persist after THA. Progressive resistance training (PRT) appear to improve several outcomes moderately in patients with hip OA. Current treatment selection is based on low-level evidence as no randomised controlled trials have compared THA to non-surgical treatment. The primary objective of this trial is to determine the effectiveness of THA followed by standard care compared to 12 weeks of supervised PRT followed by 12 weeks of optional unsupervised PRT, on changes in hip pain and function, in patients with severe hip OA after 6 months.

Materials and Methods

This is a protocol for a multicentre, parallel-group, assessor blinded, randomised controlled superiority trial. Patients aged ≥ 50 years with clinical and radiographic hip OA found eligible for THA by an orthopaedic surgeon will be randomised to THA or PRT (allocation 1:1). The primary outcome will be change in patient-reported hip pain and function, measured using the Oxford Hip Score. Key secondary outcomes will be change in the Hip disability and Osteoarthritis Outcome Score subscales, University of California Los Angeles Activity Score, 40-meter fast-paced walk test, 30-second chair stand test, and number of serious adverse events.

Results

The trial has been approved by The Regional Committees on Health Research Ethics for Southern Denmark (Project-ID: S-20180158) in February 2019 and registration was performed at ClinicalTrials.gov (NCT04070027) in August 2019. Recruitment was initiated on the 2nd of September 2019 and the final deadline will be on the 30th of June 2021, or when a sample size of 120 patients has been accomplished.

Conclusions

The results of the current trial are expected to enable evidence-based recommendations, which may be used to facilitate the shared-decision making process in the discussion of treatment strategy for the individual patient with severe hip OA. All results will be presented in peer-reviewed scientific journals and international conferences.

OC03.4

CLINICAL AND FUNCTIONAL OUTCOMES OF KINEMATIC ALIGNED TOTAL KNEE ARTHROPLASTY WITH MEDIAL PIVOT DESIGN: A SHORT-TERM FOLLOW UP

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Introduction and Objective

Kinematic Alignment (KA) is a surgical technique that restores the native knee alignment following Total Knee Arthroplasty (TKA). The association of this technique with a medial pivot implant design (MP) attempts to reestablish the physiological kinematics of the knee. Aim of this study is to analyze the clinical and radiological outcomes of patients undergoing MP-TKA with kinematic alignment, and to assess the effect of the limb alignment and the orientation of the tibial component on the clinical outcomes.

Materials and Methods

We retrospectively analyzed 63 patients who underwent kinematic aligned medial pivot TKA from September 2018 to January 2020. Patient-Related Outcomes (PROMs) and radiological measures were collected at baseline, 3 months and 12 months after surgery.

Results

We demonstrated a significant improvement in the clinical and functional outcomes starting from 3 months after surgery. This finding was also confirmed at the longest follow-up. The clinical improvement was independent from the limb alignment and from the orientation of the tibial component. The radiological analysis showed that the patient's native limb alignment was restored, and that the joint line orientation maintained the parallelism to the floor when standing. This latter result has a particular relevance, as it may positively influence the outcomes, reducing the risk of wear and mobilization of the implant.

Conclusions

The association of kinematic alignment and a medial pivot TKA implant allows for a fast recovery, good clinical and functional outcomes, independently from the final limb alignment and the tibial component orientation.

OC03.5

CT-BASED PREOPERATIVE PLANNING AND 3D-RECONSTRUCTIONS WITH ALLOGRAFT BONE IN REVERSE SHOULDER ARTHROPLASTY REVISION SURGERY ASSOCIATED WITH CRITICAL SIZE BONE DEFECT: A CASE REPORT

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Introduction and Objective

In recent years, along with the extending longevity of patients and the increase in their functional demands, the number of annually performed RSA and the incidence of complications are also increasing. When a complication occurs, the patient often needs multiple surgeries to restore the function of the upper limb. Revision implants are directly responsible for the critical reduction of the bone stock, especially in the shoulder. The purpose of this paper is to report the use of allograft bone to restore the bone stock of the glenoid in the treatment of an aseptic glenoid component loosening after a reverse shoulder arthroplasty (RSA).

Materials and Methods

An 86-years-old man came to our attention for aseptic glenoid component loosening after RSA. Plain radiographs showed a complete dislocation of the glenoid component with 2 broken screws in the neck of glenoid. CT scans confirmed the severe reduction of the glenoid bone stock and critical bone resorption and were used for the preoperative planning. To our opinion, given the critical bone defect, the only viable option was revision surgery with restoration of bone stock. We planned to use a bone graft harvested from distal bone bank femur as component augmentation. During the revision procedure the baseplate with a long central peg was implanted "on table" on the allograft and an appropriate osteotomy was made to customize the allograft on the glenoid defect according to the CT-based preoperative planning. The Bio-component was implanted with stable screws fixation on residual scapula. We decided not to replace the humeral component since it was stable and showed no signs of mobilization.

Results

The new bio-implant was stable, and the patient gained a complete functional recovery of the shoulder. The scheduled radiological assessments up to 12 months showed no signs of bone resorption or mobilization of the glenoid component.

Conclusions

The use of bone allograft in revision surgery after a RSA is a versatile and effective technique to treat severe glenoid bone loss and to improve the global stability of the implant. Furthermore, it represents a viable alternative to autologous graft since it requires shorter operative times and reduces graft site complications. There are very few data available regarding the use of allografts and, although the first studies are encouraging, further investigation is needed to determine the biological capabilities of the transplant and its validity in complex revisions after RSA.

OC03.6

PERFORMANCE OF LOWER LIMB PERIPHERAL NERVE BLOCKS AMONG DIFFERENT ORTHOPEDIC SUB-SPECIALTIES: A SINGLE INSTITUTION EXPERIENCE IN 246 PATIENTS

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Introduction and Objective

Continuous peripheral nerve blocks (cPNBs) have shown good results in pain management after orthopedic surgeries. However, the variation of performance between different subspecialties is unknown. The aim of this study is to describe our experience with cPNBs after lower limb orthopedic surgeries in different subspecialties.

Materials and Methods

This prospective cohort study was performed on collected data from cPNBs after orthopedic surgeries in lower limbs. Catheters were placed by experienced anesthesiologists using sterile technique. After catheterization, the patients were examined daily, by specially educated acute pain service nurses. The characteristics of the patients, duration of catheterization, severity of the post-operative pain, need for additional opioids, and possible complications were registered.

Results

We included 246 patients (=547 catheters). 115 (21%) femoral, 162 (30%) saphenous, 66 (12%) sciatic, and 204 (37%) popliteal sciatic nerve catheter were used. The median duration of a catheter was 3 days [IQR = 2 – 5]. The proportion of femoral, sciatic, saphenous, and popliteal nerve catheters with duration of more than two days was 81%, 79%, 73%, and 71% for, respectively. This proportion varied also between different subspecialties. 91% of the catheters remained in place for more than two days in amputations (n=56), 89% in pediatric surgery (n=79), 76% in trauma (n=217), 64% in foot and ankle surgery (n=129), and 59% in limb reconstructive surgery (n=66). The proportion of pain-free patients were 77 – 95% at rest, 63 – 88% at mobilization. 79 – 92% did not need increased opioid doses, and 50 – 67% did not require PRN opioid. 443 catheters (81%) were removed as planned. The cause of unplanned catheter removal was loss of efficacy in 69 (13%), dislodgement in 23 (4.2%), leakage in 8 (1.5%), and erythema in 4 catheters (0.73%). No major complication occurred.

Conclusions

81% of catheters remained in place until planned removal and opioid usage after surgery was lower than expected. Catheters were efficient in both adult and pediatric surgery; however, a variation was seen between orthopaedic subspecialties regarding duration of nerve catheter usage.

OC04 BIOMECHANICS

K4

NONUNIONS - JUST A BIOMECHANICAL PROBLEM?

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Nonunions occur in situations with interrupted fracture healing process and indicate conditions where the fracture has no potential to heal without further intervention. Per definition, no healing is detected nine months post operation and there is no visible progress of healing over the last three months. The classification of nonunions as hypertrophic, oligotrophic, atrophic and pseudoarthrosis, as well as aseptic or septic, identifies mechanical and biological requirements for fracture healing that have not been met. The overall treatment strategy comprises identification and elimination of the problems. However, current clinical methods to determine the state of healing are based on highly subjective radiographic evaluation or clinical examination.

A data collection telemetric system for objective continuous measurement of the load carried by a bridging smart implant was developed to assess the mechanical stability and monitor bone healing in complicated fracture situations. The first results from a clinical trial show that the system is capable to offer early warning of nonunions or poor fracture healing.

Nonunions are often multifactorial in nature and not just related to a biomechanical problem. Their successful treatment requires consideration of both biological and mechanical aspects. Disturbed vascularity and stability are the most important factors. Infection could be another complicating factor resulting in unpredictable long-time treatment. New technologies for monitoring of fracture healing in addition to radiographic evaluation and clinical examination seem to be promising for early detection of nonunions.

OC04.1

MUSCLE LENGTH AND MUSCLE FORCE CHARACTERISTICS IN PATIENTS WITH SPASTIC CEREBRAL PALSY ARE WEAKLY CORRELATED

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Introduction and Objective

Clinically, it is considered that spastic muscles of patients with cerebral palsy (CP) are shortened, and produce higher force in shorter muscle lengths. Yet, direct quantification of spastic muscles' forces is rare. Remarkably, previous intraoperative tests in which muscle forces are measured directly as a function of joint angle showed for spastic gracilis (GRA) that its passive forces are low, and only a small percentage of its maximum active force is measured in flexed knee positions. However, the relationship of force characteristics of spastic GRA with its muscle-tendon unit length (l_{MTU}) is unknown. Combining intraoperative experiments with participants' musculoskeletal models developed based on their gait analyses, we aimed to test if spastic GRA muscle (1) operates at short l_{MTU} compared to that of typically developing (TD) children, and exerts higher (2) passive and (3) active forces at shorter lengths, within gait-relevant l_{MTU} range.

Materials and Methods

Ten limbs of seven children with CP (GMFCS-II) were tested. Pre-surgery, gait analyses were conducted. Intraoperatively, isometric spastic GRA distal forces were measured in ten hip-knee joint angle combinations, in two conditions: (i) passive state and (ii) maximal activation of the GRA exclusively. In OpenSim, gait_2392 model was used for each limb to calculate l_{MTU} 's per each hip and knee angle combination and the gait-relevant l_{MTU} range, and to analyze gait relevant spastic muscle force - l_{MTU} data. l_{MTU} values were normalized for the participants' thigh lengths. Two-way ANOVA was used to compare the patients' l_{MTU} to those of the seven age-matched TD children to test the first hypothesis. In order to test the second and the third hypotheses, Spearman's rank correlation coefficient (ρ) was calculated to seek a correlation between the muscle's operational length (represented by mean l_{MTU} within gait cycle) and muscular force characteristics (the percent force at shortest l_{MTU} of peak force, either in passive or in active conditions) within gait-relevant l_{MTU} range.

Results

ANOVA showed that l_{MTU} 's of spastic GRA are shorter (on average by 15.4%) compared to those of TD. At the shortest gait-relevant l_{MTU} , the GRA passive force was 84.6 (13.7)% of the peak passive force; and the active force was 55.8 (33.9)% of the peak active force. Passive state forces show an increase at longer lengths, whereas active state force characteristics vary in a patient-specific way. Spearman's rank correlation indicated weak correlations between muscle's operational length and muscular force characteristics ($\rho = -0.30$ $P = 0.40$, and $\rho = -0.27$ $P = 0.45$, for passive and active states, respectively). Therefore, only the first hypothesis was confirmed.

Conclusions

Novel muscle force - l_{MTU} data for spastic GRA were obtained using intraoperative data and modelling combined. The modelling showed in concert with the clinical considerations that spastic GRA may be a shortened muscle. However, because the model does not distinguish the muscle-belly and tendon lengths, it cannot isolate shorter muscle belly length and how this compares to the data of TD children remains unknown. Moreover, the absence of a strong correlation between shorter operational muscle length and higher force production either in passive or in active conditions highlights the influence of other factors (e.g., muscle structural proteins, and muscle mechanical characteristics including intermuscular interactions etc.) on the pathology rather than ascribing it solely to the length of a spastic muscle itself.

OC04.2

SUPERIMPOSITION OF GROUND REACTION FORCE ON PROXIMAL TIBIAL MORPHOLOGY: AN ORIGINAL METHODOLOGY SUPPORTING DIAGNOSIS AND POST-OPERATIVE EVALUATIONS IN HIGH-TIBIAL OSTEOTOMY

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Introduction and Objective

Medial Knee Osteoarthritis (MKO) is associated with abnormal knee varism, this resulting in altered locomotion and abnormal loading at tibio-femoral condylar contacts. To prevent end-stage MKO, medial compartment decompression is selectively considered and, when required, executed via High Tibial Osteotomy (HTO). This is expected to restore normal knee alignment, load distribution and locomotion. In biomechanics, HTO efficacy may be investigated by a thorough analysis of the ground reaction forces (GRF), whose orientation with respect to patient-specific knee morphology should reflect knee misalignment. Although multi-instrumental assessments are feasible, a customized combination of medical imaging and gait analysis (GA), including GRF data, rarely is considered. The aim of this study was to report an original methodology merging Computed-Tomography (CT) with GA and GFR data in order to depict a realistic patient-specific representation of the knee loading status during motion before and after HTO.

Materials and Methods

25 MKO-affected patients were selected for HTO. All patients received pre-operative clinical scoring, and radiological/instrumental assessments; so far, these were also executed post-operatively at 6-month follow-up on 7 of these patients. State-of-the-art GA was performed during walking and more demanding motor tasks, like squatting, stair-climbing/descending, and chair-rising/sitting. An 8-camera motion capture system, combined with wireless electromyography, and force platforms for GRF tracking, was used together with an own established protocol. This marker-set was enlarged with 4 additional skin-based non-collinear markers, attached around the tibial-plateau rim. While still wearing these markers, all analyzed patients received full lower-limb X-ray in standing posture a CT scan of the knee in weight-bearing. Subsequently, relevant DICOMs were segmented to reconstruct the morphological models of the proximal tibia and the additional reference markers, for a robust anatomical reference frame to be defined on the tibia. These marker trajectories during motion were then registered to the corresponding from CT-based 3D reconstruction. Relevant registration matrices then were used to report GRF data on the reconstructed tibial model. Intersection paths of GRF vectors with respect to the tibial-plateau plane were calculated, together with their centroids.

Results

Pre-operative clinical and radiological scoring confirmed MKO and associated abnormal varism. The morphological characterization of GRF was successfully achieved pre- and post- HTO on patient-specific tibial plateau. Pre-operative GFR patterns and peaks, including those related to knee joint moments, were observed medially on the knee, as expected. In post-HTO, these resulted lateralized and much closer to the tibial plateau spine, as desired. In detail, when post- is compared to pre-op, the difference of the centroids were, on average, 54.6 ± 18.1 mm (min÷max: $36.7 \div 72.8$ mm) more lateral during walking and 52.5 ± 28.5 mm ($24.7 \div 87.6$ mm) during stair climbing. When reported in % of the tibial plateau width, these values became 69.2 ± 20.1 ($46.1 \div 81.4$) and 78.1 ± 30.1 ($43.4 \div 98.0$), respectively. Post-op also clinical scores and GA revealed a considerable overall improvement, especially in functional performances.

Conclusions

The reported novel approach allows a combination of motion data, including GFR, and tibial-plateau morphology. Relevant pre- and post-operative routine application offer a quantification of the effect of the original deformity and executed joint realignment, and an assistance for surgical planning in case of HTO as well as ideally in other orthopedic treatments.

OC04.3

THE ROLE OF THE ILIOFEMORAL LIGAMENT IN ENERGY EFFICIENT WALKING

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Introduction and Objective

The human body is designed to walk in an efficient way. As energy can be stored in elastic structures, it is no surprise that the strongest elastic structure of the human body, the iliofemoral ligament (IFL), is located in the lower limb. Numerous popular surgical hip interventions, however, affect the structural integrity of the hip capsule and there is a growing evidence that surgical repair of the capsule improves the surgical outcome. Though, the exact contribution of the iliofemoral ligament in energy efficient hip function remains unelucidated. Therefore, the objective of this study was to evaluate the influence of the IFL on energy efficient ambulation.

Materials and Methods

In order to assess the potential passive contribution of the IFL to energy efficient ambulation, we simulated walking using the large public dataset (n=50) from Schreiber in a the AnyBody musculoskeletal modeling environment with and without the inclusion of the IFL. The work required from the psoas, iliacus, sartorius, quadriceps and gluteal muscles was evaluated in both situations. Considering the large uncertainty on ligament properties a parameter study was included.

Results

A significant reduction in the active component of all hip flexors was observed when the IFL is intact. The required muscle work was found to be reduced by as much as 48% (CI: 29-62%), 61% (CI: 35-84%) and 38% (CI: 2-69%) for the psoas, iliacus, and sartorius muscle respectively. The IFL inclusion has no major effect on the required work from the quadriceps and the gluteal muscle group. The energy storage in the IFL is largest at maximal hip extension and the contribution to forward motion is the largest at the start of the swing phase.

Conclusions

The iliofemoral ligament seems to be a crucial structure in energy efficient walking. The findings support need for meticulous reconstruction of the capsule ligament in case of surgical damage.

OC04.4

DOUBLE PLATING OF UNSTABLE DISTAL FEMORAL FRACTURES: IS AUGMENTED LATERAL PLATING WITH A HELICALLY SHAPED MEDIAL PLATE BIOMECHANICALLY ADVANTAGEOUS OVER A STRAIGHT MEDIAL PLATE?

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Introduction and Objective

Plating of geriatric distal femoral fractures with Locking Compression Plate Distal Femur (LCP-DF) often requires augmentation with a supplemental medial plate to achieve sufficient stability allowing early mobilization. However, medial vital structures may be impaired by supplemental medial plating using a straight plate. Therefore, a helically shaped medial plate may be used to avoid damage of these structures. Aim of the current study was to investigate the biomechanical competence of augmented LCP-DF plating using a supplemental straight versus helically shaped medial plate.

Materials and Methods

Ten pairs of human cadaveric femora with poor bone quality were assigned pairwise for instrumentation using a lateral anatomical 15-hole LCP-DF combined with a medial 14-hole LCP, the latter being either straight or manually pre-contoured to a 90-degree helical shape. An unstable distal femoral fracture AO/OTA 33-A3 was simulated by means of osteotomies. All specimens were biomechanically tested under non-destructive quasi-static and destructive progressively increasing combined cyclic axial and torsional loading in internal rotation, with monitoring by means of optical motion tracking.

Results

Initial axial stiffness and torsional stiffness in internal and external rotation for straight double plating (548.1 ± 134.2 N/mm, 2.69 ± 0.52 Nm/° and 2.69 ± 0.50 Nm/°) was significantly higher versus helical double plating (442.9 ± 133.7 N/mm, 2.07 ± 0.32 Nm/° and 2.16 ± 0.22 Nm/°), $p \leq 0.04$. Initial interfragmentary axial displacement and flexural rotation under 500 N static loading were significantly smaller for straight plating (0.11 ± 0.14 mm and $0.21 \pm 0.10^\circ$) versus helical plating (0.31 ± 0.14 mm and $0.68 \pm 0.16^\circ$), $p < 0.01$. However, initial varus deformation under this loading remained not significantly different between the two fixation methods (straight: $0.57 \pm 0.23^\circ$, helical: $0.75 \pm 0.34^\circ$), $p = 0.08$. During dynamic loading, within the course of the first 4000 cycles the movements of the distal fragment in flexion were significantly bigger for helical over straight plating ($1.03 \pm 0.33^\circ$ versus $0.40 \pm 0.20^\circ$), $p < 0.01$. However, no significant differences were observed between the two fixation methods in terms of varus, internal rotation, axial and shear displacements at the fracture site, and number of cycles to failure.

Conclusions

Augmented lateral plating of unstable distal femoral fractures with use of supplemental helically shaped medial plate was associated with more elastic bone-implant construct behavior under static and dynamic loading compared to straight double plating. Both fixation methods resulted in comparable number of cycles to failure. From a biomechanical perspective, the more elastic helical double plating may be considered as useful alternative to straight plating, potentially reducing stress risers at the distal bone-implant interface due to its ameliorated damping capacities.

OC05 BONE BIOLOGY AND PATHOPHYSIOLOGY

OC05.1

THE IMPACT OF SYNDECAN-1 ON ANGIOGENESIS DURING BONE AGING

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Introduction and Objective

Neoangiogenesis drives the replacement of mineralized cartilage by trabecular bone during bone growth regulated by molecules like e.g. VEGF, OPG and RANKL and the close interaction of progenitors of osteoblasts, chondrocytes, endothelial cells and osteoclasts/chondroclasts. The Heparan sulfate proteoglycan Syndecan-1 (Sdc-1) plays a role in the interaction between osteoclasts and osteoblasts and the development of blood vessels. As the processes of osteogenesis and angiogenesis are closely related to each other in bone, we expected Sdc-1 to have an influence on vessel structure during aging. Therefore, angiogenesis at the growth plate in mice of different ages was compared and the influence of Syndecan-1 deficiency was characterized.

Materials and Methods

Animals: C57BL/6 (WT) and Sdc1^{-/-} mice were used for native bone analysis at 4, 12 and 18 month age. Femura were dissected, cryoprotected and embedded. Histology: Embedded bones were sectioned into 80um thick slices so that the 3D network of the vascularization of the bone could be visualized using an anti-Endomucin antibody and DAPI as counter staining. For semi-automatrical quantification of the vessel bulbs we used a custom made software. In vitro angiogenesis: For aortic ring assay, aortic tissue was isolated from 4 month old mice, cut into 0.5mm rings and embedded in collagen type I matrix. Microvessel outgrowth was quantified after 6 days of culture.

Results

We verified our custom-made software using slices of WT mice and showed that there is no variation of the number of bulbs with regard to the width of the growth plate in periphery versus center zones in all age groups which indicates a homogeneous distribution of angiogenesis throughout the interface of cartilage to newly forming bone. Furthermore, in both, WT and Sdc-1 deficient mice the number of bulbs decreased significantly with age. However, Sdc-1 knockout mice at the age of 4 and 12 month showed a highly significant decrease in angiogenesis close to the growth plate compared to WT mice, whereas in older mice these differences were gone. Quantification of microvessel outgrowth of aortic tissue revealed a significant decrease in number of vessels from rings taken from Syndecan-1 deficient mice compared to WT mice.

Conclusions

Syndecan-1 has a significant impact on neoangiogenesis in vitro and in vivo during aging as demonstrated at the chondro-osseous border of the native bone, emphasizing the importance to further characterize the function of Syndecan-1 regulated processes during enchondral ossification.

OC05.2

THE EFFECT OF CHEMICAL AND MECHANICAL DAMAGE IN A NOVEL OSTEOCHONDRAL EXPLANT FOR PTOA

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Introduction and Objective

Traditionally, osteoarthritis (OA) has been associated mostly with degradation of cartilage only. More recently, it has been established that other joint tissues, in particular bone, are also centrally involved. However, the link between these two tissues remains unclear. This relationship is particularly evident in post-traumatic OA (PTOA), where bone marrow lesions (BMLs), as well as fluctuating levels of inflammation, are present long before cartilage degradation begins. The process of bone-cartilage crosstalk has been challenging to study due to its multi-tissue complexity. Thus, the use of explant model systems have been crucial in advancing our knowledge. Thus, we developed a novel patellar explant model, to study bone cartilage crosstalk, in particular related to subchondral bone damage, as an alternative to traditional femoral head explants or cylindrical core specimens. The commonly used osteochondral explant models are limited, for our application, since they involve bone damage during harvest. The specific aim of this study was to validate this novel patellar explant model by using IL-1B to stimulate the inflammatory response and mechanical stimulation to determine the subsequent developments of PTOA.

Materials and Methods

Lewis rats (n=48) were used to obtain patellar and femoral head explants which were harvested under an institutional ethical approval license. Explants were maintained in high glucose media (containing supplements), under sterile culture conditions. Initially, we characterised undamaged patellar explants and compared them with the commonly used femoral head. First, tissue viability was assessed using an assay of metabolic activity and cell damage. Second, we created chemical and mechanical damage in the form of IL-1B treatment, and mechanical stimulation, to replicate damage. Standard biochemical assays, histological assays and microstructural assays were used to evaluate responses. For chemical damage, explants were exposed to 10ng/ml of IL-1B for 24 hours at 0, 1, 3 and 7 days after harvesting. For mechanical damage, tissues were exposed to mechanical compression at 0.5 Hz, 10 % strain for 10 cycles, for 7 days. Contralateral patellae served as controls. In both groups, sGAG, ADAMTS4, and MMP-13 were measured as an assessment of representative cartilage responses while ALP, TRAP and CTSK were assessed as a representative of bone responses. In addition to this, histomorphometric, and immunohistochemical, evaluations of each explant system were also carried out.

Results

Our results confirm that the patellar explant system is an excellent ex vivo model system to study bone-cartilage crosstalk, and one which does not induce any bone damage at the time of tissue harvest. We successfully established culture conditions to maintain viability in these explants for up to 28 days. Rat IL-1B treatment resulted in increased both proteoglycan content and bone metabolism markers after 7 days when compared with the controls. To confirm this finding, qualitative immunohistochemical staining showed chondrocytes increased expression of MMP13 after treatment with IL-1B. Furthermore, we observed that the levels of ADAMTS4 decreased in 48 hours after IL-1B exposure. Contrastingly IL-1B treatment had the opposite effect on CTSK markers when compared with the control. Mechanically compressed patellae showed a decrease in compressive moduli from day 3 to day 7, suggesting that tissue remodelling may have taken place as a compensatory mechanism in response to damage. In addition, MMP13 release decreased over 48 hours after mechanical compression, while TRAP levels were increased compared with the control.

Conclusions

Thus, we successfully demonstrated that IL-1B and mechanical stimulation affects both bone and cartilage tissues independently in this system, which may have relevance in the understanding of bone-cartilage crosstalk after injury and how this is involved in PTOA development.

OC05.3

THE EFFECT OF TESTOSTERONE TREATMENT UPON BONE REMODELLING IN TESTOSTERONE DEFICIENT APOE^{-/-} MICE FED A HIGH FAT DIET

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Introduction and Objective

Global prevalence of obesity has risen almost three-fold between 1975 and 2016. Alongside the more well-known health implications of obesity such as cardiovascular disease, cancer and type II diabetes, is the effect of male obesity on testosterone depletion and hypogonadism. Hypogonadism is a well-known contributor to the acceleration of bone loss during aging, and obesity is the single biggest risk factor for testosterone deficiency in men. Understanding the micro and macro structural changes to bone in response to testosterone depletion in combination with a high fat 'Western' diet, will advance our understanding of the relationship between obesity and bone metabolism. This study investigated the impact of surgically induced testosterone depletion and subsequent testosterone treatment upon bone remodelling in mice fed a high fat diet.

Materials and Methods

Male ApoE^{-/-} mice were split into 3 groups at 7 weeks of age and fed a high fat diet: Sham surgery with placebo treatment, orchiectomy surgery with placebo treatment, and orchiectomy surgery with testosterone treatment. Surgeries were performed at 8 weeks of age, followed by fortnightly testosterone treatment via injection. Mice were sacrificed at 25 weeks of age. Tibiae were collected and scanned *ex vivo* at 4.3µm on a SkyScan 1272 Micro-CT scanner (Bruker). Left tibiae were used for assessment of trabecular and cortical Volumes of Interest (VOIs) 0.2mm and 1.0mm respectively from the growth-plate bridge break. Tibiae were subsequently paraffin embedded and sectioned at 4µm prior to immunohistochemical evaluation of alkaline phosphatase.

Results

Trabecular bone volume and mineral density were significantly reduced in orchiectomised mice compared to sham-operated controls; and these parameters were normalised to control levels in orchiectomised mice treated with testosterone. In contrast, Trabecular thickness was significantly higher in testosterone depleted animals.

Cortical bone parameters and body weights did not significantly differ between groups.

Levels of alkaline phosphatase did not differ significantly in cortical or trabecular osteoblasts between groups.

Conclusions

Findings suggest that testosterone deficiency significantly reduces trabecular bone parameters, and testosterone therapy may be a useful intervention for the loss of bone mass in testosterone deficient males. These results indicate that testosterone therapy may be useful for the treatment of trabecular bone frailty in

testosterone deficient males. Observed changes in trabecular bone do not appear to be due to decreased mineralisation caused by osteoblast alkaline phosphatase. Ongoing work includes histology analysis to elucidate the mechanisms underpinning the changes seen in the bones of testosterone deficient animals.

OC05.4

DEVELOPMENT OF A BONE-ON-A-CHIP BASED ON A 3D OSTEOCYTIC NETWORK FOR THE SCREENING OF ANTI-OSTEOPOROTIC DRUGS

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Introduction and Objective

The osteocyte, recognized as a major orchestrator of osteoblast and osteoclast activity, is the most important key player during bone remodeling processes. Imbalances that occur during bone remodeling, caused by hormone perturbations or alterations in mechanical loading, can induce bone disease as osteoporosis. Due to limited understanding of the underlying mechanisms, current therapies for osteoporosis cannot adequately address this imbalance because current studies of osteocytes rely on conventional cell culture that cannot recapitulate local in vivo microenvironments for the lack of control of the spatial/temporal distribution of cells and biomolecules. Microfluidics is the science and technology of microscale fluid manipulating and sensing and can help fill this gap.

Materials and Methods

We used a microfluidic device to enable the culture of osteocyte-like cells (MLO-Y4 and MLO-A5) in a 3D fashion. Osteocytes were cultured in a perfused and 160 µm high channel and embedded in a bone-like extracellular matrix: osteocytes were embedded in a matrigel- and collagen-based hydrogel enriched with nanostructured hydroxyapatite crystals (HA-NP) to mimic bone. To set up the best combination of matrigel enriched with Type I collagen we used fluorescent microspheres and confocal analysis. To evaluate the viability and the expression of osteocytic markers, we used live-dead assay and immunofluorescent staining and confocal analysis combined with automated quantification. For mineralization, we performed alizarin red staining.

Results

Osteocytes in the organ-on-a-chip model showed high viability and, in respect to 2D conventional cell cultures an increased differentiation, as assessed by a live-dead assay and the staining of the osteocytic markers connexin-43 and alkaline phosphatase and the increased mineralization activity. Furthermore, the addition of HA-NP significantly increased the formation of dendrite-like structures spreading through the xyz-axes, as assessed after G-actin immunofluorescence.

Conclusions

Using a microfluidic device for MLO-Y4 and MLO-A5 cell cultures, compared to the 2D surfaces, we demonstrated a significant difference in cell differentiation and morphology. In particular, 3D cultures allowed the formation of 3D cell networks and the osteogenic phenotype. As a platform technology, this microfluidic device can function as a novel cell culture model that enables further studies of osteocytes and 3D co-culturing with other bone cells for the screening of anti-osteoporotic drugs.

OC05.5

BONE MICROARCHITECTURE IN A PRE-CLINICAL RAT MODEL FOR TYPE 2 DIABETES

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Introduction and Objective

Type 2 diabetes mellitus (T2DM), and the often concurrent obesity, causes metabolic changes that affect many organs and tissues, including bone. Despite a normal or even higher bone mineral density (BMD), T2DM has often been associated with a higher fracture risk, indicating a compromised bone quality. In this work, we use a novel congenic leptin receptor-deficient BioBreeding Diabetes Resistant rat (BBDR.cg.lepr.cp) to investigate the impact of T2DM and obesity on bone morphology and architecture at the microscale.

Materials and Methods

Two different anatomical locations, i.e., femur and cranium, were studied combining micro-computed X-ray tomography (micro-CT) with scanning electron microscopy (SEM). Micro-CT data were examined using advanced image analysis tools in three-dimensions (3D).

Results

Both parietal bones and femurs were smaller, i.e., thinner and shorter, respectively, in diabetic animals compared to healthy controls. Image analysis of the sagittal suture revealed a reduced suture width and length in diabetic animals, suggesting an altered bone apposition rate. Histomorphometry analysis from micro-CT data highlighted differences in microstructure of both trabecular and cortical femur between diabetic and healthy rats. In particular, bone volume fraction (BV/TV) was lower in the T2DM group, while trabecular spacing (Tb.Sp) was increased, overall indicating a higher porosity in diabetic trabecular bone. SEM revealed the presence of extended portions of hyper-mineralized cartilage in the distal femur of the diabetic animals.

Conclusions

Micro-CT analyses, combined with SEM imaging, suggest that T2DM impacts bone growth and remodelling, in turn leading to differences in the structural organization at the microscale.

OC05.6

OSTEONECROSIS OF THE FEMORAL HEAD IS RELATED TO IMPAIRED OSTEOBLAST FUNCTION

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Introduction and Objective

Osteonecrosis of the femoral head (ONFH) is an evolving and disabling condition that often leads to subchondral collapse in late stages. It is the underlying diagnosis for approximately 3%–12% of total hip arthroplasties (THAs) and the most frequent aetiology for young patients undergoing THA. To date, the pathophysiological mechanisms underlying ONFH remain poorly understood. In this study, we investigated whether ONFH without an obvious etiological factor is related to impaired osteoblast activities, as compared to age-matched patients with primary OA.

Materials and Methods

We cultured osteoblasts isolated from trabecular bone explants taken from the femoral head of patients with ONFH and from intertrochanteric region of patients with ONFH or with OA and compared their in vitro mineralisation capacity and secretion of paracrine factors.

Results

Compared to patients with OA, osteoblasts obtained from the intertrochanteric region of patients with ONFH showed reduced mineralisation capacity, which further decreased in osteoblasts from the femoral head of the same patient. Lower mineralisation of osteoblasts from patients with ONFH correlated with lower mRNA levels of genes encoding osteocalcin and bone sialoprotein and higher osteopontin expression. Osteoblasts from the intertrochanteric region of patients with ONFH secreted lower osteoprotegerin levels than those from patients with OA, resulting in a higher receptor activator of NF- κ B ligand (RANKL)-to-osteoprotegerin (OPG) ratio. Notably, the RANKL-to-OPG ratio, as well as the secretion of the proresorptive factors interleukin-6 and prostaglandin E₂, was higher in osteoblasts from the femoral head of patients with ONFH than in those from the intertrochanteric region.

Conclusions

ONFH is associated with a reduced mineralisation capacity of osteoblasts and increased secretion of proresorptive factors.

KS5

CELLULAR THERAPY FOR OSTEOARTHRITIS: CELL CHARACTERISATION AND MECHANISM OF ACTION

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Osteoarthritis (OA) is a major global disease with increasing prevalence. It is one of the most significant causes of disability worldwide and represents a major burden in terms of healthcare delivery and impact on the quality of life of patients. It is a cause of severe chronic pain and has given rise to alarming levels of opioid use and addiction. Despite this prevalence, there are no disease-modifying treatments which delay or reverse the degenerative changes within joints which are characteristics of the disease. All treatments are symptom-modifying with the exception of joint arthroplasty, which is currently the most common surgical procedure carried out in US hospitals. Several pharmaceutical and biological interventions have been tested in recent years, including metalloproteinase inhibitors, chondrogenic agents such as Kartogenin, IL-1 antagonists and monoclonal antibodies. So far, none of these has provided an effective disease-modifying treatment. Cellular therapies have a great deal of promise because of their anti-inflammatory and regenerative effects. Mesenchymal stromal cells (MSCs) have been widely studied as a treatment for OA in preclinical and clinical assessments with generally positive results. As the clinical testing of these cells proceeds serious questions emerge relating to the quality and consistency of the therapeutic product and the need for better standardisation with regard to, for example, the tissue source and expansion conditions. Of equal importance is the need for deeper insight into the therapeutic mechanism, specifically the activity and phenotype of cells transplanted to the OA environment, their fate and interaction with local cells.

OC06 HAND AND SHOULDER

K6

Carpal Tunnel Syndrome- a disease of cellular senescence?

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Carpal tunnel syndrome (CTS) is the most common condition affecting the hand, with a prevalence of 2-3% in most populations, and a lifetime incidence over 10%. There is consensus that CTS results from increased pressure in the carpal tunnel, which eventually affects nerve function, but, aside from direct trauma and space occupying lesions, there is no consensus on what causes the pressure to rise. In the absence of an identifiable biological mechanism, the most common treatment involves surgical opening of the carpal tunnel. Recent data suggests that CTS patients demonstrate, in the carpal tunnel synovium and subsynovial connective tissue (SSCT), evidence of cellular senescence, with a senescence associated secretory phenotype (SASP). This finding suggests the potential for a biological treatment for CTS with senolytic drugs. This presentation will review the evidence for CTS as a disease of cellular senescence, and our preliminary data on the effects of senolytics, including in a relevant animal model of CTS and SSCT fibrosis.

OC06.1

CLINICAL EFFECTIVENESS OF INTRA-OPERATIVE TRANEXAMIC ACID USE IN SHOULDER SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and Objective

Tranexamic acid (TXA) is used across surgical specialties to reduce perioperative bleeding. It has been shown to be effective in trauma, spinal surgery, and lower limb arthroplasty. The aim of this study is to investigate the clinical effectiveness of TXA in all types of shoulder surgery on bleeding and non-bleeding related outcomes.

Materials and Methods

This study was registered prospectively on the PROSPERO database (ref: CRD42020185482). A systematic review and meta-analysis of randomised controlled trials (RCTs) investigating intra-operative use of TXA versus placebo in any type of surgery to the shoulder girdle. Electronic databases searched included MEDLINE, EMBASE, PsychINFO, and the Cochrane Library. Risk of bias within studies was assessed using the Cochrane risk of bias v2.0 tool and Jadad score. Certainty of findings were reported using the GRADE approach. The primary outcome was total blood loss. Secondary outcomes included patient reported outcome measures, adverse events, and rate of blood transfusion.

Results

Eight RCTs were included in the systematic review and data from 7 of these studies pooled in the meta-analysis. A total of 708 patients were randomized across the studies (406 received TXA, 302 received placebo). Studies included patients undergoing anatomic or reverse total shoulder arthroplasty, open Latarjet surgery, and arthroscopic rotator cuff repair. Pooled analysis demonstrated significant reduction in perioperative bleeding with TXA compared to controls; estimated total blood loss (mean difference [MD], -209.66; 95% CI -389.11 to -30.21; $p=0.02$), and post-operative blood loss (via drain output) (MD, -84.8ml; 95% CI, -140.04 to -29.56; $p=0.003$). A mean difference in Visual Analogue Scale (VAS) of 2.93 was noted in favour of TXA (95% CI 0.2 to 5.66; $p=0.04$).

Conclusions

Whilst noting some risk of bias within the studies, TXA was effective in reducing blood loss and pain in shoulder surgery. There may be a benefit of TXA use in both open and arthroscopic shoulder procedures. Larger, low risk of bias, RCTs for specific surgical shoulder procedures are required.

OC06.2

ARE PROGRESSIVE SHOULDER EXERCISES FEASIBLE IN PATIENTS WITH GLENOHUMERAL OSTEOARTHRITIS OR ROTATOR CUFF TEAR ARTHROPATHY ELIGIBLE FOR SHOULDER ARTHROPLASTY?

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Introduction and Objective

Only few studies have investigated the outcome of exercises in patients with glenohumeral osteoarthritis (OA) or rotator cuff tear arthropathy (CTA), and furthermore often excluded patients with a severe degree of OA. Several studies including a Cochrane review have suggested the need for trials comparing shoulder arthroplasty to non-surgical treatments. Before initiation of such a trial, the feasibility of progressive shoulder exercises (PSE) in patients, who are eligible for shoulder arthroplasty should be investigated. The aim was to investigate whether 12 weeks of PSE is feasible in patients with OA or CTA eligible for shoulder arthroplasty. Moreover, to report changes in shoulder function and range of motion (ROM) following the exercise program.

Materials and Methods

Eighteen patients (11 women, 14 OA), mean age 70 years (range 57-80), performed 12 weeks of PSE with 1 weekly physiotherapist-supervised and 2 weekly home-based sessions. Feasibility was measured by drop-out rate, adverse events, pain and adherence to PSE. Patients completed Western Ontario Osteoarthritis of the Shoulder (WOOS) score and Disabilities of the Arm, Shoulder and Hand (DASH).

Results

Two patients dropped out and no adverse events were observed. Sixteen patients (89%) had high adherence to the physiotherapist-supervised sessions. Acceptable pain levels were reported. WOOS improved mean 23 points (95%CI:13;33), and DASH improved mean 13 points (95%CI:6;19).

Conclusions

PSE is feasible, safe and may improve shoulder pain, function and ROM in patients with OA or CTA eligible for shoulder arthroplasty. PSE is a feasible treatment that may be compared with arthroplasty in a RCT setting.

OC06.3

OUTCOMES OF LONG HEAD OF BICEPS TENOTOMY ARE COMPARABLE TO TENODESIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and Objective

There remains much debate regarding the optimal method for surgical management of patients with long head of biceps pathology. The aim of this study was to compare the outcomes of tenotomy versus tenodesis.

Materials and Methods

This systematic review and meta-analysis was registered on PROSPERO (ref: CRD42020198658). Electronic databases searched included EMBASE, Medline, PsycINFO, and Cochrane Library. Randomized controlled trials (RCTs) comparing tenotomy versus tenodesis were included. Risk of bias within studies was assessed using the Cochrane risk of bias v2.0 tool and the Jadad score. The primary outcome included patient reported functional outcome measures pooled using standardized mean difference (SMD) and a random effects model. Secondary outcome measures included visual analogue scale (VAS), rate of cosmetic deformity (Popeye sign), range of motion, operative time, and elbow flexion strength.

Results

751 patients from 10 RCTs demonstrated (369 tenotomy vs 382 tenodesis) were included in the meta-analysis. Pooled analysis of all PROMs data demonstrated comparable outcomes between tenotomy vs tenodesis (SMD 0.17 95% CI -0.02 to 0.36, $p=0.09$). Sensitivity analysis comparing RCTs involving patients with and without an intact rotator cuff did not change the primary outcome. Secondary outcomes including VAS, shoulder external rotation, and elbow flexion strength did not reveal any significant difference. Tenodesis resulted in a lower rate of Popeye deformity (OR 0.27 95% CI 0.16 to 0.45, $p<0.00001$).

Conclusions

Aside from a lower rate of cosmetic deformity, tenodesis yielded no measurable significant benefit to tenotomy for addressing pathology in the long head of biceps. This finding was irrespective of the whether the rotator cuff was intact.

OC06.4

THE EFFECTS OF CARPAL TUNNEL RELEASE SURGERY ON HANDWRITING AND DIGITAL WRITING PERFORMANCE

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Introduction and Objective

Carpal tunnel syndrome (CTS) is a very common compressive neuropathy involving the median nerve. The typical symptoms are paraesthesia, dysesthesia and loss of strength; in severe case, this compression deteriorates the sensorimotor control of the hand and interferes with the adjustment of the forces at the level of the fingers, thus affecting the components that are the basis of dexterity and control of fine movements. For these reasons, the CTS has repercussions on various activities of daily life, including writing skills. Word processing via PC and mobile device (touch-typing) require a fine control of the hand-wrist movement and of the opposition of the thumb, while in handwriting, gripping and gripping movements are carried out in a protracted manner. In modern society, present skills play a role of fundamental importance from an educational, professional and social point of view.

The aim of the study is to describe the effects of carpal tunnel release (CTR) on handwriting and digital writing performance.

Materials and Methods

We recruited patients suffering from carpal tunnel syndrome (CTS) who were candidates for CTR surgery and collected clinical and demographic data, including age, occupation, duration of symptoms and electromyography outcomes. The first trial session was carried out before surgery and the subsequent ones at 1, 2, 3, 4, 8 and 12 weeks after the CTR. These trials involved copying a 500-character paragraph by handwriting, personal computer (PC) and mobile device, for which a dedicate Google Colab web page was computed. We used as parameters the speed, expressed in words per minute (wpm), and the accuracy of copying, which was measured in number of errors (en). Moreover in each session the patient filled in the QuickDASH (Disabilities of the Arm, Shoulder, and Hand) questionnaire. We used the one-way anova to evaluate the change in the three performances and in the QuickDASH score in follow-up sessions. We used the two-way anova to detect a possible interactions between speed improvement and groups of variables, namely gender, writing frequency, schooling, diabetes, dysthyroidism and metabolic syndrome.

Results

We recruited 20 patients of whom 7 dropped out for personal reasons and 13 had completed all trial sessions. The PC writing performance had an average speed and accuracy of 15.1 ± 6.8 wpm and 13.1 ± 8.2 en, respectively, while post-operatively it returned values of 17.6 ± 5.0 wpm and 9.9 ± 5.6 en. Regarding touch-typing, a pre-operative average of 16.9 ± 5.8 wpm and 14.3 ± 14.4 en was recorded, while post-operatively an average of 21.7 ± 6.5 wpm and 11.5 ± 14.7 en was reported. Handwriting performance initially had a mean of 20.5 ± 7.1 wpm and 0.1 ± 0.6 en and after three months returned a mean of 22.4 ± 4.0 wpm and 0 ± 0 n. The QuickDASH score had a pre-operative mean of 39.1 ± 9.1 and post-operative mean of 17 ± 6 points. The only statistically significant improvements were those related to touch-typing ($P = 0.022$) and QuickDASH score ($P < 0.001$). There was no significant interaction between gender, comorbidity, writing frequency, level of schooling and recovery of writing ability.

Conclusions

The data collected showed, in agreement with previous studies, that CTS has a significant impact on the patient's writing ability, who benefits from the surgical treatment, especially in terms of touch-typing and

general manual dexterity. In addition, the recovery of writing ability did not show significant correlation with other variables.

OC07 CARTILAGE TISSUE ENGINEERING

K7

MENISCUS REPAIR: FROM BASIC SCIENCE TO PRECLINICAL STUDIES

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In the last decades, significant effort has been attempted to salvage the meniscus following injury.

Basic science approaches to meniscus repair include procedures for both meniscus regeneration and meniscus healing. Regeneration of meniscal tissue focuses on filling a defect with reparative tissue, which resembles the native structure and function of the meniscus. Procedures for meniscus healing, on the other hand, aim to accomplish adhesion between the margins of a meniscal lesion, with no attempt to regenerate or replace meniscal tissue.

Regeneration studies of tissue to fill a defect in the meniscus have shown interesting results, but complete restoration of the native meniscus has not yet been accomplished.

Healing of a meniscal lesion has been investigated in different models although none has demonstrated reproducible healing. Therefore, different paths of investigation must be undertaken, and one of these may be the cell-therapy / tissue engineering approach.

In a study from our group, we showed the capacity of chondrocyte-seeded cartilaginous scaffold to repair a bucket-handle lesion of the knee meniscus orthotopically in a large animal study. Following studies were done in order to test the potential of other scaffolds and different cell sources for the repair of the meniscal tissue. We have also evaluated the role of hypoxia in meniscal development in vitro as basis for future research in this field, as hypoxia could be considered as a promoter for meniscal cells maturation, and opens considerably opportunities in the field of meniscus tissue engineering.

OC07.1

MESENCHYMAL STROMAL CELL SPHEROIDS – EFFECT OF CELL PACKING AND BIOMATERIAL COMPOSITION ON CHONDROGENIC DIFFERENTIATION IN VITRO

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Introduction

Current cell-based treatments and marrow stimulating techniques to repair articular cartilage defects are limited in restoring the tissue in its native composition. Despite progress in cartilage tissue engineering and chondrogenesis in vitro, the main limitation of this approach is the progression towards hypertrophy during prolonged culture in pellets or embedded in biomaterials. The objectives of this study were (A) to compare human bone marrow-derived mesenchymal stromal cells (hMSC) chondrogenesis and hypertrophy in pellet culture from single cells or cell spheroids and (B) to investigate the effect of tyramine-modified hyaluronic acid (THA) and collagen I (Col) content in composite hydrogels on the chondrogenesis and hypertrophy of encapsulated hMSC spheroids.

Materials and Methods

Pellet cultures were prepared either from hMSC single cells (250'000 cells/pellet) or hMSC spheroids (282 cells/spheroid) at the same final cell concentration (250'000 cells/pellet = 887 spheroids/pellet). The effect of polymer concentration on encapsulated hMSC spheroids (887 spheroids/hydrogel) was investigated in THA-Col hydrogels (50µl) at the following concentrations (THA-Col mg/ml): Group (1) 12.5-2.5, (2) 16.7-1.7, (3) 12.5-1.7, (4) 16.7-2.5 mg/ml. All samples were cultured for 21 days in standard chondrogenic differentiation medium containing 10ng/ml TGF-β1. Chondrogenic differentiation and hypertrophy of both pellet cultures and hMSCs spheroids encapsulated in THA-Col were analysed using gene expression analysis (Aggrecan (ACAN), COL1A1, COL2A1, COL10A1), dimethylmethylene-Blue assay to quantify glycosaminoglycans (GAGs) retained in the samples and (immuno-) histological staining (Safranin-O, collagen II, aggrecan) on day 1 and day 21 (n=3 donors).

Results

The culture of hMSCs in pellets based on single cells or spheroids resulted in an increase in chondrogenic-associated markers COL2A1 (2'900-3'400-fold) and ACAN (45-47-fold) compared to respective samples on day 1 in both groups. GAGs increased in spheroid pellets to 21.2±3.4 mg/ml and in single cell pellets to 20.8±6.6 mg/ml on day 21. Comparing the levels of hypertrophic markers, single cell pellets showed 7-fold and 20-fold higher expression of COL1A1 and COL10A1 than spheroid pellets on day 21. The encapsulation of hMSC spheroids in THA-Col resulted in an upregulation of chondrogenic-associated markers and GAG content in all hydrogels with differences in cell differentiation related to the Col and THA polymer ratio, while level of hypertrophy was comparable in all groups with values similar to the spheroid pellet group. Spheroids embedded in hydrogels with lower THA content (group 1 and 3) resulted in more pronounced chondrogenic phenotype marked by upregulation of COL2A1 (3'200-4'500-fold) and ACAN (152-179-fold) relative to the respective samples on day 1. Spheroids embedded in higher THA content hydrogels (group 2 and 4) showed less pronounced chondrogenesis marked by lower upregulation of COL2A1 (980-1800-fold) and ACAN (25-68-fold, relative to day 1 samples). This was confirmed by quantification of GAGs, increasing from 2.5±1.9 and 2.5±1.7 mg/ml (day 1) to 11.4±2.5 and 9.9±3.8 mg/ml on day 21 for groups 1 and 4, respectively. (Immuno-) histological stainings resulted in a more homogenous staining in lower THA content hydrogels compared to a more local matrix deposition in samples with higher THA content.

Conclusion

The reduced level of hypertrophy in hMSC pellets prepared from cell spheroids compared to single cell pellets at same cell count might be related to the packing density of the cells with cells being more densely packed in single cell pellets compared to pellets from spheroids. Investigating the effect of polymer ratios on chondrogenesis, it seems that the THA content is the driving factor influencing hMSC chondrogenesis rather than Col content in THA-Col composites at comparable mechanical properties. This study highlights the feasibility to use hMSC spheroids as alternative approach to study in vitro chondrogenic differentiation and the suitability to investigate the effect of biomaterial composition on chondrogenesis and hMSC hypertrophy.

OC07.2

IMPLICATIONS OF POLYMER INFILTRATION IN A NEW DEVELOPED BIOACTIVE GLASS SCAFFOLDS (CAR12N) FOR CARTILAGE TISSUE ENGINEERING?

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Introduction and Objective

Regeneration of cartilage injuries is greatly limited. Therefore, cartilage injuries are often the starting point for later osteoarthritis. In the past, various bioactive glass (BG) scaffolds have been developed to promote bone healing. Due to the fact that they induce the deposition of hydroxyapatite (HA) -the main component of bone matrix, these BG types are not suitable for chondrogenesis. Hence, a novel BG (Car12N) lacking HA formation, was established. Since BG are generally brittle the combination with polymers is helpful to achieve suitable biomechanic stability. The aim of this interdisciplinary project was to investigate the effects of biodegradable polymer Poly(D,L-lactide-co-glycolide) (PLLA) infiltration into a Car12N scaffold for cartilage tissue engineering.

Materials and Methods

BG scaffolds were infiltrated with PLLA using phase separation within a solvent. Pure BG Car12N scaffolds served as control. To assess whether the polymer was homogeneously distributed the polymer to glass ratio and pore contents in the upper, middle and lower third of the scaffolds were examined by light microscopy. For a more precise characterization of the scaffold topology, the glass strut length, the glass strut diameter and the pore circumference were also measured. Leaching tests in 0.1M HCl solution over 8 days were used to allow a gel layer formation on the scaffolds surface. Non-leached and leached scaffolds were subjected to strength testing. Cytotoxicity of the scaffolds with and without polymer was tested according to standards. Scaffolds were colonized with 27.777.8 per cm³ primary porcine articular chondrocytes (pACs) or primary human mesenchymal stromal cells (hMSCs), respectively. After cultivation for up to 35 days, the vitality, quantitative DNA and sulfated glycosaminoglycan (sGAG) contents per scaffold were determined.

Results

The polymer distribution was not homogeneous in the scaffolds. There were significant differences in glass strut length and pore size. Leaching increased the biomechanical strength. All scaffolds were not cytotoxic. pACs and hMSCs were able to adhere to the scaffold with and without polymer and remained viable during the whole culturing period of 35 d. The DNA content was higher in the pAC colonized scaffolds with polymer than without polymer. The sGAG content was higher in hMSCs seeded scaffolds with polymer than in pACs seeded ones with polymer.

Conclusions

Polymer infiltration leads to an increase in mechanical stability of Car12N scaffolds and chondrogenic cells are able to colonize these composites suggesting them as a promising.

OC07.3

PHYSIOXIA ENHANCES CLONOGENICITY AND DIFFERENTIATION POTENTIAL OF VASCULAR AND AVASCULAR MENISCAL CELLS

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Introduction and Objective

The meniscus is composed of two distinct regions, a vascular outer zone and an avascular inner zone. Due to vascularization, tears within the vascular zone can be treated by suturing. However, tears in the avascular zone have a poor healing capacity and partial meniscectomy is used to prevent further pain, although this leads to early osteoarthritis. Previous studies have demonstrated that the vascular zone contains a progenitor population with multilineage differentiation potential. Isolation and propagation of these progenitors can be used to develop cell-based therapies for treating meniscal defects. In vivo, the meniscus resides under a low oxygen environment, also known as physioxia (2-7% oxygen) and previous work suggests that it promotes the meniscal phenotype. The objective of the study was to isolate progenitor populations from both meniscus regions and to examine their clonogenicity and differentiation potential under both hyperoxia (20% oxygen) and physioxia (2% oxygen). We hypothesize that physioxia will have a beneficial effect on colony formation and trilineage differentiation of meniscal cells.

Materials and Methods

Human meniscus (n =4; mean age: 64 + 6) tissue was split into vascular and avascular regions, finely cut into small pieces and then sequentially digested in pronase (70U/mL) and collagenase (200U/mL) at 37°C. Avascular and vascular meniscus cells were counted and split equally for expansion under hyperoxia and physioxia at a seeding density of 5 x 10³ cells/cm². At passage 1, cells were seeded at 2, 5 and 20 cells/cm² in 10cm dishes for observing colony formation using crystal violet assay. At passage 3, vascular and avascular meniscus cells were differentiated towards the chondrogenic, osteogenic and adipogenic lineage. Chondrogenesis was evaluated using DMMB staining for GAG deposition, osteogenesis was assessed using Alizarin Red staining for calcium deposition, whilst adipogenesis was observed using Oil-Red-O staining for fat droplets.

Results

Expansion of vascular and avascular meniscus cells showed no difference in doubling time between hyperoxic or physioxic culture. However, physioxia significantly increased the number of colonies compared to hyperoxia for both meniscus cell types (p < 0.05). Both vascular and avascular meniscus cells differentiated towards the chondrogenic, osteogenic and adipogenic lineage under both oxygen tensions. Interestingly, we observed greater DMMB, alizarin red and oil-red-o staining for vascular meniscal cells under physioxia compared to corresponding hyperoxic cultures and avascular meniscal cells.

Conclusions

Physioxia enhances the clonogenicity of vascular and avascular meniscus cells. Trilineage differentiation potential was observed from both regions with increased capacity detected under physioxia for vascular meniscal cells. Physioxic isolation of meniscal cells for the propagation of these progenitors can be used for the treatment of meniscal tears/defects.

OC07.4

EXTRACELLULAR CALCIUM DIFFERENTIALLY REGULATES CARTILAGE MATRIX PRODUCTION BY ARTICULAR CHONDROCYTES AND MESENCHYMAL STROMA CELLS

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Introduction and Objective

Current cartilage repair strategies lack adequate tissue integration capacity and often present mechanical failure at the graft-to-host tissue junction. The design of multilayered osteochondral tissue engineering (TE) constructs is an attractive approach to overcome these problems. However, calcium ion-release from resorbable bone-replacement materials was suggested to compromise chondrogenic differentiation of adjacent cartilage tissue and it is unclear whether articular chondrocytes (AC) or mesenchymal stroma cells (MSC) are more sensitive to such conditions. Aim of the study was to compare how elevated calcium levels affect cartilage matrix production during re-differentiation of AC versus chondrogenic differentiation of MSC. The results of this study will help to identify the ideal cell source for growth of neocartilage adjacent to a calcified bone replacement material for design of multilayered osteochondral TE approaches.

Materials and Methods

Expanded human AC and MSC (6-12 donors per group) were seeded in collagen type I/III scaffolds and cultured under standard chondrogenic conditions at control (1.8mM) or elevated (8.0mM) CaCl₂ for 35 days. Proteoglycan and collagen production were assessed via radiolabel-incorporation, ELISA, qPCR and Western blotting. Differences between groups or cell types were calculated using the non-parametric Wilcoxon or Mann-Whitney U test, respectively, with $p < 0.05$ considered significant.

Results

Elevated calcium significantly reduced GAG synthesis (63% of control, $p=0.04$) and chondrogenic marker expression of AC, lowering the GAG/DNA content (47% of control, $p=0.004$) and collagen type II deposition (24% of control, $p=0.05$) of neocartilage compared to control conditions. Opposite, at elevated calcium levels MSC-derived chondrocytes significantly increased GAG synthesis (130% of control, $p=0.02$) and collagen type II content (160% of control, $p=0.03$) of cartilage compared to control tissue. Chondrogenic and hypertrophic marker expression was insensitive to calcium levels in MSC-derived chondrocytes. As a result, maturation under elevated calcium allowed for a significantly higher GAG/DNA content in MSC-derived samples compared to AC constructs, although under control conditions both groups developed similarly.

Conclusions

AC and MSC showed an opposite reaction to elevation of calcium levels regarding cartilage matrix production and we propose MSC as a preferred cell source to grow chondrocytes in vicinity to calcified bone replacement materials. Since MSC remained prone to hypertrophy under elevated calcium, trizonal cartilage TE constructs, where an AC-layer is separated from the bone replacement phase by an intermediate layer of MSC appear as an ideal design for multilayered osteochondral TE with respect to calcium sensitivity of cells and protection of the upper cartilage layer from hypertrophy.

OC08 SPORTS MEDICINE

K8

OBJECTIVE MEASUREMENT OF KNEE LAXITY IN MRI - PORTO KNEE TESTING DEVICE

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Rotational laxity increases the risk of anterior cruciate ligament (ACL) injuries and residual rotational laxity can result in inferior surgical outcomes and risk of retears.

The dynamic rotatory knee stability can be assessed through manual examination, but it is limited to the surgeon's experience and it provides inaccurate measurements, highlighting the need for objective measurement of knee rotational laxity. The objective measurement of knee laxity can help to better identify patients that may benefit from conservative treatment or those that require surgical treatment with or without concomitant extra-articular procedures.

We rely in Porto Knee Testing Device (PKTD®) to accurately measure sagittal and rotatory laxity of the knee, either individually or in a combined fashion. The PKTD® is safe and can be used in combination with CT or MRI, which allows to assess both the "anatomy" and the "function" in the same examination. By this way, we may have a total ACL rupture and a stable knee not requiring surgery or, on the other hand, the same injury scenario but with an unstable knee that requires surgical intervention (with or without lateral extra-articular tenodesis). In cases of partial ACL tears, it may be possible to identify some ligamentous fibers that remain functional, where the conservative treatment or augmentation techniques can provide satisfactory results. It can also identify when a posteromedial or posterolateral instability is associated. The PKTD® can also be used to follow-up the laxity results of conservative and surgical procedures and contribute to the decision-making of return to sports.

OC08.1

TOWARDS AUTOMATED LIGAMENTOUS INJURY EVALUATION IN SYNDESMOTIC ANKLE LESIONS

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Introduction and Objective

Forced external rotation is hypothesized as the key mechanism of syndesmotic ankle injuries. This complex trauma pattern ruptures the syndesmotic ligaments and induces a three-dimensional deviation from the normal distal tibiofibular joint configuration. However, current diagnostic imaging modalities are impeded by a two-dimensional assessment, without taking into account ligamentous stabilizers. Therefore, our aim is two-fold: (1) to construct an articulated statistical shape model of the normal ankle with inclusion of ligamentous morphometry and (2) to apply this model in the assessment of a clinical cohort of patients with syndesmotic ankle injuries.

Materials and Methods

Three-dimensional models of the distal tibiofibular joint were analyzed in asymptomatic controls (N= 76; Mean age 63 +/- 19 years), patients with syndesmotic ankle injury (N = 13; Mean age 35 +/- 15 years), and their healthy contralateral equivalent (N = 13). Subsequently, the statistical shape model was generated after aligning all ankles based on the distal tibia. The position of the syndesmotic ligaments was predicted based on previously validated iterative shortest path calculation methodology. Evaluation of the model was described by means of accuracy, compactness and generalization. Canonical Correlation Analysis was performed to assess the influence of syndesmotic lesions on the distal tibiofibular joint congruency.

Results

Our presented model contained an accuracy of 0.23 +/- 0.028 mm. Mean prediction accuracy of ligament insertions was 0.53 +/- 12 mm. A statistically significant difference in anterior syndesmotic distance was found between ankles with syndesmotic lesions and healthy controls (95% CI [0.32 , 3.29], p = 0.017). There was a significant correlation between presence of syndesmotic injury and the morphological distal tibiofibular configuration (r = 0.873, p <0,001).

Conclusions

In this study, we constructed a bony and ligamentous statistical model representing the distal tibiofibular joint. Furthermore, the presented model was able to detect an elongation injury of the anterior inferior tibiofibular ligament after traumatic syndesmotic lesions in a clinical patient cohort.

OC08.2

LOCAL INFILTRATION ANAESTHESIA (LIA) IS EQUALLY EFFECTIVE AS ADDUCTOR CANAL BLOCKS (ACB) FOR PAIN RELIEF IN HAMSTRING GRAFT ANTERIOR CRUCIATE LIGAMENT (ACL) RECONSTRUCTIONS

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Introduction and Objective

Objectives: To determine the effectiveness of LIA compared to ACB in providing pain relief and reducing opiates usage in hamstring graft ACL reconstructions.

Materials and Methods

In a consecutive series of hamstring graft ACL reconstructions, patients received three different regional and/or anaesthetic techniques for pain relief. Three groups were studied: group 1: general anaesthetic (GA)+ ACB (n=38); group 2: GA + ACB + LIA (n=31) and group 3: GA+LIA (n=36). ACB was given under ultrasound guidance. LIA involved infiltration at skin incision site, capsule, periosteum and in the hamstring harvest tunnel. Analgesic medications were similar between the three groups as per standard multimodal analgesia (MMA). Patients were similar in demographics distribution and surgical technique. The postoperative pain and total morphine requirements were evaluated and recorded. The postoperative pain was assessed using the visual analogue scores (VAS) at 0hrs, 2hrs, 4hrs, weight bearing (WB) and discharge (DC).

Results

There was no statistically significant difference in opiates intake amongst the three groups. When comparing VAS scores; there were no statistical difference between the groups at any of the time intervals that VAS was measured. However, the GA+LIA group hospital's LOS (m=2.31hrs, SD=0.75) was almost half that of GA+ACB group (m=4.24hrs, SD=1.08); (conditions $t(72)=8.88$; $p=0.000$). There was no statistical significance in the incidence of adverse effects amongst the groups.

Conclusions

The LIA technique provided equally good pain relief following hamstring graft ACL reconstructions when compared to ACB, while allowing for earlier rehabilitation, mobilisation and discharge.

OC08.3

ACL GRAFT SOURCE INFLUENCES FIBROBLASTIC RESPONSE TO TENSION LOAD IN VITRO

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Introduction and Objective

Anterior cruciate ligament reconstruction (ACLR) with tendon autografts is the “gold standard” technique for surgical treatment of ACL injuries. Common tendon graft choices include patellar tendon (PT), semitendinosus/gracilis “hamstring” tendon (HT), or quadriceps tendon (QT). Healing of the graft after ACLR may be affected by graft type since the tissue is subjected to mechanical stresses during post-operative rehabilitation that play important roles in graft integration, remodeling and maturation. Abnormal mechanical loading can result in high inflammatory and degradative processes and altered extracellular matrix (ECM) synthesis and remodeling, potentially modifying tissue structure, composition, and function. Because of the importance of load and ligamentization for tendon autografts, this study was designed to compare the differential inflammatory and degradative metabolic responses to loading by three tendon types commonly used for autograft ACL reconstruction.

Materials and Methods

With IRB approval (IRB # 2009879) and informed patient consent, portions of 9 QT, 7 PT and 6 HT were recovered at the time of standard of care ACLR surgeries. Tissues were minced and digested in 0.2 mg/ml collagenase solution for two hours and were then cultured in 10% FBS at 5% CO₂, 37°C, and 95% humidity. Once confluent, cells were plated in Collagen Type I-coated BioFlex® plates (1 × 10⁵ cells/well) and cultured for 2 days prior to the application of strain. Then, media was changed to supplemented DMEM with 2% FBS for the application of strain. Fibroblasts were subjected to continuous mechanical stimulation (2-s strain and 10-s relaxation at a 0.5 Hz frequency) at three different elongation strains (mechanical stress deprivation-0%, physiologic strain-4%, and supraphysiologic strain-10%)⁹ for 6 days using the Flexcell FX-4000T strain system. Media was tested for inflammatory biomarkers (PGE₂, IL-8, Gro- α , and MCP-1) and degradation biomarkers (GAG content, MMP-1, MMP-2, MMP-3, TIMP-1, and TIMP-2). Significant (p<0.05) difference between graft sources were assessed with Kruskal-Wallis test and post-hoc analysis. Results are reported as median \pm interquartile range (IQR).

Results

Differences in Inflammation-Related Biomarker Production (Figure 1): The production of PGE₂ was significantly lower by HT fibroblasts compared to both QT and PT fibroblasts at all timepoints and strain levels. The production of Gro- α was significantly lower by HT fibroblasts compared to QT at all time points and strain levels, and significantly lower than PT on day 3 at 0% strain, and all strain levels on day 6. The production of IL-8 by PT fibroblasts was significantly lower than QT and HT fibroblast on day 3 at 10% strain.

Differences in Degradation-Related Biomarker Production (Figure 2): The production of GAG by HT fibroblasts was significantly higher compared to both QT and PT fibroblasts on day 6 at 0% strain. The production of MMP-1 by the QT fibroblasts was significantly higher compared to HT fibroblasts on day 3 of culture at all strain levels, and in the 0% and 10% strain levels on day 6 of culture. The production of MMP-1 by the QT fibroblasts was significantly higher compared to PT fibroblasts at in the 0% and 4% strain groups on day 3 of culture. The production of TIMP-1 by the HT fibroblasts was significantly lower compared to PT fibroblasts on day 3 of culture.

Conclusions

The results of this study identify potentially clinically relevant difference in the metabolic responses of tendon graft fibroblasts to strain, suggesting a lower inflammatory response by hamstring tendon fibroblasts and higher degradative response by quadriceps tendon fibroblasts. These responses may influence ACL autograft healing as well as inflammatory mediators of pain in the knee after reconstruction, which may have implications regarding graft choice and design of postoperative rehabilitation protocols for optimizing outcomes for patients undergoing ACL reconstruction.

OC08.4

IMMUNOHISTOCHEMISTRY ON OSTEOCHONDRAL ALLOGRAFTS SUGGEST IMMUNOLOGICAL IMPACT IN FAILURE MECHANISMS

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Introduction and Objective

Osteochondral allograft (OCA) transplants have been used clinically for more than 40 years as a surgical option for joint restoration, particularly for young and active patients. While immediate graft rejection responses have not been documented, it is believed that the host's immunological responses may directly impact OCA viability, incorporation, integrity, and survival, and therefore, it is of the utmost importance to further optimize OCA transplantation outcomes. The influences of sub-rejection immune responses on OCA transplantation failures have not been fully elucidated therefore aimed to further characterize cellular features of OCA failures using immunohistochemistry (IHC) in our continued hopes for the successful optimization of this valuable surgical procedure.

Materials and Methods

With IRB approval, osteochondral tissues that were resected from the knee, hip, and ankle of patients undergoing standard-of-care revision surgeries (N=23) to treat OCA failures and tissues from unused portions of OCAs (N=7) that would otherwise be discarded were recovered. Subjective histologic assessments were performed on hematoxylin and eosin-stained and toluidine blue-stained sections by a pathologist who was blinded to patient demographics, outcomes data, and tissue source. IHC for CD3, CD8, and CD20 were performed to further characterize the and allow for subjective assessment of relevant immune responses.

Results

Eleven (48%) of the failed OCAs had aggregates of CD3+, CD8+, and CD20+ lymphocytes around small blood vessels in the bone marrow spaces and adipose/collagenous tissue of the allograft, while the non-implanted healthy control OCA tissues did not show any evidence of inflammation. The remaining failed OCAs (52%) did not show a similar pattern of T- and B-cell infiltrates around blood vessels. Other histologic abnormalities associated with failed OCAs included avascular necrosis, subchondral micro and macro fractures, subchondral collapse, bacterial infection, and/or articular cartilage erosion or delamination.

Conclusions

The results from the present study support this possibility in that mixed aggregates of CD3+, CD8+, and CD20+ lymphocytes were observed around small blood vessels in approximately half of the failed OCAs. This potentially cytotoxic immune response may have contributed to the lack of functional survival of the OCA

noted in these cases, and warrants further investigation as a possible failure mechanism that may be mitigated using post-transplantation management strategies.

OC09 TRAUMA RESEARCH

K9

HUMAN AMNIOTIC MEMBRANE POTENTIAL FOR BONE REPAIR: FROM THE LAB TO THE CLINIC

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The human amniotic membrane (hAM), derived from the placenta, possesses a low (nay inexistant) immunogenicity and exerts an anti-inflammatory, anti-fibrotic, antimicrobial, antiviral and analgesic effect. It is a source of stem cells and growth factors promoting tissue regeneration. hAM acts as an anatomical barrier with adequate mechanical properties (permeability, stability, elasticity, flexibility, resorbability) preventing the proliferation of fibrous tissue and promoting early neovascularization of the surgical site. Cryopreservation and lyophilization, with sometimes additional decellularization process, are the main preservation methods for hAM storage.

We examined the use of hAM in orthopaedic and maxillofacial bone surgery, specially to shorten the induced membrane technique (Gindraux, 2017). We investigated the cell survival in cryopreserved hAM (Laurent, 2014) and the capacity of intact hAM of in vitro osteodifferentiation (Gualdi, 2019). We explored its in vivo osteogenic potential in an ectopic model (Laurent, 2017) and, with Inserm U1026 BioTis, in a calvarial defect (Fenelon, 2018). Still piloted by U1026, decellularization and/or lyophilization process were developed (Fenelon, 2019) and, processed hAM capacities was assessed for guided bone regeneration (Fenelon 2020) and induced membrane technique (Fenelon, 2021) in mice.

We reported a limited function of hAM for bone defect management. In this light, we recognized medication-related osteonecrosis of the jaw (MRONJ) as appropriate model of disease to evaluate hAM impact on both oral mucosa and bone healing. We treated height compassionate patients (stage II, III) with cryopreserved hAM. A multicentric randomized clinical study (PHRC-I 2020 funding) will be soon conducted in France (regulatory and ethical authorization in progress).

OC09.1

EFFECTS OF AGE ON FRACTURE HEALING AFTER SEVERE BLOOD LOSS

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Introduction and Objective

In multiple trauma patients, as well as in the healing of isolated fractures (Fx) with heavy bleeding (trauma haemorrhage, TH), complications occur very often. This is particularly evident in elderly patients over 65 years of age. Since these accompanying circumstances strongly influence the clinical course of treatment, the influence of age on bone regeneration after femoral fracture and severe blood loss was investigated in this study.

Materials and Methods

12 young (17-26 weeks) and 12 old (64-72 weeks) male C57BL / 6J mice per group were examined. The fracture group Fx underwent an osteotomy after applying an external fixator. The THFx group also received blood pressure-controlled trauma hemorrhage (35 mmHg for 90 minutes) and reperfusion with Ringer's solution for 30 minutes. The Sham group received only the catheter and one external fixator. μ CT scans of the femora were performed in vivo after 2 weeks and ex vivo after 3 weeks. Histological and biomechanical examinations were also carried out. The statistical significance was set at $p \leq 0.05$. The non-normally distributed data were analyzed using the Mann-Whitney-U or Kruskal-Wallis test.

Results

The histology showed less mineralized bone in the fracture gap in old animals of the Fx (25.41% [1.68%]) and THFx groups (25.50% [4.07%]) compared with the young ones (34.20% [6.36%], $p = 0.003$; 34.31% [5.12%], $p=0.009$). Moreover, a severe blood loss lead to more cartilage in both young (6.91% [5.08%]) and old animals (4.17% [1.42%]) compared to animals with only a fracture (2, 45% [1.04%], $p=0.004$; 2.95% [1.12%], $p=0.032$). In old animals (11.37 / nm^2 [17.17 / nm^2]) in contrast the young mice with an isolated fracture (33.6/ nm^2 [8.83/ nm^2]) fewer osteoclasts were present ($p=0.009$). Therefore, the severe blood loss further reduced the number of osteoclasts only in young animals (16.83/ nm^2 [6.07/ nm^2]) ($p=0.004$). In the in vivo μ CT, after 2 weeks, a lower volume of bone, cortex and callus was found in old THFx animals (3.14 mm^3 [0.64 mm^3]; 1.01 mm^3 [0.04 mm^3]; 2.07 mm^3 [0.57 mm^3]) compared with the Fx animals (4.29 mm^3 [0.74 mm^3], $p=0.008$; 1.18 mm^3 [0, 25 mm^3], $p=0.004$; 3.02 mm^3 [0.77 mm^3], $p=0.008$) After 3 weeks, the ex vivo μ CT scans also showed a reduced callus percentage in old THFx animals (61.18% [13.9 9%]), as well as a low number of trabeculae (1.81 mm^{-1} [0.23 mm^{-1}]) compared to animals without blood loss (68.72% [15.71%], $p = 0.030$; 2.06 mm^{-1} [0.37 mm^{-1}], $p=0.041$). In the biomechanical test, a reduced elasticity limit of the old THFx mice (7.75 N [3.33 N]) in contrast to the old Fx (10.24 N [3.32 N]) animals was shown ($p=0.022$).

Conclusions

A severe blood loss has a higher negative effect on the healing, morphometry, and biomechanical properties of previously fractured femora in old compared to young individuals.

OC09.2

IN VIVO PRECLINICAL APPLICATION OF AN ACTIVE FIXATOR SYSTEM FOR THE SYSTEMATIC INVESTIGATION OF THE INFLUENCE OF THE MECHANICAL ENVIRONMENT ON FRACTURE HEALING

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Introduction and Objective

It is widely accepted that interfragmentary strain stimulus promotes callus formation during secondary bone healing. However, the impact of the temporal variation of mechanical stimulation on fracture healing is still not well understood. Moreover, the minimum strain value that initiates callus formation is unknown. The goal of this study was to develop an active fixation system that allows for in vivo testing of varying temporal distribution of mechanical stimulation and that enables detection of the strain limit that initiates callus formation.

Materials and Methods

We employed a previously established wedge defect model at the sheep tibia. The model incorporates two partial osteotomies directed perpendicularly to each other, thus creating a bone fragment in the shape of a wedge. The defect was instrumented with an active fixator that tilts the wedge around its apex to create a gradient of interfragmentary strain along the cutting line. The active fixator was equipped with a force and displacement sensors to measure the stiffness of the repair tissue during the course of healing. We developed a controller that enabled programming of different stimulation protocols and their autonomous execution during the in vivo experiment. The system was implanted in two sheep for a period of five weeks. The device was configured to execute immediate stimulation for one animal (stimulation from Day 1), and delayed stimulation for the other (stimulation from Day 22). The daily stimulation protocol consisted of 1'000 loading events evenly distributed over 12 hours from 9:00 am to 9:00 pm. The healing progression was monitored by the in vivo stiffness measurements provided by the fixator and by weekly radiographs. The impact of the local strain magnitude on bone formation was qualitatively evaluated on a post-mortem high-resolution CT scan of the animal with immediate stimulation.

Results

The animals tolerated the fixator system well. Both devices operated seamlessly throughout the entire experiment. Callus formation was initiated earlier for the immediately stimulated animal which was also confirmed by a faster stiffness increase. In this pilot feasibility experiment, the initiation of callus formation was observed between 0% and 4% local interfragmentary strain.

Conclusions

We developed an autonomous stimulation system for large animal research that enables systematic investigation of fracture healing processes. The in vivo pilot study demonstrated the feasibility of the system and delivered first interesting insights on temporal stimulation impact and callus induction strain limit. These observations, however, require further validation.

OC09.3

ELECTRICAL IMPEDANCE CORRELATES WITH RADIOGRAPHIC BONE HEALING IN RABBITS

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Introduction and Objective

Home-based monitoring of fracture healing has the potential of reducing routine follow-up and improve personalized fracture care. Implantable sensors measuring electrical impedance might detect changes in the electrical current as the fracture heals. The aim was to investigate whether electrical impedance correlated with radiographic fracture healing.

Materials and Methods

Eighteen rabbits were subjected to a tibial osteotomy that was stabilized with an external fixator. Two electrodes were positioned, one electrode placed within the medullary cavity and the other on the lateral cortex, both three millimeters from the osteotomy site. Transverse electrical impedance was measured daily across the fracture site at a frequency range of 5 Hz to 1 MHz using an Analog Discovery 2 Oscilloscope with Impedance Analyzer. Biweekly x-rays were taken and analyzed blinded using a modified anterior-posterior (AP) radiographic union score of the tibia (RUST). Each animal served as its own control by performing repeated measurements from time zero until the end of follow-up.

Results

At 5 Hz measurements, a linear mixed model revealed an average impedance at day zero of 10670 +/- 272 Ohm ($p < 0.001$) and a change in impedance from day 0 to day 7 of -3330 +/- 152 ($p < 0.001$). The slope from day 0-7 was estimated as -548.6 +/- 26 ($p < 0.001$) and was steeper than the slope after day 7 which was estimated to -85.6 +/- 4 ($p < 0.001$). This indicates that the impedance decreased quicker before day 7 and slower after day 7. The coefficient of variation for difference between RUST scores, from double intra-rater measurements of 15 radiographs with a minimum of 22 days between, was 1.3. Spearman's correlation coefficient between impedance and RUST score at the 5 Hz was -0.75 ($p < 0.001$).

Conclusions

This osteotomy model showed that the electrical impedance can be measured in vivo at a distance from the fracture site with a consistent change in impedance over time. This is the first study to demonstrate a significant correlation between increasing radiographic union score and decreasing impedance. Further studies are warranted to investigate how these new and important results can further be translated into larger animal studies.

OC09.4

YOUNG MEN AND SCAPHOID FRACTURES – A QUALITATIVE INVESTIGATION OF ATTITUDES AND BEHAVIOUR

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Introduction and Objective

Scaphoid waist fractures (SWF) are notable in upper limb trauma and predominantly occur in young men. Morbidities associated with SWF include fracture non-union, premature arthritis and humpback deformity. Delayed treatment and non-adherence to fracture immobilisation increases likelihood of these complications. There is evidence that men engage in negative health behaviours such as delayed help-seeking. The Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT) conducted interviews in individuals who had sustained a SWF. Although SWIFFT showed multiple social determinants for the overall injury and healing experience, a key factor this novel study considers is age and sex. This study aimed to analyse interview data from young male participants in SWIFFT to help distinguish the experience of SWF in young men, through exploring the influence of masculinity.

Materials and Methods

A purposive sample of 12 young male participants were selected from SWIFFT. These participants were enrolled from a possibility of 13 different centres across Britain. There were 17 semi-structured interviews produced from these participants, and this was thought to be sufficient for data saturation. These interviews were evaluated through deductive thematic analysis with an open-coding approach, with respondents' experiences being compared against themes documented in men's health literature. The "Braun and Clarke (2006) Six Phases of Thematic Analysis" methodology was adopted to perform this.

Results

There were three thematic models developed in the data set, which then were further divided into subthemes. Model 1: Negative Health Behaviour Prior to Treatment, model 2: Feeling Frail and model 3: Need for Speed. Model 1 corroborated that participants were inclined to sustain the injury as a result of risk-taking and would subsequently hesitate to seek treatment. Model 2 indicated that as a result of the injury, respondents were unable to engage in physical activities and activities of daily living. Respondents exercised caution to varying extents after sustaining a SWF. Model 3 highlighted that interviewees were prone to non-adherence with fracture immobilisation and in hindsight resumed employment prematurely.

Conclusions

The findings of this study demonstrate that masculinity is significantly influential on the experience of SWF in young men. This was indicated through the results of thematic analysis strongly corresponding with behaviours established in men's health literature. Educational interventions could be of value in addressing behaviours observed in this population group, such as delayed help-seeking and non-compliance with fracture immobilisation. Further work in patient education and concordance with treatment after sustaining a SWF may be beneficial to longer term outcomes. In turn, this may reduce complications associated with SWF in young men.

OC10 ORTHOPAEDIC CLINICAL RESEARCH

K10

DEEP PHENOTYPING CHRONIC BACK PAIN PATIENTS FOR PRECISION MEDICINE

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Chronic low back pain (cLBP) is a complex, multifaceted disorder where biological, psychological, and social factors affect its onset and trajectory. Consequently, cLBP encompasses many different disease variants, with multiple patient-specific mechanisms. The goal of NIH Back Pain Consortium (BACPAC) Research Program is to develop understanding of cLBP mechanisms and to develop algorithms that optimally match specific treatments to individual patients. To accomplish this, one research activity of BACPAC is to develop theoretical models for chronic low back pain based on the current state of knowledge in the scientific community, and to interrogate the relationships implied by the theoretical models using data generated by or available to BACPAC. The models consider biopsychosocial perspectives, and encompass both peripheral (i.e. low back) and central (i.e. spinal and supra-spinal) factors as well as proposed mechanisms of action of cLBP treatments. However, absent explanations, models/algorithms may fall short of regulatory requirements and clinician expectations, and ultimately may not be embraced by physicians and patients. To address this, BACPAC is developing a clinical utility roadmap (CUR) to clarify how models will be used in practice for selecting optimal treatments, monitoring response to treatment, and reducing health care utilization. This presentation will review the goals of BACPAC and how theoretical models and CUR are being used to support computational knowledge networks to integrate data from deeply phenotyped cLBP patients.

OC10.1

THE ACCURACY OF A PATIENT SPECIFIC GUIDE MEDIATED HIGH TIBIAL OSTEOTOMY FOR POSTERIOR SLOPE AND METAPHYSEAL VARUS CORRECTION: A CASE STUDY

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Introduction and Objective

After anterior cruciate ligament reconstruction one of the risk factors for graft (re-)rupture is an increased posterior tibial slope (PTS). The current treatment for PTS is a high tibial osteotomy (HTO). This is a free-hand method, with 1 degree of tibial slope correction considered to be equal to 1 or even 1.67 mm of the anterior wedge resection. Error rates in the frontal plane reported in literature vary from 1 - 8.6 degrees, and in the sagittal plane outcomes in a range of 2 – 8 degrees are reported when planned on PTSs of 3 - 5 degrees. Therefore, the free-hand method is considered to have limited accuracy. It is expected that HTO becomes more accurate with patient specific saw guides (PSGs), with an accuracy margin reported in literature of 2 degrees. This proof of concept porcine cadaver case study aimed to investigate whether the use of PSGs improves the accuracy of HTO to less than 2 degrees. Secondly, the reproducibility of tibial slope measurement was evaluated.

Materials and Methods

Preoperative MRI images of porcine cadaver knees (n = 3) were used to create 3D anatomical bone models (Mimics, Materialise, Belgium). These 3D models were subsequently used to develop PSGs (3-Matic, Materialise, Belgium) to correct all tibiae for 3 degrees PTS and 4 degrees varus. The PSG mediated HTOs were performed by an experienced orthopaedic surgeon, after which postoperative MRI images were obtained. 3D anatomical models of postoperative tibiae were created, and tibial slopes were assessed on both pre- and postoperative tibiae. The tibial slope was defined as the angle between the mechanical axis and 3D tibial reference plane in the frontal and sagittal plane. The accuracy of the PSG mediated HTO (median and range) was defined as the difference in all possible combinations of the preoperatively planned and postoperatively obtained tibial slopes. To ensure reproducibility, the pre- and postoperative tibial slopes were measured thrice by one observer. The intra-class correlation coefficients (ICCs) were subsequently calculated to assess the intra-rater reliability (SPSS, IBM Corp., Armonk, N.Y., USA).

Results

An accuracy within 2 degrees was achieved in all three cases. The median and range in accuracy for each specimen were +0.46 (-0.57 - 1.45), +0.60 (-1.07 - 1.00), and +0.45 (-0.16 - 0.71) degrees in the frontal plane, and -0.45 (-1.97 - 1.22), -0.80 (-2.42 - 1.77), and 0.00 (-2.19 - 1.93) degrees in the sagittal plane. The pre- and postoperatively planned tibial slopes in the frontal and sagittal plane were measured with a good up to excellent reproducibility. The ICCs of the preoperative planned tibial slopes were 0.82 (95% CI, 0.11 - 1.0), and 0.77 (95% CI, 0.17 - 1.0) for the frontal and sagittal plane, respectively. Postoperative, the ICC for the frontal plane was 0.92 (95% CI, 0.43 - 1.0), and 0.67 (95% CI, -0.06 - 0.99) for the sagittal plane.

Conclusions

This proof of concept porcine case study showed an accuracy for the PSG mediated HTO within 2 degrees for each specimen. Moreover, the tibial slopes were measured with a good up to excellent reproducibility. Therefore, the PSG mediated HTO seems to be accurate and might be better than the current used free-

hand HTO method. These results offer perspective for implementation of PSG mediated HTO to correct PTS and metaphyseal varus.

OC10.2

EMERGENCY DEPARTMENT VISITS FOR NON-TRAUMATIC LOW BACK PAIN EPISODES DURING THE COVID-19 PANDEMIC: A RETROSPECTIVE ANALYSIS

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Introduction and Objective

The coronavirus (Covid-19) pandemic, first identified in China in December 2019, halted daily living with mandatory lockdowns imposed in Israel in March 2020. This halt induced a sedentary lifestyle for most citizens as well as a decreased physical activity time. These are both common risk factors for the development of low back pain (LBP) which is considered a major global medical and economical challenge effecting almost 1 in 3 people and a leading cause of Emergency Department (ED) visits. It is hypothesized that prevalence of minor LBP episodes during the first total lockdown should have increased compared to previous times. However, due to "Covid-19 fear" we expect a decrease in ED visits. We also speculate that rate of visits due to serious spinal illness (causing either immediate hospitalization or spinal surgery within 30-days of presentation) did not change.

Materials and Methods

Retrospective study based on patients visiting the ED in Tel Aviv Sourasky Medical Center During the first pandemic stage in 2020 compared to parallel periods in 2018 and 2019 due to LBP.

Results

During the first lockdown period on March 11th-April 21st, only 171 patients attended the ED due to non-traumatic LBP compared to more than 330 patients in the corresponding time during the years 2018 and 2019. This represents a statistically significant drop of 52.5% (p-value < 0.01) and 48.7% (p-value < 0.01) in LBP ED visits during the first pandemic lockdown of 2020 compared to 2019 and 2018, respectively. Additionally, there was no significant drop in immediate hospitalization or spine surgeries within 30 days following the ED visit (p-value >0.10 for all analysis types).

Conclusions

"Covid-19 fear" was probably the main reason for patients with an LBP episode to stay at home during the Covid-19 massive outbreak. Since no significant change was shown in the more severe cases, it seems that the minor LBP patients were able to contain the episode outside hospital walls. This presents an opportunity for clinicians and policy decisions makers to learn and find ways to improve our care of back pain in the community and to reduce unnecessary burden on EDs and the healthcare system.

OC10.3

A REVIEW OF OUTCOMES ASSOCIATED WITH FEMORAL NECK LENGTHENING OSTEOTOMY IN PATIENTS WITH COXA BREVIS

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Introduction and Objective

Several studies have described double and triple femoral neck lengthening osteotomies to correct coxa brevis deformity, however, no overview exists in literature. Our aim was to perform the first systematic review of the outcomes of double and triple femoral neck lengthening.

Materials and Methods

After an extensive search in Pubmed, CINAHL and Embase libraries for published articles using the following search strategy: '(((proximal femoral deformity) OR hip dysplasia) OR coxa brevis) AND (((femoral neck lengthening) OR double proximal femoral osteotomy) OR triple proximal femoral osteotomy)', we included studies reporting the results of double and triple femoral neck osteotomies. Clinical and radiological outcomes, and reported complications were extracted. The review process was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results

After evaluating 456 articles, we included 11 articles reporting 149 osteotomies in 143 patients (31% male, 64% female, 5% unspecified). Mean age of the patients was 20 years (range 7 years to 52 years). Indications were developmental hip dysplasia (51%), Perthes disease (27%), infection (6%), post-trauma (4%), congenital disorders (2%), slipped capital femoral epiphysis (1%), idiopathic (3%) and unknown (6%). The mean limb length discrepancy reduced by 12 mm (0 mm to 40 mm). In total, 65% of 101 positive Trendelenburg sign hips experienced improvement of abductor muscle strength. An 18% (9% to 36%) increase could be found in functional hip scores. Mean increase in articulo-trochanteric distance was 24 mm (10 mm to 34 mm). Five patients older than 30 years at the time of osteotomy and two younger patients with prior hip incongruency had disappointing results and required arthroplasty. In all, 12 complications occurred in 128 osteotomies, in which complications were reported.

Conclusions

This first systematic review of double and triple femoral neck lengthening osteotomies shows that favorable outcomes and few complications can be expected in coxa brevis, however, excessive caution is required in older patients with incongruent hips.

OC10.4

SHOULD WE CONTINUE TO USE ANTI-EMBOLISM GRADUATED COMPRESSION STOCKINGS?

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Introduction and Objective

The effectiveness of anti-embolic graduated compression stockings (GCSs) has recently been questioned. The aim of this study is to systematically review all the relevant randomised controlled trials published to date.

Materials and Methods

We systematically reviewed all the randomised controlled trials comparing anti-embolism stockings with no stockings. We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and CINAHL, Cochrane Musculoskeletal Injuries Group specialized register and the reference lists of articles as well as hand search results. Trials were independently assessed and data for the main outcome measures; deep vein thrombosis (DVT), pulmonary embolism and skin ulceration, were extracted by two reviewers.

Results

A total of 26 relevant RCTs involving 8279 participants were systematically reviewed. The occurrence of deep vein thrombosis was 306/4159 (7.3%) with the stocking to 492/4120 (11.9%) without the stockings (RR 0.49, 95% CI 0.39-0.62). The occurrence of pulmonary embolism was also reduced from 1.2% to 0.7% (95% 0.33-0.92). This initial finding was unsound due to the potential underreporting of negative studies and the subsequent changes to clinical practice. For the three large contemporary studies involving 5171 participants, these failed to show any statistically significant reduction in thrombosis, with DVT confirmed in 158 (6.1%) participants in those allocated to stocking, as opposed to 171 (6.6%) in the control group.

Conclusions

The current recommendations regarding the use of thrombo-embolic stockings need to be reconsidered, as their effectiveness at reducing the occurrence of post-operative deep vein thrombosis is minimal at best, based on the current evidence and clinical practices.

OC11 DISC DEGENERATION AND REGENERATION

K11

ROLE OF TIE2 POSITIVE NUCLEUS PULPOSUS PROGENITOR CELLS IN DISC DEGENERATION AND ITS USE IN REGENERATIVE MEDICINE

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Low back pain is thought to relate to intervertebral disc (IVD) degeneration. Although the mechanisms have not been clearly identified, exhaustion of nucleus pulposus cells and their producing matrix is regarded as one cause. The matrix of the IVD is continuously replenished and remodeled by tissue-specialized cells and are crucial in supporting the IVD function. However, due to aging, trauma, and genetic and lifestyle factors, the cells can lose their potency and viability, thereby limiting their collective matrix production capacity.

We have discovered the link between loss of angiopoietin-1 receptor (Tie2)-positive human NP progenitor cells (NPPC) and IVD degeneration. Tie2⁺ cells were characterized as undifferentiated cells with multipotency and possessing high self-renewal abilities. Thus we and others have proposed Tie2⁺ NPPC as a potent cell source for regenerative cell therapies against IVD degeneration. However, their utilization is hindered by low Tie2-expressing cell yields from NP tissue, in particular from commonly available older and degenerated tissue sources. Moreover, NPPC show a rapid Tie2 decrease due to cell differentiation as part of standard culture processes. As such, a need exists to optimize or develop new culture methods that enable the maintenance of Tie2-expressing NPPC. Trials to overcome these difficulties will be shared.

OC11.1

TRACTION TO OPTIMIZE INTERVERTEBRAL DISC MECHANOBIOLOGY: A BOVINE ORGAN MODEL FEASIBILITY STUDY

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Introduction and Objective

Low back pain (LBP) is a major cause of long-term disability in adults worldwide and it is frequently attributed to intervertebral disc (IVD) degeneration. So far, no consensus has been reached regarding appropriate treatment and LBP management outcomes remain disappointing. Spine unloading or traction protocols are common non-surgical approaches to treat LBP. These treatments are widely used and result in pain relief, decreased disability or reduced need for surgery. However, the underlying mechanisms -namely, the IVD unloading mechanobiology- have not yet been studied. The aim of this first study was to assess the feasibility of IVD unloading in a large animal organ culture set-up and evaluate its impact on mechanobiology.

Materials and Methods

Bovine tail discs (diameter 16.1 mm \pm 1.2 mm), including the endplates, were isolated and prepared for culture. Beside the day0 sample that was processed directly, three other discs were cultured for 3 days and processed on day4. One disc was loaded in the bioreactor according to a previously established physiological (compressive) loading protocol (2h/day, 0.2Hz). The two other discs were embedded in biocompatible resin, leaving the cartilage endplate free to permit nutrient diffusion, and fitted in the traction holder; one of these discs was kept in free swelling conditions, whereas the second was submitted to cyclic traction loading (2h/day, 0.2Hz) corresponding to 30% of the animal body weight corrected for organ culture.

Results

The cell viability assessed on lactate dehydrogenase and ethidium homodimer stained histological slides was not different between the three cultured discs. This means that the disc viability was not affected neither by the embedding, nor by the traction itself. Compared to the physiologically loaded disc, the gene expression of COL1, COL2 and ACAN was higher in the nucleus pulposus and inner annulus fibrosus of the traction treated disc. In the outer annulus fibrosus of this disc TAGLN and MKX were higher expressed upon traction than in the physiologically loaded disc.

Conclusions

Based on these preliminary data, we can conclude that large animal organ culture allows effective unloading of the disc, while preserving cell viability and modulating cellular gene expression responses. This sets the ground for future experiments and opens the door to an evidence-based improvement of clinical spine traction protocols and LBP management overall.

OC11.2

NOTOCHORDAL CELLS IN DISC REGENERATION

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Introduction and Objective

Intervertebral disc (IVD) degeneration accompanying with low back pain is a serious worldwide problem. Even though, surgical treatments are available for pain relief, there is an urgent need to establish enduring cell-based remedies. Notochordal (NC) cells as the ancestor of nucleus pulposus (NP) cells in human IVD are a promising therapeutic target. It has been reported that the loss of NC cells after childhood could promote the onset of disc degeneration. Thus, we firstly, aimed to optimise the culture of NC cells in vitro without using the FCS in alginate (3D) culture systems, secondly, investigate their behaviour in healthy and degenerate niche and lastly, co-culture these cells with degenerated NP cells to assess their regeneration potentials.

Materials and Methods

Porcine NC cells were extracted using pronase treatment followed by overnight digestion in 0.01% collagenase II. After extraction, cells were culture in 1.2% alginate beads (gold standard 3D culture) in either low glucose DMEM or α MEM medium. Cells were harvested after 24 hours, 1 week and 2 weeks for gene expression analysis and formalin fixed paraffin embedding. Quantitative Real-Time PCR and Immunostaining were performed for analysis of NC markers (KRT18, FOXA2 and T) and COL I as a negative marker. Next, NC cells were cultured in healthy and degenerate medium to assess their viability and behaviour.

Results

A mixed phenotype of NC and NP cells was observed in alginate bead cultures. NC phenotype was observed within all culture conditions with production of GAGs and maintenance of vacuolated phenotype. Gene expression analysis showed no significant difference between the culture of NC cells in low glucose DMEM and α MEM medium. Interestingly, NC cell viability was maintained in both healthy and degenerate media, despite observing more dead cells in degenerate conditions. Current investigations are comparing the behaviour of NC cells in healthy and degenerate niche.

Conclusions

Investigating the preservation of NC phenotype in alginate culture and studying their behaviour between healthy and degenerate conditions would lead us to better understand their characteristics in different niches and how we can further use them in therapeutic purposes for disc degeneration.

OC11.3

MICRORNAS ASSOCIATED WITH TLR-2-INDUCED INFLAMMATION IN INTERVERTEBRAL DISC PATHOPHYSIOLOGY

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Introduction and Objective

Intervertebral disc (IVD) degeneration is one of the major contributors to low back pain, the leading cause of disability worldwide. This multifactorial pathological process involves the degradation of the extracellular matrix, inflammation, and cell loss due to apoptosis and senescence. While the deterioration of the extracellular matrix and cell loss lead to structural collapse of the IVD, increased levels of inflammation result in innervation and the development of pain. Amongst the known regulators of inflammation, toll-like receptors (TLRs) and more specifically TLR-2 have been shown to be specifically relevant in IVD degeneration. As strong post-transcriptional regulators, microRNAs (miRNAs) and their dysregulation has been connected to multiple pathologies, including degenerative diseases such as osteoarthritis and IVD degeneration. However, the role of miRNAs in TLR signalling in the IVD is still poorly understood and was hence investigated in this study.

Materials and Methods

Human Nucleus pulposus (hNP) and Annulus fibrosus (hAF) cells (n=5) were treated with the TLR-2/6 specific agonist PAM2CSK4 (100 ng/mL for 6 hours) in order to activate the TLR2 signalling pathway. After the activation both miRNA and mRNA were isolated, followed by next-generation sequencing and qPCR analysis of proinflammatory cytokines respectively. Furthermore, cell supernatants were used to analyze the secretion of proinflammatory cytokines with enzyme-linked immunosorbent assay. TLR-2 knockdown (siRNA) cells were used as a control. Statistical analysis was conducted by performing Kolmogorov-Smirnov test and a two-tailed Student's t-test using GraphPad Prism version 9.0.2 for Windows (GraphPad Software, La Jolla California USA).

Results

TLR-2 activation resulted in the induction of an inflammatory cell response, with a significant increase in gene expression of interleukin (IL)-6 (525 ± 180 fold change, $p < 0.05$) and IL-8 (7513 ± 1907 fold change, $p < 0.05$) and protein secretion of IL-6 (30.5 ± 8.1 pg/mL) and IL-8 (28.9 ± 5.4 pg/mL). TLR-2 activation was furthermore associated with changes in the miRNA profile of hNP and hAF cells. Specifically, we identified 10 differentially expressed miRNAs in response to TLR-2 activation, amongst which were miR-335-3p (1.45 log₂ FC, $p < 0.05$), miR-125b-1-3p (0.55 log₂ FC, $p < 0.05$), and miR-181a-3p (-1.05 log₂ FC, $p < 0.05$).

Conclusions

The identified miRNAs are known to be associated with osteoarthritis (miR-335-3p), inflammation and IVD degeneration (miR-125-1-3p and miR-181a-3p), but the link to TLR signalling has not been previously reported. Experiments to validate the identified miRNAs and elucidate their functional role are undergoing. The identification of these miRNAs provides an opportunity to further investigate miRNAs in the context of TLR activation and inflammation and to enhance our understanding of underlying molecular mechanisms behind disc degeneration, inflammation, and TLR dysregulation.

OC11.4

THE IN VITRO EFFECTS OF MSC SECRETOME ON HUMAN NUCLEUS PULPOSUS CELLS IN A 3D CULTURE MODEL

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Introduction and Objective

Low back pain (LBP) is a disorder strongly associated with intervertebral disc degeneration (IDD) with an important impact on the quality of life of affected people. To date, LBP treatment is based on conservative methods with the aim to reduce back pain without restoring the degenerative environment of the disc. The main cause of IDD is the drastic reduction of the proteoglycan content within the nucleus pulposus (NP), eventually leading to the loss of disc water content, micro-architecture, biochemical and mechanical properties. A promising approach for disc regeneration is represented by the transplantation of mesenchymal stromal cells (MSCs). The exact mechanism remains unknown. Growing evidence suggests that MSCs can influence cells and modulate cells' behaviour by secreting a set of bioactive factors. MSCs secretome is composed of several molecules such as soluble protein, lipids, nucleic acids and extracellular vesicles (EVs) involved in inflammation, immunomodulation, cell survival and intercellular communication. The aim of this study was to evaluate the in vitro effects of MSCs secretome on human NP cells (hNPCs) in a 3D culture model with and without inflammatory stimulus.

Materials and Methods

MSCs secretome was collected from bone marrow-MSCs (BM-MSCs) and adipose tissue-MSCs (ASCs) after centrifugation and obtained by culturing cells without fetal bovine serum (FBS) for 48 hours. hNPCs were isolated from surgical specimens through digestion with type II collagenase, culture expanded in vitro, encapsulated in alginate beads (three-dimensional culture system) and treated with growth medium (controls), BM-MSCs or ASCs secretome with or without interleukin-1 beta (IL-1b). After 7 days, total RNA was extracted and reverse-transcribed. Gene expression levels of catabolic and anabolic genes were analyzed through real time-polymerase chain reaction (qPCR). Cell proliferation and glycosaminoglycan (GAG) production was assessed by flow cytometry and 1,9-dimethylmethylene blue (DMMB), respectively. hNPCs in alginate beads were stained with Live/Dead assay and detected using confocal immunofluorescence microscopy. Data were analyzed using Graphpad prism 8 and expressed as mean \pm S.D. One-way ANOVA analysis was used to compare differences among the groups under exam.

Results

Our results reported an increase of hNPCs proliferation after treatment with both MSCs-secretomes. In detail, cell proliferation levels increased at 7 days after ASC-secretome ($p \leq 0,05$) and BM-secretome ($p \geq 0,05$) treatment compared to control. Live/dead staining showed that cell death was reduced by BM-secretome ($p \leq 0,05$); in combined treatment of BM-secretome with IL1b 10ng/mL ($p \leq 0,05$) at 7 days compared to control. There is not a significant difference between treated and untreated hNPCs' GAG synthesis. In addition, gene expression levels resulted to be modulated by MSCs-secretomes under study compared to controls.

Conclusions

Although the cell-therapy may be considered an attractive and safe option, MSCs require long and expensive processes. In conclusion, our experimental conditions supported as BM-MSCs and ASCs secretomes could represent cell-free alternative approaches in IDD, overcoming translational limits of cell therapy to the clinical practice.

OC12 DISC DEGENERATION AND REGENERATION

K12

WNT REGULATION IN BONE OF TYPE 2 DIABETES PATIENTS

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Fragility fractures are skeletal complications associated with type 2 diabetes (T2D) causing disability, hospitalization, impaired quality of life, and increased mortality. Increased circulating sclerostin and accumulation of advanced glycation end-products (AGEs) are two potential mechanisms underlying low bone turnover and increased fracture risk. We have recently shown that T2D affects the expression of genes controlling bone formation (SOST and RUNX2) and that accumulation of AGEs is associated with impaired bone formation in T2D. We hypothesized that Wnt/B-catenin target genes are down-regulated in bone of T2D subjects as a consequence of decreased SOST and AGEs accumulation. To this end, we studied gene expression in extracts of bone samples obtained from femoral heads of 14 subjects with relatively well-controlled T2D (HbA1c $6.5 \pm 1.7\%$) and 21 control, non-diabetic postmenopausal women (age >65 years) undergoing hip replacement. There were no differences in age ($73.2 \pm .8$ vs. 75.2 ± 8.5 years) or BMI (27.7 ± 5.6 vs. 29.9 ± 5.4 kg/m²) between control and T2D groups, respectively. Expression of LEF1 mRNA was significantly lower in T2D compared to non-diabetic subjects ($p=0.002$), while DKK1 was not different between groups ($p=0.108$). Correlation analysis showed that DKK1 ($r^2=0.038$; $p=0.043$) and HbA1c ($r^2=0.503$; $p=0.048$) increased with age in T2D. COL1A1 mRNA trended lower in T2D compared to controls ($p=0.056$). Bone volume ($9,333 \pm 1,443$ vs. $15,53 \pm 2,442$ mm²; $p=0.048$), mineralized volume ($9,278 \pm 1,418$ vs. $15,45 \pm 2,444$ mm²; $p=0.048$) and BV/TV ($0,2125 \pm 0,03114$ vs. $0,3719 \pm 0,03196$ %; $p=0.002$) measured by bone histomorphometry were lower in T2D compared to controls. Our data show that even in patients with relatively good glycemic control, T2D decreases expression of Wnt/B-catenin target genes and COL1A1, associated with decreased bone density. These results may help understand the mechanisms underlying bone fragility in T2D.

OC12.1

MALUNION AFTER TRAUMA - KNEE ARTHRITIS CORRELATES WITH MALALIGNMENT

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Introduction and Objective

Malunion after trauma can lead to coronal plane malalignment in the lower limb. The mechanical hypothesis suggests that this alters the load distribution in the knee joint and that this increased load may predispose to compartmental arthritis. This is generally accepted in the orthopaedic community and serves as the basis guiding deformity correction after malunion as well as congenital or insidious onset malalignment. Much of the literature surrounding the contribution of lower limb alignment to arthritis comes from cohort studies of incident osteoarthritis. There has been a causation dilemma perpetuated in a number of studies - suggesting malalignment does not contribute to, but is instead a consequence of, compartmental arthritis. In this investigation the relationship between compartmental (medial or lateral) arthritis and coronal plane malalignment (varus or valgus) in patients with post traumatic unilateral limb deformity was examined. This represents a specific niche cohort of patients in which worsened compartmental knee arthritis after extra-articular injury must rationally be attributed to malalignment.

Materials and Methods

The picture archiving system was searched to identify all 1160 long leg x ray films available at a major metropolitan trauma center over a 12-year period. Images were screened for inclusion and exclusion criteria, namely patients >10 years after traumatic long bone fracture without contralateral injury or arthroplasty to give 39 cases. Alignment was measured according to established surgical standards on long leg films by 3 independent reviewers, and arthritis scores Osteoarthritis Research Society International (OARSI) and Kellegren-Lawrence (KL) were recorded independently for each compartment of both knees. Malalignment was defined conservatively as mechanical axis deviation outside of 0-20 mm medial from centre of the knee, to give 27 patients. Comparison of mean compartmental arthritis score was performed for patients with varus and valgus malalignment, using Analysis of Variance and linear regression.

Results

In knees with varus malalignment there was a greater mean arthritis score in the medial compartment compared to the contralateral knee, with OARSI scores 5.69 vs 3.86 (0.32, 3.35 95% CI; $p < 0.05$) and KL 2.92 vs 1.92 (0.38, 1.62; $p < 0.005$). There was a similar trend in valgus knees for the lateral compartment OARSI 2.98 vs 1.84 (CI -0.16, 2.42; $p = 0.1$) and KL 1.76 vs 1.31 (CI -0.12, 1.01; $p = 0.17$), but the evidence was not conclusive. OARSI arthritis score was significantly associated with absolute MAD (0.7/10mm MAD, $p < 0.0005$) and Time (0.6/decade, $p = 0.01$) in a linear regression model.

Conclusions

Malalignment in the coronal plane is correlated with worsened arthritis scores in the medial compartment for varus deformity and may similarly result in worsened lateral compartment arthritis in valgus knees. These findings support the mechanical hypothesis that arthritis may be related to altered stress distribution at the knee, larger studies may provide further conclusive evidence.

OC12.2

WEIGHT-BEARING ALLOWED FOLLOWING INTERNAL FIXATION OF ANKLE FRACTURES, A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Introduction and Objective

Postoperative management regimes vary following open reduction and internal fixation of unstable ankle fractures. There is an evolving understanding that poorer outcomes could be associated with non-weight bearing protocols and immobilisation. Traditional non-weight bearing cast immobilisation may prevent loss of fixation, and this practice continues in many centres. The aim of this systematic review and meta-analysis is to compare the complication rate and functional outcomes of early weight-bearing (EWB) versus late weight-bearing (LWB) following open reduction and internal fixation of ankle fractures.

Materials and Methods

We performed a systematic review with a meta-analysis of controlled trials and comparative cohort studies. MEDLINE (via PubMed), Embase and the Cochrane Library electronic databases were searched inclusive of all date up to the search time. We included all studies that investigated the effect of weight-bearing following adults ankle fracture fixation by any means. All ankle fracture types, including isolated lateral malleolus fractures, isolated medial malleolus fractures, bi-malleolar fractures, tri-malleolar fractures and Syndesmosis injuries, were included. All weight-bearing protocols were considered in this review, i.e. immediate weight-bearing (IMW) within 24 hours of surgery, early weight-bearing (EWB) within three weeks of surgery, non-weight-bearing for 4 to 6 weeks from the surgery date (or late weight-bearing LWB). Studies that investigated mobilisation but not weight-bearing, non-English language publications and tibial Plafond fractures were excluded from this systematic review. We assessed the risk of bias using ROB 2 tools for randomised controlled trials and ROBINS-1 for cohort studies. Data extraction was performed using Covidence online software and meta-analysis by using RevMan 5.3.

Results

After full-text review, fourteen studies (871 patients with a mean age ranged from 35 to 57 years) were deemed eligible for this systematic review; ten randomised controlled trials and four comparative cohort studies. Most of the included studies were rated as having some concern with regard to the risk of bias. There is no important difference in the infection rate between protected EWB and LWB groups (696 patients in 12 studies). The risk ratio (RR) is 1.30, [95% CI 0.74 to 2.30], $I^2 = 0\%$, $P = 0.36$). Other complications were rare. The Olerud-Molander Ankle Score (OMAS) was the widely used patient-reported outcome measure after ankle fracture fixation among the studies. The result of the six weeks OMAS analysis (three RCTs) was markedly in favour of the early weight-bearing group (MD = 10.08 [95% CI 5.13 to 15.02], $I^2 = 0\%$, $P < 0.0001$).

Conclusions

The risk of postoperative complications is an essential factor when considering EWB. We found that the overall incidence of surgical site infection was 6%. When comparing the two groups, the incidence was 5.2% and 6.8% for the LWB and EWB groups. This difference is not clinically important. On the other hand, significantly better early functional outcome scores were detected in the EWB group. These results are not

without limitations. Protected early weight-bearing following open reduction and internal fixation of ankle fractures is potentially safe and improve short-term functional outcome. Further good-quality randomised controlled trials would be needed before we could draw a more precise conclusion.

OC12.3

DO PATIENTS WITH NEUROMUSCULAR DISORDERS HAVE A HIGHER RISK OF DISLOCATION OF HIP HEMIARTHROPLASTY?

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Introduction and Objective

Dislocation of a hip hemiarthroplasty is a significant complication with a high mortality rate in elderly patients. Previous studies have shown a higher risk of dislocation in patients with neuromuscular conditions. In this study, we reviewed our larger cohort of patients to identify if there is a link between neuromuscular disorders and dislocation of hip hemiarthroplasty in patients with neuromuscular conditions.

Materials and Methods

We have retrospectively analysed a single-centre data that was collected over 34 years for patients with intracapsular neck of femur fracture who underwent hip hemiarthroplasty. The study population was composed of four groups: patients with no neuromuscular disorders, patients with Parkinson's disease, patients with previous stroke, and patients with mental impairment.

Results

A total of 3827 patients were included in the analysis. 3371 patients had no neuromuscular condition (Group I) with a dislocation rate of 1.1%. 219 patients had Parkinsonism (Group II) with a dislocation rate of 3.2%, 104 patients had a previous stroke with weakness on the fracture side with a dislocation rate of 1.0% (Group III), and 984 patients had severe mental impairment with a dislocation rate of 1.8% (Group IV). The increased dislocation rate for those with Parkinson's disease was statistically significant ($p=0.02$) while none of the other neuromuscular conditions were statistically significant.

Conclusions

Our study has shown an increased risk of dislocation of hemiarthroplasty in patients with Parkinson's disease in comparison to other groups. No increase was apparent for patients with mental impairment or weakness from a previous stroke.

OC12.4

THE INFLUENCE OF THE UBIQUITIN-EDITING ENZYME A20 AFTER MAJOR TRAUMA AND SUBSEQUENT REMOTE LUNG INJURY IN RELATION TO THE SUPPRESSION OF NF-KAPPAB SIGNALING

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Introduction and Objective

Hemorrhagic shock and fractures are the most common injuries within multiple injured patients, inducing systemic and local inflammation in NF-kappaB-dependent manner. Alcohol intoxication, showing a high incidence with severe injuries, has immunomodulatory properties and implicates NF-kappaB downregulation. However, the mechanism is largely unknown. A20 deubiquitinase is a critical negative regulator of NF-kappaB activity and inflammation. Here, we investigate the role of A20 as a modifier of NF-kappaB-driven inflammation and remote lung injury in severely injured and alcohol-intoxicated mice.

Materials and Methods

Mice were randomly divided into four groups. Either sodium chloride or ethanol (35%, EtOH) was administrated by intragastral gavage one hour before trauma induction. In the trauma group, the animals underwent an osteotomy with external fracture fixation (Fx) followed by a pressure-controlled hemorrhagic shock (35±5 mmHg; 90 minutes) with subsequent resuscitation (H/R). Sham-operated animals underwent only surgical procedures. Mice were sacrificed at 24 hours. Fatty vacuoles and thus, the alcohol intoxication were evaluated by Oil red O staining of the liver. To assess the lung injury, hematoxylin eosin staining, determination of total protein concentration in bronchoalveolar lavage (BALF) and calculation of the lung injury score (LIS) were performed. Lungs were stained for neutrophil elastase, CXCL1 and active caspase-3 to determine neutrophil invasion, pro-inflammatory changes and apoptosis, respectively. The expression level of A20 was evaluated by immunofluorescence microscopy.

Results

EtOH induced significant fatty changes in the liver. Fx+H/R led to trauma-induced lung injury, significantly enhancing the total protein concentration in the BALF and the histomorphological LIS compared to sham animals. In turn, EtOH reduced the lung injury in Fx+H/R. The expression of CXCL1 and activated caspase-3 as well as the pulmonary neutrophil infiltration were significantly enhanced in Fx+H/R vs. sham, whereas A20 protein expression was reduced. EtOH+Fx+H/R caused reduced pulmonary neutrophil invasion, CXCL1 expression, and apoptosis compared to Fx+H/R, whereas the A20 protein expression in the lungs was increased.

Conclusions

In murine Fx+H/R trauma model, EtOH ameliorates the extent of the remote lung injury. The immunosuppressive effect may be caused by elevated pulmonary levels of A20 deubiquitinase, indicating a suppression of NF-kappaB activation.

OC13 BIOMECHANICS

K13

PATIENT SPECIFIC INSTRUMENTATION IN HIGH TIBIAL OSTEOTOMY: STATE OF THE ART AND PRELIMINARY RESULTS OF A NEW CUSTOMISED 3-D PRINTED DEVICE

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The medial opening-wedge high tibial osteotomy (OW-HTO) is an accepted option to treat the isolated medial compartment osteoarthritis (OA) in varus knee. Despite satisfactory outcomes were described in literature, consistent complication rate has been reported and the provided accuracy of coronal alignment correction using conventional HTO techniques falls short.

Patient specific instrumentations has been introduced with the aim to reduce complications and to improve the intra-operative accuracy according to the pre-operative plan, which is responsible for the clinical result of the surgery.

In this talk, an overview of the clinical results of HTO patient specific instrumentation available in literature will be performed.

Moreover, preliminary intra-operative and clinical results of a new customised 3-D printed cutting guide and fixation plate for OW-HTO will be presented.

OC13.1

A LONGITUDINAL STUDY ON THE GEOMETRICAL, STRUCTURAL AND MATERIAL PROPERTIES OF TYPE-2 DIABETIC BONE USING A ZUCKER DIABETIC FATTY (ZDF) RAT MODEL

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Introduction and Objective

Individuals with type 2 diabetes (T2D) have a 3-fold increased risk of bone fracture compared to non-diabetics, with the majority of fractures occurring in the hip, vertebrae and wrists. However, unlike osteoporosis, in T2D, increased bone fragility is generally not accompanied by a reduction in bone mineral density (BMD). This implies that T2D is explained by poorer bone quality, whereby the intrinsic properties of the bone tissue itself are impaired, rather than bone mass. Yet, the mechanics remain unclear. The objective of this study is to (1) assess the fracture mechanics of bone at the structural and tissue level; and (2) investigate for changes in the composition of bone tissue along with measuring total fluorescent advanced glycation end products (fAGEs) from the skin, as T2D progresses with age in Zucker diabetic fatty (ZDF (fa/fa)) and lean Zucker (ZL (fa/+)) rats.

Materials and Methods

Right ulnae and skin sections were harvested from ZDF (fa/fa) (T2D) and ZL (fa/+) (Control) rats at 12 and 46 weeks (wks) of age (n = 8, per strain and age) and frozen. Right ulnae were thawed for 12 hrs before micro-CT (μ CT) scanning to assess the microstructure and measure BMD. After scanning, ulnae were loaded until failure via three-point bending. Fourier transform-infrared microspectroscopy (FTIR) was used to measure various bone mineral- and collagen-related parameters such as, mineral-to-matrix ratio and nonenzymatic cross-link ratio. Finally, fAGEs were measured from skin sections using fluorescence spectrometry and an absorbance assay, reported in units of ng quinine/ mg collagen.

Results

At 12 and 46 wks bone size was significantly smaller in length ($p < 0.01$), cortical area ($p < 0.001$) and cross-sectional moment of inertia ($p < 0.001$) in T2D rats compared to age-matched controls. A slight reduction in BMD was observed in T2D rats compared to controls at both ages, however, this was not significant. Structural properties of T2D bone were significantly altered at 12 and 46 wks, with bending rigidity increasing approximately 2.5-fold and 1.5-fold in control and T2D rats with age, respectively ($p < 0.0001$). Similarly, yield and ultimate moment significantly reduced in T2D rats with age in comparison to controls ($p < 0.0001$). Energy absorbed to failure was significantly reduced in T2D rats at 46 weeks of age compared to controls ($p < 0.01$). The amount of energy absorbed to failure increased approximately 1.4-fold from 12 to 46 wks in control rats, however, in T2D rats a reduction was seen with age, although not significant. At 12 wks, there was no significant deficits in tissue material properties, whereas, at 46 wks a significant reduction in yield stress, yield strain and ultimate stress was observed for T2D rats in comparison to controls ($p < 0.05$).

Conclusions

These findings show that longitudinal growth is impaired as early as 12 wks of age and by 46 wks bone size is significantly reduced in T2D rats compared to controls. The reduction in T2D structural properties is likely attributed to the bone geometry deficits. At 12 wks of age, the tissue material properties are not altered in T2D bone versus controls. However, at 46 wks, bone strength is reduced in T2D, leading to the conclusion that tissue properties are altered as the disease progresses.

OC13.2

MEDIAL HELICAL VERSUS LATERAL STRAIGHT PLATING OF DISTAL FEMORAL FRACTURES. A BIOMECHANICAL COMPARATIVE STUDY

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Introduction and Objective

Distal femoral fractures are commonly treated with a straight plate fixed to the lateral aspects of both proximal and distal fragments. However, the lateral approach may not always be desirable due to persisting soft-tissue or additional vascular injury necessitating a medial approach. These problems may be overcome by pre-contouring the plate in helically shaped fashion, allowing its distal part to be fixed to the medial aspect of the femoral condyle. The objective of this study was to investigate the biomechanical competence of medial femoral helical plating versus conventional straight lateral plating in an artificial distal femoral fracture model.

Materials and Methods

Twelve left artificial femora were instrumented with a 15-hole Locking Compression Plate – Distal Femur (LCP-DF) plate, using either conventional lateral plating technique with the plate left non-contoured, or the medial helical plating technique by pre-contouring the plate to a 180° helical shape and fixing its distal end to the medial femoral condyle (n=6). An unstable extraarticular distal femoral fracture was subsequently simulated by means of an osteotomy gap. All specimens were tested under quasi-static and progressively increasing cyclic axial and torsional loading until failure. Interfragmentary movements were monitored by means of optical motion tracking.

Results

Initial axial stiffness was significantly higher for helical (185.6±50.1 N/mm) versus straight (56.0±14.4) plating, $p < 0.01$. However, initial torsional stiffness in internal and external rotation remained not significantly different between the two fixation techniques (helical plating: 1.59±0.17 Nm/° and 1.52±0.13 Nm/°; straight plating: 1.50±0.12 Nm/° and 1.43±0.13 Nm/°), $p \geq 0.21$. Helical plating was associated with significantly higher initial interfragmentary movements under 500 N static compression compared to straight plating in terms of flexion (2.76±1.02° versus 0.87±0.77°) and shear displacement under 6 Nm static rotation in internal (1.23±0.28° versus 0.40±0.42°) and external (1.21±0.40° versus 0.57±0.33°) rotation, $p \leq 0.01$. In addition, helical plating demonstrated significantly lower initial varus/valgus deformation than straight plating (4.08±1.49° versus 6.60±0.47°), $p < 0.01$. Within the first 10000 cycles of dynamic loading, helical plating revealed significantly bigger flexural movements and significantly lower varus/valgus deformation versus straight plating, $p = 0.02$. No significant differences were observed between the two fixation techniques in terms of axial and shear displacement, $p \geq 0.76$. Cycles to failure was significantly higher for helical plating (13752±1518) compared to straight plating (9727±836), $p < 0.01$.

Conclusions

Although helical plating using a pre-contoured LCP-DF was associated with higher shear and flexion movements, it demonstrated improved initial axial stability and resistance against varus/valgus deformation compared to straight lateral plating. Moreover, helical plate constructs demonstrated significantly improved endurance to failure, which may be attributed to the less progressively increasing lever bending moment arm inherent to this novel fixation technique. From a biomechanical perspective, helical plating may be considered as a valid alternative fixation technique to standard straight lateral plating of unstable distal femoral fractures.

OC13.3

RADIOLOGICAL COMPARISON OF THREE TECHNIQUES OF SCAPHOLUNATE RECONSTRUCTION FOR SCAPHOLUNATE INSTABILITY: A CADAVER STUDY

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Introduction and Objective

Scapholunate instability is the most common cause of carpal instability. When this instability is left untreated, the mechanical relationship between the carpal bones is permanently disrupted, resulting in progressive degenerative changes in the radiocarpal and midcarpal joints. Different tenodesis methods are used in the treatment of acute or early chronic reducible scapholunate instability, where arthritis has not developed yet and the scapholunate ligament cannot be repaired. Although it has been reported that pain is reduced in the early follow up in clinical studies with these methods, radiological results differ between studies. The deterioration of these radiological parameters is associated with wrist osteoarthritis as previously stated. Therefore, more studies are needed to determine the tenodesis method that will improve the wrist biomechanics better and will last longer. In our study, two new tenodesis methods, spiral antipronation tenodesis, and anatomic front and back reconstruction (ANAFAB) were radiologically compared with triple ligament tenodesis (TLT), in the cadaver wrists.

Materials and Methods

The study was carried out on a total of 16 fresh frozen cadaver wrists. Samples were randomly allocated to the groups treated with 3 different scapholunate instability treatment methods. These are TLT (n: 6), spiral antipronation tenodesis (n: 5) and ANAFAB tenodesis (n: 5) groups. In all samples SLIL, DCSS, STT, DIC, RSC and LRL ligaments were cut in the same way to create scapholunate instability. Wrist CT scans were taken on the samples in 4 different states, in intact, after the ligaments were cut, after the reconstruction and after the movement cycle. In all of these 4 states, wrist CTs were taken in 6 different wrist positions. For every state and every position through tomography images; Scapholunate (SL) distance, Scapholunate (SL) angle, Radioscaphoid (RS) angle, Radiolunate (RL) angle, Capitulum (CL) angle, Dorsal scaphoid translation (Dt) measurements were made.

Results

Scapholunate distances means were different between intact and cut states only in neutral and clenched fist positions for all groups (p values <0.001). Mean differences were similar between the groups (p > 0.100). In neutral position, for SL center distance, mean difference between cut and reconstruction states were not different between the groups (p=0.497) but it was noted that only TLT group could not restore to the intact state. In neutral position, for SL angle, compared with the cut state, TLT and ANAFAB significantly reduced the angle (TLT: 20° (p=0.005), ANAFAB: 28° (p<0.001)) whereas antipronation tenodesis could not (13°, p=0.080). In clenched fist position, for SL angle, compared with the intact state, only ANAFAB group restored the angle, TLT and antipronation groups were significantly worse than the intact state (TLT: p<0.001, antipronation: p=0.001). In clenched fist position, for RL angle, compared with the intact state, ANAFAB and TLT groups restored the angle but antipronation group was significantly worse than the intact state (p<0.001). In neutral position, for RS angle, compared with the cut state, only ANAFAB significantly reduced the angle (11°, p<0.001) whereas TLT and antipronation groups could not (TLT: 6° (p=0.567), antipronation: 4° (p=0.128)).

Conclusions

In the presence of severe scapholunate instability in which a several number of secondary stabilizers are injured, the ANAFAB tenodesis method may be preferred to the classical method, TLT tenodesis. The results of spiral antipronation tenodesis were not better than the TLT.

OC13.4

THE FLEXION - EXTENSION AXIS OF THE KNEE AND ITS RELATIONSHIP TO THE ROTATIONAL ALIGNMENT OF TIBIA IN KNEE OSTEOARTHRITIS. THE CONCEPT OF PROXIMAL TIBIAL TWIST

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Introduction and Objective

The geometry of the proximal tibia and distal femur is intimately linked with the biomechanics of the knee and it is to be considered in total knee arthroplasty (TKA) component positioning. The aim of the present study was to evaluate the proximal tibial torsion in relation to the flexion-extension axis of the knee in healthy and pathological cohort affected by knee osteoarthritis (OA).

Materials and Methods

We retrospectively analyzed computed tomography scans of OA knee of 59 patients prior to TKA and non-arthritic knee of 39 patients as control. Posterior condylar angle (PCA), femoral tibial torsion (TEAs-PTC and TEAs-PTT), proximal tibial torsion (PTC-PTT and PCAx-PTC) and distance between fibial tuberosity and the trochlear groove (TT-TG) were measured.

Results

No differences were found for gender, age, TG-TT and PCAn angles. Statistically significant differences were found for all the other angles considered. Significant relation was found between Tibial Torsion and TEA-PTT angles, between PCAx-PTC and TEA-PTC, between TEA-PTT and TEA-PTC and between PCAx-PTC and TEA-PTT. All measures, except TG-TT and PCAn angles, showed high validity (AUC > 75%) in detecting OA, with TEA-PTT displaying the highest validity with an AUC of 94.38%.

Conclusions

This is the first study to find significant differences in terms of proximal tibia geometry and anatomy between non arthritic and OA knees. It is conceivable that such anatomy could be implicated in the development of OA. Based on our data, the TEAs is a valid reference for correct positioning of tibial component in TKA. Indeed, setting the tibial component parallel to TEAs makes the prosthetic knee more similar to the native non-arthritic knee.

OC14 HIP ARTHROPLASTY

K14

HYBRID COOPERATIVE COMPLEX OF HYALURONIC ACID AND SODIUM CHONDROITIN, CLINICAL EVIDENCES

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Hyaluronic acid (HA) is responsible for the viscoelastic properties of synovial fluid and cartilage. Compared to healthy joints, synovial fluid in osteoarthritic joints contains HA of lower concentration and molecular weight. Hyaluronic acid hybrid complexes are composed by long and short HA chains linked by H bonds. These rheological characteristics and viscoelastic properties were produced by thermal patented process without chemical modification. Chondroitin sulfate (CS) is one of the essential components of the articular cartilage matrix and plays a key role in cartilage's mechanical and elastic properties. Biotechnological chondroitin (CB) is produced through fermentative/biotechnological processes and, unlike CS, is not sulfated. It has been shown that CB to play a more significant role in the phenotypic maintenance of chondrocytes than chondroitin sulfate and increases their viability and proliferation. A recent A Single-Arm, Open-Label, Pilot Study was conducted to evaluate the safety and efficacy of a single-dose intra-articular injection of Hybrid Hyaluronic acid and Sodium Chondroitin in the Treatment of Symptomatic Hip Osteoarthritis. A single injection of HS-SC was well tolerated and safe in the treatment of symptomatic hip OA. The treatment demonstrated a rapid significant improvement in pain (VAS) and function (Lequesne's Index) up to 6 months of follow-up.

OC14.1

RESTORING GLOBAL OFFSET AND LOWER LIMB LENGTH IN TOTAL HIP ARTHROPLASTY WITH A 3 OFFSET OPTION DOUBLE-TAPERED STEM. A MONOCENTRIC FIVE-YEARS FOLLOW-UP EXPERIENCE

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Introduction and Objective

A proper restoration of hip biomechanics is fundamental to achieve satisfactory outcomes after total hip arthroplasty (THA). A global hip offset (GO) postoperatively reduction of more than 5 mm was known to impair hip functionality after THA. This study aimed to verify the restoration of the GO radiographic parameter after primary THA by the use of a cementless femoral stem available in three different offset options without length changing.

Materials and Methods

From a consecutive series of 201 patients (201 hips) underwent primary cementless THA in our centre with a minimum 3-year follow up, 80 patients (80 hips) were available for complete radiographic evaluation for GO and limb length (LL) and clinical evaluation with Harris hip score (HHS). All patients received the same femoral stem with three different offset options (option A with - 5 mm offset, option B and option C with + 5 mm offset, constant for each sizes) without changing stem length.

Results

Mean GO significantly increased by + 3 mm ($P < 0.05$) and mean LL significantly decreased by + 5 mm ($P < 0.05$) after surgery, meaning that postoperatively the limb length of the operated side increased by + 5 mm. HHS significantly improved from 56.3 points preoperatively to 95.8 postoperatively ($P < 0.001$). Offset option A was used in 1 hip (1%), B in 59 hips (74%) and C in 20 hips (25%).

Conclusions

The femur is lateralized with a mean of + 5mm after surgery than, the native anatomy, whatever type of stem was used. Thus, the use of this 3-offset options femoral stem is effective in restoring the native biomechanical hip parameters as GO, even if 2 offset options were considered sufficient to restore GO.

OC14.2

ANTERIOR AND LATERAL APPROACH COMPARISON IN FEMORAL NECK FRACTURES: RADIOGRAPHIC ANALYSIS OF HIP HEMIARTHROPLASTY

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Introduction and Objective

Interest for direct anterior approach (DAA) in hip hemiarthroplasty (HHA) has greatly increased in recent years, however which is the best surgical approach in hip replacement treating femoral neck fractures (FNFs) is already unclear. The aim of this study is to perform a radiographic and perioperative complications analysis by comparing the direct anterior approach (DAA) with the direct lateral approach (DLA) in patients treated with hemiarthroplasty for FNFs.

Materials and Methods

Patients with FNFs surgically treated between 2016-2020 with HHA were enrolled. The radiographical outcomes of DAA and DLA are compared. Several peri-operative and post-operative variables were evaluated: mean surgery time, complications as periprosthetic fractures or episodes of dislocation, the average of post-operative diaphyseal filling of the stem (Canal Fill Index, CFI), the extent of heterotopic ossification (HO) (simplified Brooker classification) and metadiaphyseal bone loss (Paprosky classification) within one year from surgery.

Results

86 patients underwent HHA by DAA and 80 patients by DLA. The two groups are qualitatively comparable. No statistically significant differences were showed in all variables analyzed ($p > 0.05$). The average of surgical time of DAA were 61 minutes compared to 67 of DLA. No differences were showed in the post-operative CFI (DAA 0.71 ± 6.1 ; DLA 0.76 ± 13.5), the extent of the HO (DAA 79.07% low; DLA 75% low) and metadiaphyseal bone loss (DAA Grade I 91.86%; DLA Grade I 93.75%). Regarding perioperative complications, we have discovered only one periprosthetic fracture each group. Although there was no statistically significant difference, we highlighted a higher number of dislocations in the group of DLA (2 episodes vs no one).

Conclusions

In this study we have shown that the DAA is an adequate surgical choice comparing with the classical DLA for FNFs treated with HHA. The analysis of our radiographic parameters and perioperative complications have not shown a significant difference between the two surgical approach. This study is limited by a purely radiographic analysis without addition of clinical parameters.

OC14.3

EXPERIMENTAL BONE STRAIN EVOLUTION ASSOCIATED OF HIP PRESS-FIT ACETABULUM LOOSEING

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Introduction and Objective

The patients with a total hip arthroplasty is growing in world mainly in Europe and USA, and this solution present a high success at 10years in several orthopaedic registers. The application of total press-fit hip fixation presents the most used solution, but presents some failures associated to the acetabular component fixation, associated to the load transfer and bone loss at long term. The aim of this work is to investigate the influence of different acetabular bone loss in the strain distribution in iliac bone. To evaluate implant fixation, an experimental study was performed using acetabular press-fit component simulating different acetabular bone loss and measuring the strain distribution.

Materials and Methods

The experimental samples developed was based in an iliac bone model of Sawbones supplier and a acetabular component Titanium (Stryker) in a condition press-fit fixation and was implanted according surgical procedure with 45° inclination angle and 20° in the anteversion angle. Were developed five models with same initial bone, one with intact condition simulating the cartilage between bones and four with different bone loss around the acetabular component. These four models representing the evolution of bone support of acetabular components presented in the literature. The evolution of bone loss was imposed with a CAD CAM process in same iliac bone model. The models were instrumented with 5 rosettes in critical region at the cortical bone to measure the strain evolution along the process.

Results

The results of strain gauges present the influence of acetabular component implantation, reducing the bone strains and presented the effect of the strain shielding. The acetabular component works as a shield in the load transfer. The critical region is the posterior region with highest principal strains and the strain effect was observed with different bone loss around acetabular component. The maximum value of principal strain was observed in the intact condition in the anterior region, with 950µε. In the posterior superior region, the effect of bone loss is more important presenting a reduction of 500% in the strains. The effect of bone loss is presented in the strains induced with acetabular implantation, in the first step of implantation the maximum strain was 950µε and in the last model the value was 50µε, indicating lower press-fit fixation.

Conclusions

The models developed allows study the effect of bone loss and acetabular implant fixation in the load transfer at the hip articulation. The results presented a critical region as the anterior-superior and the effect of strain shielding was observed in comparison with intact articulation. The results of press-fit fixation present a reduction of implant stability along bone loss. The process of bone fixation developed present some limitation associated to the bone adhesion in the interface, not considered.

Acknowledgement

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OC14.4

EXPERIENCE, RESULTS, CRITICAL ISSUE AND TECHNICAL INNOVATIONS AIMED AT IMPROVING SURVIVAL RATES OF ANTIPROTRUSIO CAGES

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Introduction and Objective

The surgical strategy for acetabular component revision is determined by available host bone stock. Acetabular bone deficiencies vary from cavitory or segmental defects to complete discontinuity. For segmental acetabular defects with more than 50% of the graft supporting the cup it is recommended the application of reinforcement ring or ilioischial antiprotrusion devices. Acetabular reconstruction with the use of the antiprotrusion cage (APC) and allografts represents a reliable procedure to manage severe periprosthetic deficiencies with highly successful long-term outcomes in revision arthroplasty.

Objective

We present our experience, results, critical issues and technical innovations aimed at improving survival rates of antiprotrusion cages.

Materials and Methods

From 2004 to 2019 we performed 69 revisions of the acetabulum using defrosted morcellized bone graft and the Burch Schneider anti-protrusion cage. The approach was direct lateral in 25 cases, direct anterior in 44. Patients were re-evaluated with standard radiography and clinical examination.

Results

Eight patients died from causes not related to surgery, and two patients were not available for follow up. Five patients were reviewed for, respectively, non-osseointegration of the ring, post-traumatic loosening with rupture of the screws preceded by the appearance of supero-medial radiolucency, post-traumatic rupture of the distal flange, post-traumatic rupture of the cemented polyethylene-ceramic insert, and dislocation treated with new dual-mobility insert. Among these cases, the first three did not show macroscopic signs of osseointegration of the ring, and the only areas of stability were represented by the bone-cement contact at the holes in the ring. Although radiographic studies have shown fast remodeling of the bone graft and the implant survival range from 70% to 100% in the 10-year follow up, the actual osseointegration of the ring has yet to be clarified. To improve osseointegration of the currently available APC whose metal surface in contact with the bone is sandblasted, we combined the main features of the APC design long validated by surgical experience with the 3D-Metal Technology for high porosity of the external surface already applied to and validated with the press fit cups. The new APC design is produced with the 3D-Metal technology using Titanium alloy (Ti6Al4V ELI) that Improves fatigue resistance, primary stability and favorable environment for bone graft ingrowth. We preview the results of the first cases with short-term follow up.

Conclusions

Acetabular reconstruction with impacted morcellized bone graft and APC is a current and reliable surgical technique that allows the restoration of bone loss with a high survival rate of the implant in the medium to long term. The new 3D Metal Cage is designed to offer high friction for the initial stability. The high porosity of the 3D Metal structure creates a favorable environment for bone growth, thus providing valid secondary fixation reproducing the results achieved with the 3D metal press fit cup.

OC15 BIOMATERIALS

K15

INJECTABLE BIOACTIVE BIOMATERIALS FOR BONE REPAIR AND REGENERATION

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Minimally invasive surgery for the restoration of bone tissues lost due to diseases and trauma is preferred by the health care system as the related costs are continuously increasing. Recently, efforts have been paid to optimize injectable calcium phosphate (CaP) cements which have been recognized as excellent alloplastic material for osseous augmentation because of their unique combination of osteoconductivity, biocompatibility and mouldability. The sol-gel synthesis approach appears to be the most suitable route towards performing injectable calcium phosphates. Different strategies used to prepare bioactive and osteoinductive injectable CaP are reported. CaP gels complexed with phosphoserine-tethered poly(ϵ -lysine) dendrons (G3-K PS) designed to interact with the ceramic phase and able to induce osteogenic differentiation of human mesenchymal stem cells (hMSCs) is discussed. Recently, attention has been given to the modification of hydroxyapatite with Strontium (Sr) due to its dual mode of action, simultaneously increasing bone formation (stimulating osteoblast differentiation) while decreasing bone resorption (inhibiting osteoclast differentiation). The effect of systems based on strontium modified hydroxyapatite (Sr-HA) at different composition on proliferation and osteogenic differentiation of hMSC is described. One more approach is based on the use of antimicrobial injectable materials. It has been demonstrated that some imidazolium, pyridinium and quaternary ammonium ionic liquids (IL) have antimicrobial activity against some different clinically significant bacterial and fungal pathogens. Here, we report several systems based on IL at different alkyl-chain length incorporated in Hydroxyapatite (HA) through the sol-gel process to obtain an injectable material with simultaneous opposite responses toward osteoblasts and microbial proliferation.

OC15.1

BONE BEYOND BORDERS – MONETITE-BASED CALCIUM PHOSPHATE INDUCES BONE FORMATION OUTSIDE THE SKELETAL ENVELOPE IN AN OVIS ARIES OCCIPITAL BONE MODEL

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Introduction and Objective

Calcium phosphates are among the most commonly used bone graft substitute materials. Compositions containing predominantly monetite (~84.7%) with smaller additions of beta-tricalcium phosphate (β -TCP; ~8.3%) and calcium pyrophosphate (Ca-PP; ~6.8%) have previously been demonstrated to exhibit osteoinductive properties. Such a multi-component calcium phosphate bioceramic was fashioned in the form of hollowed-out, dome-shaped devices (15 mm diameter, 4 mm height), each reinforced with a 3D printed Ti6Al4V ELI frame. With the aim to induce bone formation beyond the skeletal envelope, these devices were investigated in vivo using a sheep (*Ovis aries*) occipital bone model.

Materials and Methods

The bioceramic composition was prepared from a mixture of β -TCP/dicalcium pyrophosphate and monocalcium phosphate monohydrate powders mixed with glycerol. The Ti6Al4V ELI frame was positioned into a dome-shaped mould and bioceramic paste was poured over the frame and allowed to set, in sterile water, prior to removal from the mould. In adult female sheep (n=7), the devices were positioned directly over the bone and stabilised using self-drilling screws. After 52 weeks, the devices were retrieved, resin embedded, and used for X-ray micro-computed tomography (micro-CT), histology, backscattered electron scanning electron microscopy (BSE-SEM), energy dispersive X-ray spectroscopy (EDX), micro-Raman spectroscopy, and Fourier transform infrared spectroscopy (FTIR).

Results

The bioceramic composition (Ca/P: ~0.85 at. %) transforms to carbonated apatite (Ca/P: ~1.2 at. %, Mg/Ca: ~0.03 at. %), in vivo, largely at the expense of monetite and Ca-PP whereas β -TCP remains detectable. Discrete particles of Ca-PP are identified by correlative BSE-SEM and micro-Raman spectroscopy. Together with chemical transformation, physical degradation is evident within the bulk of the bioceramic. Beyond the confines of the skeletal envelope, de novo bone occupies ~53–84% (~73 \pm 11%; mean \pm standard deviation) of the hollowed-out space. Low porosity and the arrangement of remodelled bone into a concentric lamellar pattern is indicative of cortical-like structure. Such areas are typically surrounded by yet unremodelled, and microstructurally disordered, woven bone that stains intensely with blue cationic dyes, owing to relatively higher acid phosphate content. This pattern indicates a recurring sequence of woven bone formation followed by remodelling. Bone formation is also visible within the bioceramic. Recently remodelled and areas of ongoing remodelling are identified by relatively lower mineral density than the surrounding woven bone. Dendritic extensions of osteocytes appear to extend into the bioceramic surface. Both micro-Raman spectroscopy and FTIR reveal little, if any, detectable difference between the mineral and organic phases of the extracellular matrix, between de novo and native bone.

Conclusions

The bioceramic composition undergoes physical degradation, but remains largely intact by 52 weeks in vivo, and only partially transforms to carbonated apatite. In addition to very high bone volume within the hollowed-out bioceramic device, the overall composition and microstructure of de novo bone are similar to

native bone. Notably, the mineral phase of bone in response to, and in direct contact with the β -TCP, monetite, and Ca-PP, remains exclusively carbonated apatite.

OC15.2

CHLORHEXIDINE TRIPHOSPHATE LOADED BONE CEMENT: HANDLING, SETTING, MECHANICAL, RELEASE AND ANTIMICROBIAL PROPERTIES

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Introduction and Objective

The continued effectiveness of antibiotic loaded bone cements is threatened by antibiotic resistance. The common antiseptic, chlorhexidine (CHX), is a potential alternative to antibiotics in bone cements, but conventional salts are highly soluble, causing burst release and rapid decline to subinhibitory local CHX concentrations. Here, chlorhexidine triphosphate (CHX-TP), a low solubility CHX salt, is investigated as an alternative antimicrobial in PMMA bone cements. The aim was to assess duration of antimicrobial release and antimicrobial efficacy, along with handling, setting and mechanical properties of CHX-TP loaded cements, compared with an existing cement formulation containing gentamicin.

Materials and Methods

Palacos R (Heraeus Medical, Newbury, UK) with 0, 1, 4, 7 and 12% CHX-TP (w/w) cements were prepared by combining solid CHX-TP with Palacos R components, and compared with Palacos R+G. All cements were prepared without vacuum and under ISO 5833:2002 conditions. Cements were tested under ISO 5833:2002 for compressive and bending properties, setting time, maximum temperature and doughing time. Antimicrobial release from the cements into deionised water was studied and antimicrobial efficacy of unaged and aged cements against *Staphylococcus aureus* (ATCC 29213) was assessed using a disc diffusion assay.

Results

Compressive strength of CHX-TP loaded cements was not significantly different to Palacos R or Palacos R+G ($p > 0.05$, all exceeding ISO 5833:2002 minimum of 70 MPa). Mean bending strength was significantly lower with CHX-TP loading ($p < 0.05$) than bending strength of Palacos R and Palacos R+G, though all bending moduli exceeded the ISO 5833:2002 minimum (1800 MPa). All cements studied were within the ISO 5833:2002 limits for setting time (3 to 15 min), doughing time (≤ 5 min) and maximum temperature (90 °C). Mean doughing time for Palacos R, Palacos R+G and Palacos R + 12 % CHX-TP respectively: 52.5 s, 45 s and 45 s. Mean setting time and mean maximum temperature for Palacos R, Palacos R+G and Palacos R + 1, 4, 7 and 12% CHX-TP respectively: 11.00 min (73 °C), 11.25 min (72 °C), 12.25 min (66 °C), 10.50 min (70 °C), 10.00 min (70 °C), 10.75 min (62 °C). Sustained CHX release into deionised water was observed from all Palacos R + CHX-TP cements. Duration varied according to CHX-TP dosing and diminished over time, although to an extent that itself varied with dosing. 1 % CHX-TP ceased releasing CHX at 6.9 weeks; 4 % CHX-TP ceased at 67.7 weeks; 7 % and 12 % CHX-TP were ongoing at 75.5 weeks. Palacos R+G cements ceased releasing detectable levels of gentamicin after 14.4 weeks. Palacos R+G and Palacos R + CHX-TP cement discs showed efficacy against *S. aureus* (ATCC 29213) when applied as prepared (unaged) to *S. aureus* bacterial lawns in disc diffusion assays, with CHX-TP cements showing dose dependency. Zone of inhibition (ZOI) size was significantly reduced for Palacos R+G cements and Palacos R + 1% CHX-TP cements after 1 week and 6 weeks aging, compared to ZOI from unaged cements ($p < 0.05$). ZOI size produced by Palacos R + 4, 7, and 12 % CHX-TP cements did not decline significantly after 6 weeks aging ($p > 0.05$).

Conclusions

CHX-TP can be incorporated into the Palacos R cement matrix up to 12% w/w without deterioration of compressive strength, bending modulus, doughing time, setting time or maximum temperature. Bending strength was significantly reduced at all CHX-TP loadings studied. Palacos R + 4, 7 and 12% CHX-TP cements provided sustained CHX release, exceeding the duration of gentamicin release from Palacos R+G, and showed sustained efficacy against *S. Aureus* after 6 weeks aging, which was not achieved by Palacos R+G cements.

OC15.3

NEW COATINGS FOR ORTHOREGENERATION: THE ROLE OF BIOMIMETIC COMPOSITION AND MULTISCALE MORPHOLOGICAL CUES IN DIRECTING CELLS RESPONSE

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Introduction and Objective

The choice of appropriate characteristics is crucial to favor a firm bonding between orthopedic implants and the host bone and to permit bone regeneration. In particular, the morphology and composition of the biointerface plays a crucial role in orchestrating precise cellular responses. Here, to modulate the biointerface, we propose new biomimetic coatings, having multi-scale nano- to micro- morphological cues and a composition mimicking the mineral phase of bone.

Materials and Methods

Films on various substrates are obtained by Ionized Jet Deposition (IJD), by ablation of biogenic apatite and annealing at 400°C for 1 hour. Films are proposed for functionalization of metallic implants, but application to heat sensitive porous (3D printed) substrates is also shown, as it permits to further boost biomimicry (by addition of collagen/gelatin), thus reproducing the architecture of cancellous bone. In IJD, coatings thickness can be selected by tuning deposition duration. Here, a 450 nm thickness is selected based on preliminary results. Micro-rough titanium alloy (Ti6Al4V) disks (roughness 5 µm) are used as a substrate for the deposition and as a control. The coatings are characterized in terms of composition (GI-XRD, EDS, FT-IR microscopy), morphology (FEG-SEM, AFM, data processing by ImageJ), mechanical properties (micro-scratch test) and dissolution profile in medium (pH 7.4, FEG-SEM). Then, their behavior is characterized in vitro (human bone marrow-derived mesenchymal stromal cells - hMSCs), by studying cells early adhesion (focal adhesion by vinculin staining), viability (Alamar Blue), morphology (SEM) and differentiation (expression of RUNX2, ALPL, SPARC and COL1A1, BMP2, BGLAP, osteocalcin, alkaline phosphatase, collagen type I) at 3, 7 and 14 days.

Results

Films exhibit a biomimetic composition, as they are constituted by a nanocrystalline multi-doped carbonated hydroxyapatite. EDS indicates the presence of trace ions sodium ($0,11 \pm 0,02$ wt%) and magnesium ($0,47 \pm 0,05$ wt%), uniformly distributed in the coating in a percentage close to native bone. These ion-substitutions are crucial, as each ion modifies apatite solubility and ion-release in the peri-implant

environment and has important biological role. Films have a high adhesion to the substrates and a suitable dissolution profile. The morphology is highly rough, as films are composed by nanosized grains (minimum diameter 40 nm) aggregated in multi-scale clusters (diameter range: 100 nm-2 μ m). Morphology of the aggregates can be tuned by selecting deposition duration and also depends on the morphology, roughness and composition of the substrate. Because of the nanoscale thickness of the films, they do not alter the microscale features of the implants. For fibrous substrates, films grow onto the fibers surface, with no pore occlusion or damage to substrate composition. Coatings do not alter the metabolic activity of MSCs but influence their early adhesion, morphology and differentiation. More in detail, MSCs on coated disks show a branched shape, while those on the controls show a more spindle and elongated morphology. Coatings increase hMSCs early adhesion, as a higher density and a greater area of focal adhesions are observed at 24 hours. Finally, they can trigger a signaling pathway that promotes the osteogenic differentiation of hMSCs, as confirmed by quantification of osteocalcin, alkaline phosphatase and collagen, even in the absence of osteogenesis-inducing factors.

Conclusions

The topographical and chemical cues of the biomimetic nanostructured coating are perceived by hMSCs, showing that combining morphological and biomimetic cues is a promising route for the development of cells-instructive biomaterials for orthopedics. In vivo tests on rabbit models are in progress.

OC15.4

USE OF CROSSLINKED WHARTON'S JELLY IN GUIDED BONE REGENERATION

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Introduction and Objective

Guided Bone Regeneration (GBR) uses biodegradable collagen membranes of animal origin tissues (dermis and pericardium). Their barrier effect prevents soft tissues to interfere with the regeneration of alveolar bone. However, their xenogeneic origin involves heavy chemical treatments which impact their bioactivity. Wharton's Jelly (WJ) from the umbilical cord is a recoverable surgery waste. WJ is mostly made from collagen fibers, proteoglycans, hyaluronic acid, and growth factors. WJ with immunologically privileged status and bioactive properties lends credence to its use as an allograft. Nevertheless, low mechanical properties limit its use in bone regenerative strategies. Herein, our objective is to develop a crosslinked WJ-based membrane to improve its strength and thus its potential use as a GBR membrane.

Materials and Methods

The umbilical cords are collected after delivery and then stored at -20°C until use. The WJ membranes (1 x 5 x 12 mm) were obtained after the removal of blood vessels and amniotic tissue, washed, lyophilized, and stored at -20°C. WJ membranes were incubated in genipin solutions in decreasing concentrations (0.3 g / 100 mL - 0.03 g / 100 mL) for 24 hours at 37°C. The crosslinking degree was estimated by ninhydrin and confirmed by FTIR (Fourier-transform infrared spectroscopy) assays. The swelling rate was obtained after the rehydration of dry crosslinked WJ-membrane for 10 min in D-PBS. The mechanical properties were assessed in hydrated conditions on a tensile bench. The resistance to the degradation was evaluated by collagenase digestion (1 mg/mL for 60 hours) assay. The cytotoxicity of crosslinked WJ-membrane was evaluated in accordance with the standard ISO.10993-5 (i.e. Mitochondrial activity and Lactate Dehydrogenase release) against Mesenchymal Stem Cells (MSCs). Finally, the MSCs colonization and proliferation were followed after 21 days of culture on crosslinked WJ-membranes.

Results

The increase of crosslinking rates from 30% to 90% of the WJ membrane was demonstrated by the ninhydrin assay. FTIR analysis showed a prominent peak at 1732 cm⁻¹, confirming the incorporation of genipin in the WJ. The swelling rate of crosslinked WJ-membrane decreased with an increase of the crosslinking rate. An increase in elastic modulus and an increase in the resistance to the collagenase degradation were observed along with an increase in the crosslinking degree. Cytotoxicity investigations did not elicit a harmful effect of the genipin, however, a poor MSCs adhesion on the crosslinked membrane was observed.

Conclusions

Our results show that a membrane can be developed from Wharton's jelly. The mechanical and degradation properties can be improved by crosslinking with genipin without inducing any cytotoxicity effect. However, the percentage of crosslinking has an influence on the adhesion of the cells to the membranes. The crosslinked WJ-membrane bioactivity and the osteo-regenerative potential in vitro/in vivo will be evaluate.

OC16 CELL-BASED THERAPY

K16

RESPINE: EUROPEAN CLINICAL TRIAL OF MESENCHYMAL STROMAL CELLS IN DEGENERATIVE DISC DISEASE

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The World Health Organisation (WHO) has included low back pain in its list of twelve priority diseases. Notably, Degenerative disc disease (DDD) presents a large, unmet medical need which results in a disabling loss of mechanical function. Today, no efficient therapy is available. Chronic cases often receive surgery, which may lead to biomechanical problems and accelerated degeneration of adjacent segments. Our consortium partners have developed and studied mesenchymal stem cell-based, regenerative therapies trials. In previous phase 2 trial, patients exhibited rapid and progressive improvement of functional and pain indexes after 1 year with no significant side effects. To develop the world's first rigorously proven, effective treatment of DDD, EUROSPINE aims to assess, via a multicentre, randomized, controlled, phase 2b clinical trial including 112 patients with DDD, the efficacy of an allogenic intervertebral mesenchymal stem cell (MSC)-based therapy. This innovative therapy aims to rapidly and sustainably (at least 24 months) reduce pain and disability. In addition, the consortium aims to provide new knowledge on immune response & safety associated with allogeneic BM-MSC intradiscal injection. This simple procedure would be cost-effective, minimally invasive, and standardised. At the end of the RESPINE trial, we aim to propose a broadly available and clinically applicable treatment for DDD, marketed by European SMEs.

OC16.1

INTRA-ARTICULAR INJECTION OF MESENCHYMAL STROMAL CELLS ENCAPSULATED IN MICRO-MOLDED ALGINATE PARTICLES FOR THE TREATMENT OF POST-TRAUMATIC KNEE OSTEOARTHRITIS IN RABBIT

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Introduction and Objective

Osteoarthritis (OA) is the most common inflammatory and degenerative joint disease. Mesenchymal Stromal Cells (MSCs), with their chondro-protective and immune-regulatory properties, have been considered as a new approach to treat OA. Considering the risk of cell leakage outside the articular space and the poor survival rate after intra-articular (IA) injection, we hypothesized that cell encapsulation in cytoprotective hydrogels could overcome these limitations and provide cells with a suitable 3D microenvironment supporting their biological activity. We previously generated micromolded alginate particles (diameter 150 μm) and demonstrated the long-term viability of microencapsulated MSCs isolated from human adipose tissue (hASCs). Encapsulated cells maintained their in vitro ability to sense and respond to a pro-inflammatory environment (IFN- γ /TNF- α or synovial fluids from OA patients) by secreting PGE₂, IDO, HGF and TGF- β . In this study, we evaluated the anti-OA efficacy of these microencapsulated hASCs in a post-traumatic OA model in rabbits.

Materials and Methods

OA was surgically induced by anterior cruciate ligament transection (ACLT)-mediated destabilization of the right knee in rabbits (n=24). Eight weeks after surgery, destabilized joints were injected (IA, 26G needle) with 200 μL of either PBS, blank microparticles, non-encapsulated or microencapsulated cells (5×10^5 cells). Six weeks after injection, rabbits were euthanized and all destabilized (right) and sham-operated (left contralateral) joints were dissected and analyzed for OA severity. Tibial subchondral bone histomorphometric parameters were measured by quantitative micro-computed tomography (micro-CT). Histological sections of samples were analyzed after Safranin-O staining and quantitatively assessed according to a modified Osteoarthritis Research Society International (OARSI) scoring system. Immunohistochemical detection of NITEGE was performed to assess the extracellular matrix degradation.

Results

Micro-CT analysis of destabilized joints confirmed that the rabbit ACLT significantly affected the tibial subchondral bone architecture as early as eight weeks, as revealed by significant changes of the subchondral bone parameters of operated joints compared to the sham operated joints. In particular, destabilized joints exhibited a Bone Volume/Tissue Volume ratio (BV/TV) ranging from 53.4% to 56.6%, compared to a mean BV/TV of 65.4% for sham operated joints. All destabilized joints also exhibited a significantly increased modified OARSI score, ranging from 7.4 ± 0.4 for those injected with encapsulated cells to 8.9 ± 0.2 for those injected with PBS, as compared to 4.8 ± 0.4 for sham-operated joints. Of interest, we identified a slight, while not significant, reduction of the severity of OA lesions after injection of

microencapsulated cells using the modified OARSI scoring. Finally, semi-quantitative analysis of NITEGE immunostaining revealed a significant increase in all destabilized joints that were injected with PBS or blank microparticles, in comparison with sham ones. On the contrary, NITEGE immunostaining in destabilized joints that were injected with non-encapsulated or encapsulated hASC revealed a significant reduced NITEGE immunostaining, indicating a decreased matrix degradation.

Conclusions

Our data suggest that the microencapsulated hASCs exerted their anti-OA properties after IA injection in rabbit knees, as evidenced by the tendency toward a reduced modified OARSI score, and most importantly a significant reduction in NITEGE immunostaining associated matrix degradation. Further studies are now warranted to investigate the anti-OA efficacy of microencapsulated hASCs in the long-term.

OC16.2

AUTOLOGOUS MESENCHYMAL STEM CELLS IN THE TREATMENT OF SPINAL ANEURYSMAL BONE CYST

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Introduction and Objective

Aneurysmal bone cyst (ABC) of the spine is a locally aggressive benign lesion which can be treated by en bloc resection with wide margin to reduce the risk of local recurrence. To avoid morbidity associated with surgery, selective arterial embolization (SAE) can be considered the first-line treatment for ABCs of the spine. Other emerging treatments for ABCs include bisphosphonates, percutaneous doxycycline, sclerotherapy and Denosumab. In addition, we previously introduced the use of autologous bone marrow concentrate (BMC) injection therapy to stimulate bone healing and regeneration in ABC of the spine. One of the potential advantages of such a method is that surgical treatments are not necessary, thus allowing for both a minimally invasive approach and the treatment of poorly accessible lesions. In this prospective study we described the clinical and radiological outcomes of percutaneous injection of autologous BMC in a series of patients affected by ABCs of the spine and followed for at least one year.

Materials and Methods

Fourteen patients (6 male, 8 female) were treated between June 2014 to December 2019 with BMC injection for ABC of the spine. The mean age was 17.85 years. The mean follow up was 37.4 months (range 12- 60 months). The dimension of the cyst and the degree of ossification were measured by Computed Tomography (CT) scans before the treatment and during follow-up visits.

Results

Six patients received a single dose of BMC, five patients received two doses and in three patients three doses of BMC were administered. The mean ossification of the cyst (expressed in Hounsfield units) increased statistically from 43.48 ± 2.36 HU to 161.71 ± 23.48 HU during follow-up time and the ossification was associated to an improvement of the clinical outcomes. The mean ossification over time was significantly higher in patients treated with a single injection compared to patients treated with multiple injections. No significant difference in ossification was found between cervical and non-cervical localization of the cyst. Moreover, the initial size of the cyst was not statistically associated with the degree of ossification during follow-up. We also observed that five out of six female patients (83.3%) were less than sixteen years old and four of these (66.7%) were managed with a single dose of BMC injection, while a higher percentage of male patients (6/8, 75%) were more than sixteen years old and more than one injection was administered to them.

Conclusions

The results of this study reinforce our previous evidence on the use of BMC as a valid alternative for spinal ABC management when SAE is contraindicated or ineffective. The initial size of the cyst and its localization does not influence the efficacy of the treatment. However, BMC injection could be indicated as treatment of choice for spinal ABC in young adolescent women.

OC16.3

HIGH-THROUGHPUT CHARACTERIZATION OF MICRO-FRAGMENTED ADIPOSE TISSUE FOR THE TREATMENT OF MUSCULOSKELETAL DISORDERS: COMPARISON WITH UNPROCESSED LIPOASPIRATE

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Introduction and Objective

The use of microfragmented adipose tissue (mFAT) for the treatment of musculoskeletal disorders, especially osteoarthritis, is gaining popularity following the positive results reported in recent case series and clinical trials. The purpose of this study is to characterize mFAT in terms of structure, cell content and secretome (i.e. protein and microvesicles released as paracrine mediators), and to compare it with unprocessed lipoaspirate tissue, in order to understand the possible mechanisms of action and the benefit derived from tissue processing.

Materials and Methods

Unprocessed lipoaspirate (LA) and mFAT were obtained from 7 donors. Each tissue sample was divided in four aliquots: A) fixed in formalin for histological evaluation; B) enzymatically digested to harvest cells with the exclusion of adipocytes; C) cultured for 24 hours in serum-free DMEM to harvest secretome; D) freshly frozen for proteomic evaluation. Hematoxylin and eosin staining, as well as immunohistochemistry for CD31, CD90, CD146 were performed on aliquot A. Cell count, viability, senescence and immunophenotype were assessed on aliquot B. Culture medium from aliquot C was collected and used for proteomic analysis and micro-RNA extraction and quantitation from extracellular vesicles. Aliquot D was lysed, protein were extracted and analyzed using a high-throughput proteomic approach.

Results

Histological investigations showed a lower red blood cell content in mFAT with respect to LA, while the presence of blood vessels (CD31+), stromal cells (CD90) and pericytes (CD146) was similar in all samples. These results were confirmed by flow cytometry, with reduction of erythrocytes (CD235a+) by 76% and reduction of lymphocytes (CD45+) by 79% in mFAT compared to LA. Otherwise, the proportions of stromal cells, pericytes and endothelial cells in LA and mFAT remained comparable. The percentage of senescent cells resulted similar before and after tissue processing, with very low values (< 5%). The analysis of the miRNAs contained in the extracellular vesicles in culture media identified 376 miRNAs in LA secretome and 381 in mFAT secretome. A high correlation in the expression of these miRNAs within subjects (LA and mFAT of each donor) was observed ($R^2 > 0.8$), indicating that processing in mFAT does not significantly alter the portfolio of miRNAs associated with extracellular vesicles. Proteomic analysis of secretome revealed that 217 proteins significantly differ between LA and mFAT. In particular, protein associated with acute phase were less represented in mFAT secretome, while intracellular proteins were more frequent. Proteomic analysis of tissues demonstrated a reduction of protein related to extracellular matrix and of proteins closely related to peripheral blood contamination in mFAT with respect to LA.

Conclusions

Taken together, these results suggest that processing of LA into mFAT allow for removal of blood elements, in terms of red blood cells, lymphocytes, acute phase and complement system proteins, and for the reduction of extracellular matrix components. Otherwise, tissue structure, cell populations, cell viability and senescence are not influenced by tissue processing. Then, microfragmentation process represents a safe and efficient method for the application of adipose tissue properties to musculoskeletal disorders, allowing

for the maintenance of all the effector elements for tissue regeneration while removing possible detrimental agents such as inflammatory mediators.

OC16.4

CHARACTERIZATION AND COMPARISON OF DIFFERENT METHODS TO OBTAIN MINIMALLY MANIPULATED ADIPOSE TISSUE FOR THE TREATMENT OF OSTEOARTHRITIS

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Introduction and Objective

Osteoarthritis (OA) represents one of the leading cause of disability all over the world. Cell therapies, mainly based on mesenchymal stem cells (MSCs), have shown to modulate the pathogenesis of OA in basic, preclinical and clinical studies. Adipose tissue (AT) have emerged as a rich and promising source of MSCs called adipose derived stem cells (ASCs). Different systems are available for processing lipoaspirate to purify the samples from oily and haemorrhagic fractions, minimizing the risk of complications and maximizing the biological yield for subsequent grafting. However, few studies compared the efficacy of the different processing devices already used in clinical practice. This study aims to characterize the products obtained by the use of two different systems such as micro-fragmentation or nano-fragmentation comparing them with the starting material (AT) and the collagenase isolated ASCs.

Materials and Methods

AT from 12 donors arrived without selection to the laboratories: 4 lipoaspirated (LA), 4 micro-fragmented (mF) and 4 nano-fragmented (nF). The samples were divided into three aliquots for paraffin embedding, RNA extraction and digestion with collagenase for ASCs isolation. Paraffin embedded tissue sections were stained with hematoxylin-eosin to analyze morphology. RNA was extracted, retro-transcribed and analyzed with real-time PCR to analyze the expression of pluripotency genes (SOX2, NANOG and POU5F1) and inflammatory genes (IL-1beta and iNOS). Data were analyzed using Graphpad Prism 8.0 and expressed as mean \pm SD. One-way ANOVA followed by Tukey test was used to compare the different groups.

Results

The LA comprised small lobules, with intact cell membranes and structurally integer adipocytes. mF samples showed the presence of integer adipocytes, small lobules and higher amount of cell clusters. nF samples showed the almost completely absence of adipocytes, a high amount of cells without lipid content and a high amount of stromal matrix. Real-time PCR results showed the lowest expression levels of pluripotency genes in LA samples that were assumed equal to 1.0 and used to calculate the expression levels of the other samples. mF showed expression levels of pluripotency genes similar to AT. nF showed expression levels of pluripotency genes higher than AT and mF, but without statistically significant differences. ASCs showed statistically significant higher expression levels of these genes compared to LA and mF ($p \leq 0.001$). Likewise, the expression of inflammatory genes resulted to be lowest in LA samples (assumed equal to 1.0), higher in mF samples and in nF samples without statistical significance. As expected, the highest values were found in ASCs isolated cells compared to all the other samples ($p \leq 0.0001$).

Conclusions

These results confirmed that micro-fragmentation (mF) and nano-fragmentation (nF) permitted to separate a cell mixture enriched in ASCs from a lipoaspirate sample without activating the inflammatory pathways. Both processing methods gave a minimally manipulated product suitable for OA cell therapy application. Further studies are needed to elucidate possible different activities of the ASCs enriched AT-derivatives.

OC17 BIOMECHANICS

K17

KEEPING THE HEAD LEVEL DURING AXIAL ROTATION - THE EFFECT ON COUPLED ROTATIONS IN THE CERVICAL SPINE

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Some activities of daily living require that the head be kept level during axial rotation of the cervical spine (Kinematically Constrained Axial Rotation). One such activity is looking over one's shoulder when walking or driving. The kinematic constraint of keeping the head level during axial rotation means that the segmental axis of rotation may not be aligned with the global axis of rotation of the cervical spine. Most of the literature on cervical spine axial rotation is based on experiments where the segmental axis of rotation is aligned with the global axis of rotation (Traditional Axial Rotation). There are only a few clinical and biomechanical studies that have examined kinematically constrained cervical axial rotation. We performed a series of biomechanical experiments in which we tested cervical spines in traditional and kinematically constrained axial rotation. The resulting primary and coupled motions of the segments showed that kinematically constrained axial rotation is distinct from traditional axial rotation. Our findings and the findings of other kinematically constrained axial rotation studies will be compared and contrasted with data from traditional axial rotation studies.

OC17.1

BIOMECHANICAL ANALYSIS OF RECENTLY RELEASED CEPHALOMEDULLARY NAILS FOR TROCHANTERIC FEMORAL FRACTURE FIXATION IN A HUMAN CADAVERIC MODEL

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Introduction and Objective

Trochanteric fractures are associated with increasing incidence and represent serious adverse effect of osteoporosis. Their cephalomedullary nailing in poor bone stock can be challenging and associated with insufficient implant fixation in the femoral head. Despite ongoing implant improvements, the rate of mechanical complications in the treatment of unstable trochanteric fractures is high. Recently, two novel concepts for nailing with use of a helical blade – with or without bone cement augmentation – or an interlocking screw have demonstrated advantages as compared with single screw systems regarding rotational stability and cut-out resistance. However, these two concepts have not been subjected to direct biomechanical comparison so far. The aims of this study were to investigate in a human cadaveric model with low bone density (1) the biomechanical competence of cephalomedullary nailing with use of a helical blade versus an interlocking screw, and (2) the effect of cement augmentation on the fixation strength of the helical blade.

Materials and Methods

Twelve osteoporotic and osteopenic femoral pairs were assigned for pairwise implantation using either short TFN-ADVANCED Proximal Femoral Nailing System (TFNA) with a helical blade head element, offering the option for cement augmentation, or short TRIGEN INTERTAN Intertrochanteric Antegrade Nail (InterTAN) with an interlocking screw. Six osteoporotic femora, implanted with TFNA, were augmented with 3 ml cement. Four study groups were created – group 1 (TFNA) paired with group 2 (InterTAN), and group 3 (TFNA augmented) paired with group 4 (InterTAN). An unstable pertrochanteric OTA/AO 31-A2.2 fracture was simulated. All specimens were biomechanically tested until failure under progressively increasing cyclic loading featuring physiologic loading trajectory, with monitoring via motion tracking.

Results

T-score in groups 3 and 4 was significantly lower compared with groups 1 and 2, $p=0.03$. Stiffness (N/mm) in groups 1 to 4 was 335.7 ± 65.3 , 326.9 ± 62.2 , 371.5 ± 63.8 and 301.6 ± 85.9 , being significantly different between groups 3 and 4, $p=0.03$. Varus ($^{\circ}$) and femoral head rotation around neck axis ($^{\circ}$) after 10,000 cycles were 1.9 ± 0.9 and 0.3 ± 0.2 in group 1, 2.2 ± 0.7 and 0.7 ± 0.4 in group 2, 1.5 ± 1.3 and 0.3 ± 0.2 in group 3, and 3.5 ± 2.8 and 0.9 ± 0.6 in group 4, both with significant difference between groups 3 and 4, $p\leq 0.04$. Cycles to failure and failure load (N) at 5° varus in groups 1 to 4 were 21428 ± 6020 and 1571.4 ± 301.0 , 20611 ± 7453 and 1530.6 ± 372.7 , 21739 ± 4248 and 1587.0 ± 212.4 , and 18622 ± 6733 and 1431.1 ± 336.7 , both significantly different between groups 3 and 4, $p=0.04$.

Conclusions

From a biomechanical perspective, cephalomedullary nailing of trochanteric fractures with use of helical blades is comparable to interlocking screw fixation in femoral head fragments with low bone density. Moreover, bone cement augmentation of helical blades considerably improves their fixation strength in poor bone quality.

OC17.2

ANGULAR STABLE INTRAMEDULLARY NAILING IMPROVES CONSTRUCT STABILITY IN A DISTAL TIBIA FRACTURE MODEL - A BIOMECHANICAL STUDY

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Introduction and Objective

Intramedullary nails are frequently used for treatment of unstable distal tibia fractures. However, insufficient fixation of the distal fragment could result in delayed healing, malunion or nonunion. The quality of fixation may be adversely affected by the design of both the nail and locking screws, as well as by the fracture pattern and bone density. Recently, a novel concept for angular stable nailing has been developed that maintains the principle of relative stability and introduces improvements expected to reduce nail toggling, screw migration and secondary loss of reduction. It incorporates polyether ether ketone (PEEK) inlays integrated in the distal and proximal canal portions of the nail for angular stable screw locking. The nail can be used with new standard locking screws and low-profile retaining locking screws, both designed to enhance cortical fixation. The low-profile screws are with threaded head, anchoring in the bone and increasing the surface contact area due to the head's increased diameter.

The objective of this study was to investigate the biomechanical competence of the novel angular stable intramedullary nail concept for treatment of unstable distal tibia fractures, compared with four other nail designs in an artificial bone model under dynamic loading.

Materials and Methods

The distal 70 mm of thirty artificial tibiae (Synbone) were assigned to 5 groups for distal locking using either four different commercially available nails – group 1: Expert Tibia Nail (DePuy Synthes); group 2: TRIGEN META-NAIL with Internal Hex Captured Screws (Smith & Nephew); group 3: T2 Alpha with Locking Screws (Stryker); group 4: Natural Nail System featuring Stabilize Technology (Zimmer) – or the novel angular stable TN-Advanced nail with low-profile screws (group 5, DePuy Synthes). The distal locking in all groups was performed using 2 mediolateral screws. All specimens were biomechanically tested under quasi-static and progressively increasing combined cyclic axial and torsional loading in internal rotation until failure, with monitoring by means of motion tracking.

Results

Initial nail toggling of the distal tibia fragment in group 5 was significantly lower as compared with group 3 in varus ($p=0.04$) or with groups 2 and 4 in flexion ($p\leq 0.02$). In addition, the toggling in varus was significantly lower in group 1 versus group 4 ($p<0.01$). Moreover, during dynamic loading, within the course of the first 10,000 cycles the movements of the distal fragment in terms of varus, flexion, internal rotation, as well as axial and shear displacements at the fracture site, were all significantly lower in group 5 compared with group 4 ($p<0.01$). Additionally, group 5 demonstrated significantly lower values for flexion versus groups 2 and 3 ($p\leq 0.04$), for internal rotation versus group 1 ($p=0.03$), and for axial displacement versus group 3 ($p=0.03$). A trend to significantly lower values was detected in group 5 versus group 1 for varus, flexion and shear displacement – with p ranging between 0.05 and 0.07 – and versus group 3 for shear displacement ($p=0.07$). Cycles to failure were highest in group 5 with a significant difference to group 4 ($p<0.01$).

Conclusions

From a biomechanical perspective, the novel angular stable intramedullary nail concept with integrated PEEK inlays and low-profile screws provides ameliorated resistance against nail toggling and loss of

reduction under static and dynamic loading compared with other commercially available intramedullary nails used for fixation of unstable distal tibia fractures.

OC17.3

GAIT VARIABILITY BEFORE AND AFTER TOTAL KNEE ARTHROPLASTY: A COMPARISON OF MEDIAL PIVOT AND POSTERIOR STABILIZED IMPLANTS

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Introduction and Objective

Gait variability is the amplitude of the fluctuations in the time series with respect to the mean of kinematic (e.g., joint angles) or kinetic (e.g., joint moments) measurements. Although gait variability increases with normal ageing or pathological mechanisms, such as knee osteoarthritis (OA). The purpose was to determine if a patient who underwent a total knee arthroplasty (TKA) can reduce gait variability.

Materials and Methods

Twenty-five patients awaiting TKA were randomly assigned to receive either medial pivot (MP, m=7/f=6, age=62.4±6.2 years) or posterior stabilized (PS, m=7/f=5, age=63.7±8.9 years) implants, and were compared to 13 controls (CTRL, m=7/f=6, age=63.9±4.3 years). All patients completed a gait analysis within one month prior and 12 months following surgery, CTRLs completed the protocol once. A waveform F-Test Method (WFM) was used to compare the variance in knee biomechanics variables at each interval of the gait cycle.

Results

Preoperatively, the PS group had greater sagittal knee angle variability compared to the MP (32-58% gait cycle) and CTRL (21-53% gait cycle) groups. Postoperatively, no difference in sagittal knee angle variability existed between any of the groups. Preoperatively, sagittal knee moment variability was greater in the MP (2-39% gait cycle) and PS (5-19% and 42-57% gait cycle) groups compared to the CTRL. Postoperatively, sagittal knee moment was lower in the MP (49-55% gait cycle) and greater in the PS (23-36% gait cycle) compared to the CTRL. Knee power variability was greater preoperatively in the MP (52-61% gait cycle) and PS (52-62% gait cycle) compared to the CTRL. Postoperatively, knee power variability was lower in the MP (17-22% and 45-50% gait cycle) and PS (6-23%, 34-41% and 45-49% gait cycle) compared to the CTRL group.

Conclusions

Preoperatively, knee OA patients have greater variability in knee moments than CTRLs during the transition from double-limb support to single-limb support on the affected limb. This indicates knee instability as patients are adopting a gait strategy that refers to knee muscle contraction avoidance. The MP group showed greater knee stability postoperatively as they had lower knee moment and power variability compared to the CTRL. The significance of having less variability than CTRLs is not well understood at this time. Future research on muscle activity is needed to determine if neuromuscular adaptations are causing these reductions in variability after TKA.

OC17.4

PULLEY PLASTY TECHNIQUES VERSUS RESECTION OF SINGLE FLEXOR DIGITORUM SUPERFICIALIS SLIP AND VENTING TECHNIQUE COMPARISON AFTER BOTH TENDON REPAIR IN ZONE II. A BIOMECHANICAL STUDY

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Introduction and Objective

Zone 2 flexor tendon injuries are still one of the challenges for hand surgeons. It is not always possible to achieve perfect results in hand functions after these injuries. There is no consensus in the literature regarding the treatment of zone 2 flexor tendon injuries, tendon repair and surgical technique to be applied to the A2 pulley. The narrow fibro-osseous canal structure in zone 2 can cause adhesions and loss of motion due to the increase in tendon volume due to surgical repair. Different surgical techniques have been defined to prevent this situation. In our study, in the treatment of zone 2 flexor tendon injuries; Among the surgical techniques to be performed in addition to FDP tendon repair; We aimed to compare the biomechanical results of single FDS slip repair, A2 pulley release and two different pulley plasty methods (Kapandji and V-Y pulley plasty).

Materials and Methods

In our study, 12 human upper extremity cadavers preserved with modified Larssen solution (MLS) and amputated at the mid ½ level of the arm were used. A total of 36 fingers (second, third and the fourth fingers were used for each cadaver) were divided into four groups and 9 fingers were used for each group. With the finger fully flexed, the FDS and FDP tendons were cut right in the middle of the A2 pulley and repaired with the cruciate four-strand technique. The surgical techniques described above were applied to the groups. Photographs of fingers with different loads (50 - 700 gr) were taken before and after the application. Proximal interphalangeal (PIP) joint angle, PIP joint maximum flexion angle and bowstring distance were measured. The gliding coefficient was calculated by applying the PIP joint angle to the single-phase exponential association equation.

Results

Gliding coefficient after repair increased by $\%21.46 \pm 44.41$, $\%62.71 \pm 116.9$, $\%26.8 \pm 35.35$ and $\%20.39 \pm 28.78$ in single FDS slip repair, A2 pulley release, V-Y pulley plasty and Kapandji plasty respectively. The gliding coefficient increased significantly in all groups after surgical applications ($p < 0.05$). PIP joint maximum flexion angle decreased by $\%3.17 \pm 7.92$, $\%12.82 \pm 10.94$, $\%8.33 \pm 3.29$ and $\%7.35 \pm 5.02$ in single FDS slip repair, A2 pulley release, V-Y pulley plasty and Kapandji plasty respectively. PIP joint maximum flexion angle decreased significantly after surgery in all groups ($p < 0.05$). However, there was no statistically significant difference between surgical techniques for gliding coefficient and PIP joint maximum flexion angle. Bowstring distance between single FDS slip repair, kapandji pulley plasty and V-Y pulley plasty showed no significant difference in most loads ($p > 0.05$). Bowstring distance was significantly increased in the A2 pulley release group compared to the other three groups ($p < 0.05$).

Conclusion

Digital motion was negatively affected after flexor tendon repair. Similar results were found in terms of gliding coefficient and maximum flexion angle among different surgical methods. As single FDS slip repair preserves the anatomical structure of the A2 pulley therefore we prefer it as an ideal method for zone 2 flexor tendon repair. However, resection of FDS slip may jeopardizes nutrition to the flexor digitorum profundus tendon which weakens the repair site. Therefore the results must be confirmed by an in vivo study before a clinical recommendation can be made.

Keywords: Flexor tendon; injury; pulley plasty; cadaver;

OC18 BONE BIOLOGY AND PATHOPHYSIOLOGY

K18

DECONSTRUCTING BONE TUMORS: NEW TOOLS FOR PERSONALISED TREATMENTS

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In the past decades, a huge amount of effort has been devoted to translate evidence based on standard preclinical models of bone tumours to effective tools for clinical applications. Although cancer is a genetic disease, hence the emphasis on -omics approaches, the complexity of cancer tissue, a mix of competing clones of transformed elements that react differently to microenvironmental stimuli, may hardly be reproduced by standard approaches. Cost, biological differences and ethical concerns are increasingly recognized as weaknesses of animal models. To overcome these limitations and provide reliable, reproducible, and affordable tools for predicting the effectiveness of treatments, environmental-controlled 3D cultures and co-cultures (spheroids, organoids) coupled with microfluidics and advanced imaging have recently being considered as effective instrument to increase knowledge on the pathophysiology of bone tumours and define effective therapeutic solutions.

OC18.1

AN EX VIVO MODEL OF LOAD-INDUCED CORTICAL BONE REMODELLING

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Introduction and Objective

Bone remodelling is a continuous process whereby osteocytes regulate the activity of osteoblasts and osteoclasts to repair loading-induced microdamage. While many in vitro studies have established the role of paracrine factors (e.g., RANKL/OPG) and cellular pathways involved in bone homeostasis, these techniques are generally limited to two-dimensional cell culture, which neglects the role of the native extracellular matrix in maintaining the phenotype of osteocyte. Recently, ex vivo models have been used to understand cell physiology and mechanobiology in the presence of the native matrix. Such approaches could be applicable to study the mechanisms of bone repair, whilst also enabling exploration of biomechanical cues. However, to date an ex vivo model of bone remodelling in cortical bone has not been developed. In this study, the objective was to develop an ex vivo model where cortical bone was subjected to cyclic strains to study the remodelling of bone.

Materials and Methods

Ex vivo model of bone remodelling induced by cyclic loading: At the day of culling, beam-shape bovine bone samples were cut and preserved in PBS + 5% Pen/Strep + 2 mM L-Glut overnight at 37°C. Cyclic strains were applied with a three-point bend system to induce damage with a regime at 16.66 mm/min for 5,000 cycles in sterile PBS in Evolve® bags (maximum strain 6%). A control group was cultured under static conditions.

Metabolic activity: Alamar Blue assays were performed after 1 and 7 days of ex vivo culture for each group (Static, Loaded) and normalized to weight.

Bone remodelling: ALP activity was assessed in the media at day 1 and 7. After 24 hours cell culture conditioned media (CM) was collected from each group and stored at -80°C. RAW264.7 cells were cultured with CM for 6 days, after which the samples were stained for TRAP, to determine osteoclastogenesis, and imaged.

Histomorphometry: Samples were cultured with calcein for 3 days to label bone formation between day 4 and 7. Fluorescent images were captured at day 7. μ CT scanning was performed at 3 μ m resolution after labelling samples with BaSO₄ precipitate to quantify bone damage.

Results

Bone was sectioned and cultured to maintain live osteoblasts and osteocytes. CM that was obtained 24 hours after cyclic loading and added to RAW264.7 cells cultures, resulted in significantly increased osteoclastogenic potential compared to that from static samples ($4.245 \pm 1.65\%$ vs $0.88 \pm 0.48\%$, $p < 0.001$). Calcein and HE staining indicated the presence of structures similar to bone remodelling cones in both groups after 7 days of culture. Also, 7 days post-loading, matrix microdamage in the stimulated area, detected with the BaSO₄ precipitate, were not significantly increased under the load point in loaded samples ($0.11 \pm 0.05\%$ of bone volume), while at the support areas it was significantly higher ($0.2387 \pm 0.06\%$, $p < 0.001$) compared to the static ($0.062 \pm 0.02\%$).

Conclusions

This study demonstrates that (1) cyclic strains applied on ex vivo bovine cortical bone successfully induced remodelling as characterized by the formation of bone resorption cones, along with an increase of osteoclast formation, and (2) there was an induction of microdamage post loading as shown by the significant increases in microdamage labelled. This supports previous in vivo studies with an increase in osteoclastogenesis up to 7 days post loading. This is the first evidence of the development of an ex vivo model to study osteon remodelling that could be applied to study bone physiology and repair.

OC18.2

MICRORNA-29A MITIGATES AGE-MEDIATED OSTEOPOROSIS THROUGH COMPROMISING METHYL DNA ACTIVATION OF OXIDATIVE STRESS AND INFLAMMATION

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Introduction and Objective

Senescent bone cell overburden accelerates osteoporosis. Epigenetic alteration, including microRNA signalling and DNA methylation, is one of prominent features of cellular senescence. This study aimed to investigate what role microRNA-29a signalling may play in the development of senile osteoporosis.

Materials and Methods

Bone biopsy and serum were harvested from 13 young patients and 15 senior patients who required spine surgery. Bone mass, microstructure, and biomechanics of miR-29a knockout mice (miR-29aKO) and miR-29a transgenic mice (miR-29aTg) were probed using mCT imaging and three-point bending material test. Senescent cells were probed using senescence-associated β -galactosidase (SA- β -gal) staining. Transcriptomic landscapes of osteoblasts were characterized using whole genome microarray and KEGG bioinformatics. miR-29a and senescence markers p16^{INK4a}, p21^{Waf/cipl} and inflammatory cytokines were quantified using RT-PCR. DNA methylome was probed using methylation-specific PCR and 5-methylcytosine immunoblotting.

Results

Senescent osteoblast overburden, DNA hypermethylation and oxidative damage together with significant decreases in serum miR-29a levels were present in bone specimens of aged patients. miR-29aKO mice showed a phenotype of skeletal underdevelopment, low bone mineral density and weak biomechanics. miR-29a knockout worsened age-induced bone mass and microstructure deterioration. Of note, aged miR-29aTg mice showed less bone loss and fatty marrow than aged wild-type mice. Transgenic overexpression of miR-29a compromised age-dysregulated osteogenic differentiation capacity of bone-marrow mesenchymal cells. In vitro, miR-29a promoted transcriptomic landscapes of antioxidant proteins in osteoblasts. The microRNA interrupted DNA methyltransferase (Dnmt3b)-mediated DNA methylation, inhibiting reactive oxygen radicals burst, IL-6 and RANKL production, and a plethora of senescent activity, including increased p16^{INK4a}, p21^{Waf/cipl} signalling and SA- β -gal activity.

Conclusions

miR-29a loss is correlated with human age-mediated osteoporosis. miR-29a signalling is indispensable in bone mass homeostasis and microstructure integrity. Gain of miR-29a function is advantageous to delay age-induced bone loss through promoting antioxidant proteins to inhibit DNA hypermethylation-mediated osteoblast senescence. Collective investigations shine light onto the anabolic effects miR-29a signalling to bone integrity and highlight a new epigenetic protection strategy through controlling microRNA signalling to delay osteoblast senescence and senile osteoporosis development.

OC18.3

DECREASED BONE STRUCTURE IN MICE WITH XXY KARYOTYPE (KLINEFELTER SYNDROME) MAY BE INFLUENCED BY THE SUPERNUMERARY X-CHROMOSOME AND X-CHROMOSOME INACTIVATION (XCI)

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Introduction and Objective

Klinefelter Syndrome (KS, karyotype 47,XXY) is the most frequent chromosomal aneuploidy in males, as well as the most common cause of infertility in men. Patients suffer from a lack of testosterone, i.e. hypergonadotropic hypogonadism provoking infertility, but KS men also show an increased predisposition to osteoporosis and a higher risk of bone fracture. In a mouse model for human KS, bone analysis of adult mice revealed a decrease in bone mass that could not be rescued by testosterone replacement, suggesting a gene dosage effect originating from the supernumerary X-chromosome on bone metabolism. Usually, X chromosome inactivation (XCI) compensates for the dosage imbalance of X-chromosomal genes between sexes. Some studies suggested that expression of genes that escape silencing of the supernumerary X-chromosome (e.g. androgen receptor) has an impact on sex differences, but may also cause pathological changes in males. As a promising new such candidate for a musculoskeletal escape gene, we identified the integral membrane protein (ITM) 2a, which is encoded on the X-chromosome and related to enchondral ossification. The aim of the project was to characterize systemic bone loss in the course of aging in our KS mouse model, and whether the supernumerary X-chromosome causes differences in expression of genes related to bone development.

Materials and Methods

Bone structure of 24 month (=aged) old male wild type (WT) and 41, XXY mice (B6Ei.Lt-Y) were analysed by μ CT. Afterwards bones were paraffin embedded and cut. In addition, tissue of brain, liver, kidney, lung and heart were also isolated and embedded for IHC staining. Using an anti-ITM2a antibody, expression and cellular localization of ITM2a was evaluated. IHC was also performed on musculoskeletal tissue of WT embryos (E18.5) and neonatal mice to determine possible age-related differences.

Results

In 24 month old mice, the analysis of the lumbar vertebrae revealed a significantly lower BV/TV, trabecular bone volume and trabecular number in the XXY- group compared to WT. Trabecular thickness appeared lower but did not reach significance, with the cortical thickness being significantly higher in the XXY- group. High expression of ITM2a was detected in bone slices of both karyotypes in the chondrocytes inside the growth plate, as well as in megakaryocytes and leucocytes as well as endothelial cells of blood vessels inside the bone marrow. Osteocytes, along with erythrocytes and erythropoietic stem cells were negative for ITM2a. Other organs that showed ITM2a positive staining were kidney (blood vessels), heart (muscle) and brain (different structures). Liver and lung tissue were negative for ITM2a. No obvious difference in the intensity of the ITM2a-expression was observed between the WT and the XXY-karyotype. Analyses of embryonic bone tissue (WT) showed high expression of ITM2a in proliferating, hypertrophic and resting chondrocytes in the growth plates of tibia and femur. In comparison, the neonatal animals (WT) did not show any protein-expression in chondrocytes. Furthermore, within the metaphysis of both, embryonic and neonatal bones, endothelial cells and osteoblasts were ITM2a-positive. Further analyses of bones and tissues from young mice (4-6 month) are ongoing.

Conclusions

Bone analyses revealed a significant reduction in trabecular bone mass along with fewer and thinner trabeculae in XXY mice compared to the WT, especially in the spine. ITM2a expression was visible in different cell types inside the bone, and in addition, different expression patterns at different stages of development (embryonic/neonatal) were observed. However, we have not found a significant difference in the quantity of ITM2a between tissues of XXY-karyotypes and WT. Further analyses of X-chromosomal encoded and therefore dysregulated modulators in XXY-karyotype mice and patients may reveal new sex chromosomal effector proteins in bone metabolism.

OC18.4

PERIPROSTHETIC ATYPICAL FEMORAL FRACTURES EXIST. PREVALENCE ON 115 PERIPROSTHETIC FEMORAL FRACTURES AROUND A PRIMARY HIP STEM

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Introduction and Objective

Some periprosthetic femoral fractures (PFFs) present history and radiographic aspect consistent with an atypical femoral fracture (AFF), fulfilling the criteria for AFF except that PFFs by themselves are excluded from the diagnosis of AFFs. The aim of this study was to evaluate in a single Institution series of PFFs if any of them could be considered a periprosthetic atypical femoral fracture (PAFF), and their prevalence.

Materials and Methods

Surgical records were searched for PFFs around a primary hip stem from January 2013 to December 2019. Cases were classified according to Vancouver classification. Demographic and medical history were extracted. Fisher's exact test was used for statistical analysis.

Results

One-hundred-fifteen PFFs were identified, 59 of them were type B1 and 16 were type C. Radiographs and medical records were available for all patients. Twenty-four patients (32%) have been treated with bisphosphonates (BPs) for longer than 4 years. Four patients presented a fracture with characteristics of PAFF. When enlarged to all PFFs of the series, no other PAFF was found: prevalence of PAFFs was 5.3% for type B1 and C cases and 3.5% for all surgically treated PFFs. Statistical significative difference between PAFFs and PFFs was found for prolonged BPs assumption and for the level of fracture clear of the stem.

Conclusions

Fracture with characteristics of AFFs can also happen over a prosthetic stem, configuring themselves as PAFFs, and they are related to prolonged BPs use. As a correct diagnosis is mandatory for proper treatment, a revision of criteria for AFFs should be considered, accepting that PAFFs exist.

OC19 INFECTION

K19

NOVEL ANTIMICROBIAL APPROACHES TO PREVENT ORTHOPEDIC DEVICE-RELATED INFECTION

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Orthopedic device-related bone infection is one of the most distressing complications of the surgical fixation of fractures. Despite best practice in medical and surgical interventions, the rate of infection remains stubbornly persistent, and current estimates indicate that treatment failure rates are also significant. As we approach the limit of the effectiveness of current anti-infective preventative and therapeutic strategies, novel approaches to infection management assume great importance. This presentation will describe our efforts to develop and test various hydrogels to serve as customized antibiotic delivery vehicles for infection prevention and treatment. Hydrogels offer solutions for many of the challenges faced by complex trauma wounds as they are not restricted spatially within a poorly defined surgical field, they often degrade rapidly with no compatibility issues, and releases 100% of the loaded antibiotic. The preliminary data set proving efficacy in preventing and treating infection in both rabbit and sheep studies will be described, including local antibiotic concentrations in the intramedullary canal over time, compared to that of the more conventional antibiotic loaded bone cement. These two technologies show potential for the prevention and treatment of infection in trauma patients, with a clear focus on optimized antibiotic delivery tailored for complex wounds.

OC19.1

INTRA-RATER RELIABILITY OF DIGITAL THERMOGRAPHY IN DETECTING PIN SITE INFECTION; A PROOF OF CONCEPT STUDY

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Introduction and Objective

Digital infra-red thermography may have the capability of identifying local inflammations. Nevertheless, the role of thermography in diagnosing pin site infection has not been explored yet and the reliability and validity of this method for pin site surveillance is in question. The purpose of this study was to explore the capability and intra-rater reliability of thermography in detecting pin site infection.

Materials and Methods

This explorative proof of concept study follows GRRAS -guidelines for reporting reliability and agreement studies. After clinical assessment of pin sites by one examiner using Modified Gordon Pin Infection Classification (Grade 0 - 6), thermographic images of the pin sites were captured with a FLIR C3 camera and analyzed by the FLIR tools software package. The maximum skin temperature around the pin site and the maximum temperature for the whole thermographic picture was measured. Intra-rater agreement was established and test-retests were performed with different camera angles.

Results

Thirteen (4 females) patients (age 9-72 years) were included. Indications for frames: 4 fracture, 2 deformity correction, 1 lengthening, 6 bone transport. Days from surgery to thermography ranged from 27 to 385 days. Overall, 231 pin sites were included. Eleven pin sites were diagnosed with early signs of infection: five grade 1, five grade 2, one grade 3. Mean pin site temperature was 33.9 °C (29.0-35.4). With 34 °C as cut-off value for infection, sensitivity was 73%, specificity 67%, positive predictive value 10% and negative predictive value 98%. Intra-rater reliability for thermography was ICC 0.85 (0.77-0.92). The temperature measured was influenced by the camera positioning in relation to pin site with a variance of 0.2.

Conclusions

Measurements of pin sites using the handheld FLIR C3 infrared camera was a reliable method and the temperature was related to infection grading. This study demonstrates that digital thermography with a handheld camera might be used for monitoring the pin sites after operations to detect early infection, however, future larger prospective studies are necessary.

OC19.2

THERMAL IMAGING OF SURFACE TEMPERATURE CHANGES IN SEPTIC ARTHRITIS

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Introduction and Objective

Septic arthritis is an acute infective presentation of the joint calling for urgent intervention, thus making the differential diagnosis process difficult. An increase in temperature in the area containing the suspected septic arthritis is one of the clinically important findings. In this study, it was aimed to investigate whether or not the temperature changes obtained through thermal camera can be used as a new additional diagnostic tool in the differential diagnosis of septic arthritis.

Materials and Methods

The study was approved by the local ethics committee as a prospective cohort. A total of 49 patients, 15 septic and 34 non-septic ones, both male and female ones from all ages admitted to the emergency room or evaluated with the consultation of another clinics who were also present with a pre-diagnosis of arthritis (septic or non-septic) in the knee (with complaints of redness, swelling, pain, effusion, increased temperature, edema, and inability to walk) were included in the study. The patients with non-joint inflammatory problems and a history of surgery in the same joint were excluded from the study. The temperature increase in the joint area with suspected septic arthritis was observed, and the difference in temperature changes of this suspicious area with the joint area of the contralateral extremity was compared after which the diagnosis of septic arthritis was confirmed by taking culture with routine intra-articular fluid aspiration, which is the gold standard for definitive diagnosis.

Results

The mean age of the patients was 39.89 ± 27.65 °C. A significant difference was found between the group with and without septic arthritis in terms of ASO, sedimentation, and leukocyte increase in the analysis of joint fluid ($p < 0.05$). When the thermal measurements were compared, the mean temperature was 37.93 °C in the septic group, while it was 36.79 °C in the non-septic group, which showed a significant difference ($p < 0.000^*$). The mean temperature difference in both joints was 3.40 °C in the septic group, while 0.94 °C in the non-septic group ($p < 0.000^*$). While the mean temperature was 37.10 °C in the group with septic arthritis, it was measured to be 35.89 °C in the group without ($p < 0.020$). A very strong positive correlation was found between the difference between the mean temperatures of both groups and the values of the hottest and coldest temperature points ($r = 0.960$, $r = 0.902$).

Conclusions

In the diagnosis of septic arthritis, a thermal imager can be used as a non-invasive diagnostic tool. With the help of this device, a quantitative value, in addition to palpation, can be given to the local temperature increase in the joint, which is an important finding in the clinic of septic arthritis. In future studies, specially designed thermal devices developed with special software for septic arthritis can be developed.

OC19.3

MANAGEMENT OF CONTAMINATED BONE DEFECTS USING A BONE SUBSTITUTE ELUTING DIFFERENT ANTIBIOTICS

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Introduction and Objective

Management of bone loss associated with bone contamination or infection represents a double biological and clinical challenge frequent in traumatology. The advent of new biomaterials can allow a different approach in the treatment of bone gap. The purpose of this study was to evaluate the prophylactic and therapeutic effectiveness of addition of a new absorbable bone substitute (BS) eluting different antibiotics in reconstruction of bone defects after infections and fractures with soft tissue damage.

Materials and Methods

We conducted a review of patients with contaminated or infected bone defects treated using a new biomaterial, a porous composite of collagen matrices and Beta tricalcium phosphate (β TCP), able to provide a long-term release of different antibiotics. We have included treatment of osteomyelitis and osteosynthesis of exposed fracture (Gustilo Anderson 1-3b) or fractures with soft tissue damage and high risk of contamination. Surgical technique included debridement filling bone defect with BS eluting antibiotics, osteosynthesis (plate, nail, external fixator, kirschner wire), soft tissue coverage, and systemic antibiotic therapy. Radiographic and clinical data including complications (wound dehiscence, superficial or deep infection, osteomyelitis) were collected.

Results

We treated 25 patients (21 male, 4 female) with mean age 47 yrs. (range 21-83). The locations treated (for incidence) was: 9 femurs (7 plates, 2 nail), 7 calcanei (one bilateral), 3 tibias, 2 forearms, 2 metatarsi, 2 hands, 1 elbow. 6 patients had large bone loss. 7 patients had bone infections (4 were Cierny Madern 4); 8 patients had osteosynthesis of exposed fractures Gustilo Anderson 1-3b (9 plate, one bilateral calcaneus). 8 patients had treatment for pseudoarthrosis of exposed fractures (6 femurs, 1 forearm, 1 metatarsus) and 3 patients a prophylactic treatment for calcaneal fractures with soft tissue damage. 4 deep infection were treated with multiple surgical debridement and new filling bone defect with BS eluting antibiotic with infection eradication. We have used a combination of vancomycin and gentamicin on 15 cases, vancomycin alone on 4 cases, combination of vancomycin and amikacin on 1 case and amikacin and Linezolid in a targeted multi drug resistance. At final follow-up functional outcome was good in all cases with bone healing.

Conclusions

Extensive debridement is a fundamental requisite for eradication of bone infections and contamination. Filling of the bone void with loaded bio-composite eluting diversifiable local antibiotics with synergistic anti-biofilm activity is desirable. Treatment of this bone defects are advantaged when combining his reconstruction with BS and the possibility of release high antibiotic concentration at least for 10 days. This is an important complementing prophylactic and therapeutic antimicrobial option with adjuvant role to systemic therapy that enlarges the success rate.

OC19.4

PATHOGENICITY OF *C. ACNES* FOLLOWING INTERACTION WITH HUMAN MESENCHYMAL STEM CELLS

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Introduction and Objective

Found in bone-associated prosthesis, *Cutibacterium acnes* (*C. acnes*) is isolated in more than 50% of osteoarticular prosthesis infections, particularly those involving shoulder prostheses. Ongoing controversies exist concerning the origin of *C. acnes* infection. Few reports construct a reasonable hypothesis about probable contaminant displaced from the superficial skin into the surgical wound. Indeed, despite strict aseptic procedures, transecting the sebaceous glands after incision might result in *C. acnes* leakage into the surgical wound. More recently, the presence of commensal *C. acnes* in deep intra-articular tissues was reported. *C. acnes* was thus detected in the intracellular compartment of macrophages and stromal cells in 62.5% of the tested patients who did not undergo skin penetration. Among bone stromal cells, mesenchymal stem cells (MSCs) are predominantly found in bone marrow and periosteum. MSCs are the source of osteogenic lines of cells capable of forming bone matter. In this study, the pathogenicity of *C. acnes* in bone repair context was investigated.

Materials and Methods

Human bone marrow derived MSCs were challenged with *C. acnes* clinical strains harvested from non-infected bone site (Cb). The behaviour of Cb strain was compared to *C. acnes* took from orthopaedic implant-associated infection (Ci). The infective capabilities of both strains was determined following gentamicin-based antibiotic protection assay. The morphology and ultrastructural analysis of infected MSCs was performed respectively through CLSM pictures of Phalloidin[®] stained MSCs cytoskeleton and DAPI labelled Cb, and transmission and scanning electron microscopies. The virulence of intracellular Ci and Cb (Ci-MSCs and Cb-MSCs) was investigated by biofilm formation on non-living bone materials; and the immunomodulatory response of infected MSCs was investigated (PGE-2 and IDO secretion detected by ELISA). Bone cells (osteoblasts and PMA differentiated macrophages) were then challenged with Cb-MSCs and Ci-MSCs. Intracellular accumulation of ROS within infected macrophages was assessed by flow cytometry after 2 h of infection and the catalase production by Cb-MSC and Ci-MSC was evaluated. Statistical analyses were performed using Mann & Whitney test.

Results

Following MSCs infection by *C. acnes*, the rate of viable bacteria inside MSCs was about 4% and 6% for Cb and Ci, respectively. Cb showed however a lower invasiveness in comparison to Ci (0.6-fold, $p=0.01$), confirming the higher pathogenicity of Ci. The ultrastructural and morphology analysis of infected MSCs confirmed the presence of bacteria free in MSCs cytoplasm, localized between F-actin fibers of MSCs, which preserved their elongated morphology. Considering the high level of secreted immunomodulatory mediators (PGE-2 and IDO), our results suggest that Cb-infected MSCs could promote a transition of macrophages from a primarily pro-inflammatory M1 to a more anti-inflammatory M2 phenotype. In comparison with Cb, Cb-MSCs increased significantly the formation of biofilm on TA6V and PEEK but reduced the biofilm formation on 316L SS. Ci-MSCs showed a significant increase in biofilm formation on PEEK vs Ci, while no difference in biofilm formation was noticed on TA6V and 316L SS. Regarding the ability of MSCs bacteria to infect osteoblasts, our results showed a higher infective capabilities of Cb-MSCs versus Cb (>2 -fold, $p=0.02$), while no difference was noticed between Ci and Ci-MSCs. Along with an increase in catalase production by Cb-MSCs, we noticed its higher persistence to macrophage degradation.

Conclusions

Taken together, our results demonstrate a shift in commensal Cb to pathogenic following infection. Indeed, Cb- MSCs acquires features that (i) increase biofilm formation on orthopedic based materials, (ii) increase the osteoblast infection and (iii) develop resistance to the macrophage degradation, through the increase of catalase production. Overall, these results showed a direct impact of *C. acnes* on bone marrow derived MSCs, providing new insights into the development of *C. acnes* during implant-associated infections.

OC20 KNEE ARTHROPLASTY

K20

THE HOFFA'S FAT PAD FUNCTION IN THE OSTEOARTHRITIC PROCESS OF THE KNEE JOINT

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The knee joint has also a periarticular adipose tissue, which is known as Hoffa's fat pad (IPFP). IPFP has a dual function in the joint it reduces the concentration of Nitric Oxide, the release of glycosaminoglycans and the expression of MMP1 in the cartilage, but it also contains MSC and macrophages. Our hypothesis is that synovial fluid contains elements, not all of which are understood, which act as messengers and alter the "homeostasis" of the knee and the metabolism of all the cellular components of the joint, including the MSC of Hoffa's fat pad, thus making them another piece in the puzzle as far as OA of the knee is concerned.

The IPFP of 37 patients with OA and 36 patients with ACL rupture were analyzed. Isolation, primary culture, and a functional and proteomic study of MSCs from IPFP were performed.

Our results show that OA of the knee, in its more severe phases, also affects the MSC's of IPFP, which is a new actor in the OA degenerative process and which can contribute to the origin, onset and progression of the disease. A differential protein profile between OA and ACL patients were identified.

Infrapatellar pad should be regarded as an adipose tissue with its own characteristics and it's also able to produce and excrete important inflammatory mediators directly into the knee joint.

OC20.1

THE EFFECTS OF KINESIOPHOBIA ON OUTCOME FOLLOWING TOTAL KNEE REPLACEMENT: A SYSTEMATIC REVIEW

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Introduction and Objective

Kinesiophobia, the fear of physical movement and activity related to injury vulnerability, has been linked to sub-optimal outcomes following total knee replacement (TKR). This systematic review has two aims: to define the relationship between kinesiophobia and functional outcomes, pain and range of motion following TKR, and to evaluate published treatments for kinesiophobia following TKR.

Materials and Methods

A primary search was performed in March 2020. English-language studies recruiting adult primary TKR patients, using the Tampa Scale of Kinesiophobia (TSK) were included. Study quality was assessed using the Newcastle Ottawa Scale for cohort or case control studies, and the Cochrane Collaboration Risk of Bias tool for randomised controlled trials.

Results

All thirteen included papers (82 identified) showed adequately low risk of methodological bias. TSK1 (activity avoidance) correlated with WOMAC functional score at 12 months in three studies ($r=0.20$ $p<0.05$, $R=0.317$ $p=0.001$, and correlation coefficient 0.197 $p=0.005$). TSK score significantly correlated with mean active range of motion (ROM) at six months (105.33 ($SD=12.34$) vs 85.53 ($SD=14.77$) $p=0.000$) post-operation. Three post-operative interventions improved TSK score vs control following TKR: a home-based functional exercise programme (TSK -14.30 ($SD=0.80$) vs -2.10 ($SD=0.80$) $p<0.001$), an outpatient CBT programme (TSK 27.76 ($SD=4.56$) vs 36.54 ($SD=3.58$), and video-based psychological treatment (TSK 24 ($SD=5$) vs 29 ($SD=5$) $p<0.01$).

Conclusions

Kinesiophobia negatively affects functional outcomes up until one year post-operatively, while active ROM is reduced up to six months post procedure. Post-operative functional and psychological interventions can improve kinesiophobia following TKR.

OC20.2

TIBIAL TUBERCLE OSTEOTOMY IN DIFFICULT EXPOSURE DURING TOTAL KNEE ARTHROPLASTY: MIDTERM RESULTS EXPERIENCE OF A MONOCENTRIC STUDY

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Introduction and Objective

Difficult primary total knee arthroplasty (TKA) and revision TKA are high demanding procedures. Joint exposure is the first issue to face off, in order to achieve a good result. Aim of this study is to evaluate the clinical and radiological outcomes of a series of patients, who underwent TKA and revision TKA, where tibial tubercle osteotomy (TTO) was performed.

Materials and Methods

We retrospectively reviewed a cohort of 79 consecutive TKAs where TTO was performed, from our Institution registry. Patients were assessed clinically and radiographically at their last follow-up (mean, 7.4 ± 3.7 years). Clinical evaluation included the Knee Society Score (KSS), the pain visual analogue scale (VAS), and range of motion. Radiological assessment included the evaluation of radiolucent lines, osteolysis, cortical bone hypertrophy, time of bone healing of the TTO fragment, and the hardware complication.

Results

KSS raised from 40.7 ± 3.1 to 75 ± 4.3 ($p < 0.0001$). Knee flexion increased from $78.7 \pm 9.9^\circ$ to $95.0 \pm 9.5^\circ$ ($p < 0.0001$), and VAS improved from 7.9 ± 0.9 to 3.8 ± 1 ($p < 0.0001$). No signs of loosening or evolutive radiolucency lines were found. Osteolytic areas around the stem were detected. No significant association was found between the implant design and the outcomes, while aseptic loosening showed significantly better results. Complications were: 4 painful hardware, 3 late periprosthetic infections, 1 extension lag of 5° , and 3 flexion lag.

Conclusions

Our experience suggests the use of TTO to improve the surgical approach in difficult primary TKA or revision TKA. A strict surgical technique leads to good results with low risk of complications

OC20.3

LITERATURE REVIEW ON OUTCOMES OF TOTAL KNEE ARTHROPLASTY IN POST-TRAUMATIC VS PRIMARY OSTEOARTHRITIS: IS THERE ANY DIFFERENCE?

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Introduction and Objective

Evidence in literature is contradicting regarding outcomes of total knee arthroplasty (TKA) in post-traumatic osteoarthritis (PTOA) and whether they are inferior to TKA in primary osteoarthritis (OA). The aim of this review was to find out if any difference exists in the results of TKA between the two indications.

Materials and Methods

The electronic databases MEDLINE, EMBASE, The Cochrane Collaboration, and PubMed were searched and screened in duplicate for relevant studies. The selected studies were further subjected to quality assessment using the modified Coleman method. The primary outcome measure was patient reported outcome, and secondary outcome measures were infection, revision, stiffness, and patella tendon rupture.

Results

A total of 18 studies involved 1129 patients with a mean age of 60.6 years (range 45.7-69) and follow up of 6.3 years. The time interval from index injury to TKA was 9.1 years. Knee Society Score (KSS) in PTOA reported in 12/18 studies showed functional improvement from 42.5 to 70 post-TKA exceeding minimally clinically important difference. In TKA for primary OA vs PTOA, deep peri-prosthetic joint infection (PJI) was reported in 1.9% vs 5.4% of patients, whilst revision of prosthesis at an average of 6 years post-operatively was performed in 2.6 vs 9.7% of patients.

Conclusions

TKA is a successful treatment option for PTOA. However, the risk of significant complications like PJI and implant failure requiring revision is higher than primary OA cases. Patients should be counselled about those risks. Further well-designed comparative cohort-matched studies are needed to compare outcomes between the two populations.

OC20.4

OVERSTUFF IN MECHANICALLY ALIGNED TOTAL KNEE REPLACEMENT: MORPHOMETRIC STUDY WITH CLINICAL CORRELATIONS OF BONE RESECTIONS

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Introduction and Objective

TKA have shown both excellent long-term survival rate and symptoms and knee function improvement. Despite the good results, the literature reports dissatisfaction rates around 20%.

This rate of dissatisfaction could be due to the overstuff that mechanically aligned prostheses could produce during the range of motion. Either size discrepancy between bone resection and prosthetic component and constitutional mechanical tibiofemoral alignment (MTFA) alteration might increase soft tissue tension within the joint, inducing pain and functional limitation.

Materials and Methods

Total knee arthroplasties performed between July 2019 and September 2020 were examined and then divided into two groups based on the presence (Group A) or absence (Group B) of patellofemoral overstuff, defined as a thickness difference of more than 2 mm between chosen component and bone resection performed, taking into account at least one of the following: femoral medial and lateral condyle, medial or lateral trochlea and patella. Based on pre and post-operative MTFA measurements, Group A was further divided into two subgroups whether the considered alignment was modified or not. Patients were assessed pre-operatively and at 6 months post-op using the Knee Society Score (KSS), Oxford Knee Score (OKS), Forgotten Joint Score (FJS), Visual Analogue Scale (VAS) and Range of Motion (ROM).

Results

One hundred total knee arthroplasties were included in the present study, 69 in Group A and 31 in group B. Mean age and BMI of patients was respectively 71 and 29.2. The greatest percentage of Patellofemoral Overstuff was found at the distal lateral femoral condyle. OKS, KSS functional score, and FJS were statistically significant higher in patients without Patellofemoral Overstuff.

Therefore, Group A patients with a non-modified MTFA demonstrated statistically significant better KSS, ROM and FJS.

Conclusions

Patellofemoral Overstuff decrease post-operative clinical scores in patients treated with TKA. The conventional mechanically aligned positioning of TKA components might be the primary cause of prosthetic overstuffing leading to worsened clinical results.

Level of evidence: III; Prospective Cohort Observational study;

OC21 TRAUMA RESEARCH

K21

GRAFTING TECHNIQUES IN MANAGEMENT OF GREAT BONE DEFECTS

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Treatment of large bone defects represents a great challenge for orthopedic surgeons. The main causes are congenital abnormalities, traumas, osteomyelitis and bone resection due to cancer. Each surgical method for bone reconstruction leads its own burden of complications. The gold standard is considered the autologous bone graft, either of cancellous or cortical origin, but due to graft resorption and a limitation for large defect, allograft techniques have been identified. In the bone defect, these include the placement of cadaver bone or cement spacer to create the 'Biological Chamber' to restore bone regeneration, according to the Masquelet technique.

We report eight patients, with large bone defect (for various etiologies and with an average size defect of 13.3 cm) in the lower and upper limbs, who underwent surgery at our Traumatology Department, between January 2019 and October 2020. Three patients were treated with both cortical and cancellous autologous bone grafts, while five received cortical or cement spacer allografts from donors. They underwent pre and postoperative radiographs and complete osseointegration was observed in all patients already undergoing monthly radiographic checks, with a restoration of length and range of motion.

In our study, both the two stage-Masquelet and the cortical bone graft from a cadaver donor proved to be valid techniques in patients with very extensive defects to reconstruct the defect, restore the length, minimize implant left in situ and achieve complete functional recovery.

OC21.1

ARTHROSCOPIC EVACUATION OF HEMATOMA IN DISLOCATED AND ARTICULAR FRACTURES: CAN ARTHROFIBROSIS AND EARLY SECONDARY ARTHROSIS BE PREVENTED?

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Introduction and Objective

Joint malleolar fractures have been estimated around 9% of all fractures. They are characterized by different both early and late complications. Among the latter, arthrofibrosis and early secondary arthrosis represent the two most common ones. Moreover, these two complications could be considered related to each other. Their real cause is still under investigation, even if residual post-operative hematoma and acute post-traumatic synovitis appear to be the most accredited. Supporting this hypothesis, joint debridement and the evacuation of the post-operative hematoma could represent a possible solution. The aim of this prospective study is to evaluate the role of arthroscopic lavage and debridement during internal fixation in order to prevent late joint complications.

Materials and Methods

Sixty consecutive patients who reported dislocated articular ankle fractures with surgical indication of open reduction and internal fixation (ORIF) have been included in this study. 27 patients underwent ORIF surgery associated with arthroscopic washout and debridement, while 33 patients, representing the control group, underwent just internal reduction and osteosynthesis. Patients with pure dislocations, non-articular fractures, polytrauma, previous local trauma, metabolic and connective pathologies were excluded. Follow-up was performed at 40 days (T1), 3 (T2) and 6 months (T3) after trauma for all patients. If necessary, some have been re-evaluated 12 months after the trauma. Efficacy of the treatment was evaluated through the VAS scale, Maryland scale, search for local complications such as dehiscence or infections, and finally radiographic evaluation. T-Student was estimated in order to individuate statistical significance.

Results

VAS scale showed higher values for the case group than the control group with mean values of 2.7 and 4.2 at T1 and 2.1 and 3.8 at T2, respectively. At 6 months follow-up, the VAS values resulted similar with 2.6 for the case group and 2.8 for the control group. The same projections were found for the Maryland scale, with values of 61.5 and 40.7 at T1, 80.8 and 68.0 at T2 and 87.8 and 85.0 with no significant differences at T3 respectively. No significant differences were detected for complications or radiographic evaluation.

Conclusions

Our study has shown significance differences in terms of pain and time for recovery only in the very short term follow up. Although our study, due to the specific limits, cannot be considered diriment, on the basis of the data, we could hypothesize that the aforementioned hypothesis may remain valid for the non-acute hematoma or that the cause of the arthrofibrosis should be sought somewhere else. However, evidence is low, and further research is needed.

OC21.2

A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE WIDE-AWAKE LOCAL ANAESTHETIC NO TOURNIQUET TECHNIQUE FOR DISTAL RADIUS FRACTURE FIXATION

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Introduction and Objective

Wide awake local anaesthetic no tourniquet (WALANT) is being used for a wide variety of hand and wrist surgery. It has recently been used in distal radius fracture fixation. The purpose of this systematic review and meta-analysis was to assess the effectiveness of the WALANT technique in open reduction internal fixation.

Materials and Methods

Pubmed, Embase, and Scopus databases were searched on 02/03/21 with the following search terms: radius, WALANT, local anesthetic, wide awake surgery. The primary outcome measure was conversion to general anaesthetic and mean intra-operative visual analogue scale (VAS) pain scores. Secondary measures were operative times, mean intraoperative blood loss, post-operative functional and radiological outcomes.

Results

110 articles were identified; eight studies were deemed eligible with 212 in the WALANT group and 247 in the comparative groups of regional anaesthesia and general Anaesthesia (GA). Two patients in the WALANT group required conversion to general anaesthesia due to anxiety rather than pain. Intra-operative VAS pain scores in the WALANT and regional anaesthetic group were 1.75 and 2.86 respectively ($p < 0.001$). There was no statistically significant difference in Q-DASH scores, range of motion or radiological outcomes. There was a slight increase in mean blood loss in the WALANT group compared with those given a GA or regional anaesthetic with tourniquet (22.5ml vs 12.15ml, $p < 0.001$).

Conclusions

The WALANT technique is a viable option for anaesthetic when performing distal radius fracture fixation. It is well tolerated, giving similar post-operative outcomes to other anaesthetic methods. It is a potentially useful technique in a centre with an underresourced anaesthetic department or for patients who may not tolerate regional and general anaesthetic methods. Adequate patient counselling prior to the procedure should be performed with appropriate patient selection.

OC21.3

A MULTICENTRE EVALUATION OF FIBULA NAIL OUTCOMES (MEFNO)

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Introduction and Objective

Lower limb fractures are amongst the most common surgically managed orthopaedic injuries, with open reduction and internal fixation (ORIF) as the conventional method of treatment of the fibula. In recent years, dedicated intramedullary implants have emerged for fibula fixation in tandem with the move towards minimally invasive surgery in high-risk patients. This is the largest multicentre review to date with the aim of establishing the clinical outcomes following intramedullary nail (IMN) fixation of the fibula and to identify the absolute indication for fibula IMN fixation.

Materials and Methods

A retrospective study of adult patients in all UK hospitals, who underwent fibula nail fixation between 01/01/2018 and 31/10/2020 was performed. Primary outcome measures included time to union, infection rate, other post-operative complications associated with the fixation and length of hospital stay. The secondary outcome measure was to identify the indication for fibula nailing. Data tabulation was performed using Microsoft Excel and analysis was performed using SPSS Version 23 (SPSS Statistics).

Results

2 Major Trauma Centres (MTCs) and 9 Trauma Units (TUs) were eligible for inclusion. 102 patients were included and 91% were classified as ankle fractures of 68% (n=69) were Weber B, 24% (n=24) Weber C and 8% (n=9) were either distal tibial fractures with an associated fibula fracture or pilon fractures. The mean age was 64 years of which 45 were male patients and 57 were female. The average BMI was 30.03kg/m² and 44% of patients were ASA 3. 74% of patients had poor pre-op skin condition including swelling and open wounds. The calculated infection rate for fibula nail was 4.9% and metal-work complication rate was 4.9%. The average time to union was 13 weeks and length of inpatient stay was 15 days (SD +/- 12 days).

Conclusions

MEFNO has demonstrated that fibula nail is an ideal implant in patients who have a physiologically higher risk of surgery, poor skin condition and a complex fracture pattern. The time to union, complication and infection risks are lower than that reported in literature for ankle ORIFs.

OC21.4

SLIPPED CAPITAL FEMORAL EPIPHYSIS: GAIT ALTERATIONS IN CHILDREN TREATED WITH IN SITU FIXATION COMPARED TO TYPICALLY DEVELOPED CHILDREN

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Introduction and Objective

Slipped Capital Femoral Epiphysis (SCFE) is one of the most common hip disorders in children and is characterized by a proximal femoral deformity, resulting in early osteoarthritis. Several studies have suggested that SCFE patients after in situ fixation show an altered gait pattern. Early identification of gait alterations might lead to earlier intervention programs to prevent osteoarthritis. The aim of this study is to analyse gait alterations in SCFE patients after in situ fixation compared to typically developed children, using the Computer Assisted Rehabilitation Environment (CAREN) system.

Materials and Methods

This is a cross-sectional, multi-center case-control study in the Netherlands. Eight SCFE patients and eight age- and sex-matched typically developed were included from two hospitals. Primary outcomes were kinematic parameters (absolute joint angles), studied with gait analysis using statistical parametric mapping (SPM). Secondary outcomes were spatiotemporal parameters, the Notzli alpha angle, muscle activation patterns (EMG), and clinical questionnaires (VAS, Borg CR10, SF-36, and HOOS), analyzed using non-parametric statistical methods.

Results

Patients (mean BMI=28±9 kg/m²) showed altered gait patterns, with significantly increased external hip rotation and decreased downward pelvic obliquity during the pre-swing phase of the gait cycle compared to typically developed (mean BMI=22±3 kg/m²). Walking speed, cadence, % stance time, and step length were reduced in SCFE patients. Coefficient of variances of cadence, stance time, and step length were increased. Patients had a mean alpha angle of 64, SD=7.9. Clinical questionnaires showed that general health (SF-36) was 80±25, energy/fatigue (SF-36) was 67±15, pain (VAS) was 0±1.5, and total HOOS score was 85±18.

Conclusions

SCFE patients after in situ fixation appear to have developed a compensation mechanism, showing slight alterations in gait parameters, good general health, little functional limitations of the hip, and no self-reported pain. Cam deformities, altered joint loading, and this compensation mechanism might influence long-term early osteoarthritis. BMI reduction should be implemented in care plans, as obesity might also play a role in unfavorable long-term outcomes.

OC22 TISSUE ENGINEERING

K22

ENGINEERED AND DEVITALIZED EXTRACELLULAR MATRICES AS OFF-THE-SHELF OSTEOINDUCTIVE GRAFTS

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Design criteria for tissue-engineered materials in regenerative medicine include robust biological effectiveness, off-the-shelf availability, and scalable manufacturing under standardized conditions. For bone repair, existing strategies rely on primary autologous cells, associated with unpredictable performance, limited availability and complex logistic. Here, we report the manufacturing of engineered and devitalized human hypertrophic cartilage (HyC) as cell-free material inducing bone formation by recapitulating the developmental process of endochondral ossification. Our strategy relies on a customized human mesenchymal line expressing Bone Morphogenetic Protein-2 (BMP-2), critically required for robust chondrogenesis and concomitant extracellular matrix (ECM) enrichment. Following apoptosis-driven devitalization, lyophilization and storage, the resulting material exhibited unprecedented osteoinductive properties, unmatched by synthetic delivery of BMP-2 or by living engineered grafts. Scalability and pre-clinical efficacy were demonstrated by bioreactor-based production and subsequent orthotopic assessment. Our findings exemplify the broader paradigm of customized ECMs, engineered to activate specific regenerative processes by programming human cell lines as biological factory units.

OC22.1

THE EFFECTS OF GRAPHENE-CONTAINING POLYCAPROLACTONE SCAFFOLDS ON HEALING IN LARGE OSTEOCHONDRAL DEFECT MODEL

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Introduction and Objective

Several in vitro studies have shed light on the osteogenic and chondrogenic potential of graphene and its derivatives. Now it is possible to combine the different biomaterial properties of graphene and 3D printing scaffolds produced by tissue engineering for cartilage repair. Owing to the limited repair capacity of articular cartilage and bone, it is essential to develop tissue-engineered scaffolds for patients suffering from joint disease and trauma. However, chondral lesions cannot be considered independently of the underlying bone tissue. Both the microcirculation and the mechanical support provided with bone tissue must be repaired. One of the distinctive features that distinguish graphene from other nanomaterials is that it can have an inductive effect on both bone and cartilage tissue. In this study, the effect of different concentrations of graphene on the in vivo performance of single-layer poly-ε-caprolactone based-scaffolds is examined. Our hypothesis is that graphene nanoplatelet- containing, robocast PCL scaffolds can be an effective treatment option for large osteochondral defect treatment. For this purpose, different proportions of graphene- containing (1%,3%,5%,10 wt%) PCL scaffolds were studied in a 5mm diameter osteochondral defect model created in the rabbit knee.

Materials and Methods

In the study graphene-containing (1, 3, 5, 10 wt%), porous and oriented poly-ε-caprolactone-based scaffolds were prepared by robocasting method to use in the regeneration of large osteochondral defects. Methods: The scaffolds were implanted into the full-thickness osteochondral defect in a rabbit model to evaluate the regeneration of defect in vivo. For this purpose, twenty female New Zealand white rabbits were used and they were euthanized at 4 and 8 weeks of implantation. The reparative osteochondral tissues were harvested from rabbit distal femurs and then processed for gross appearance assessment, radiographic imaging, histopathological and immunohistochemical examinations.

Results

Results revealed that, graphene- containing graft materials caused significant amelioration at the defect areas. Graphene-containing graft materials improved the fibrous, chondroid and osseous tissue regeneration compared to the control group. The expressions of bone morphogenetic protein-2 (BMP-2), collagen-1 (col-1), vascular endothelial growth factor (VEGF) and alkaline phosphatase (ALP) expressions were more prominent in graphene- containing PCL implanted groups. Results also revealed that the ameliorative effect of graphene increased by the elevation in concentration. The most prominent healing was observed in 10 wt% graphene-containing PCL based composite scaffold implanted group.

Conclusions

This study demonstrated that graphene- containing, robocast PCL scaffolds has efficacy in the treatment of large osteochondral defect. Subchondral new bone formation and chondrogenesis were observed based on immunohistochemical examinations. 3D printed PCL platforms have great potential for the investigation of the osteochondral regeneration mechanism. The efficacy of graphene-containing PCL scaffolds on osteogenesis, vascularization, and mineralization was shown at different graphene concentrations at 4th and 8th weeks. Immunohistochemical studies showed statistical significance in the 5wt% and 10 wt%

graphene-containing groups compared to the 1wt% and 3 wt% graphene-containing groups at the end of the eighth week.

OC22.2

LONG BONE HEALING IN RAT SEGMENTAL FEMUR DEFECT WITH USE OF GRAPHENE-COATED BORATE-BASED 13-93B3 BIOACTIVE GLASS SCAFFOLDS

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Introduction and Objective

Bone is a tissue which continually regenerates and also having the ability to heal after injuries however, healing of large defects requires intensive surgical treatment. Bioactive glasses are unique materials that can be utilized in both bone and skin regeneration and repair. They are degradable in physiological fluids and have osteoconductive, osteoinductive and osteostimulative properties. Osteoinductive growth factors such as Bone Morphogenetic Proteins (BMP), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF), Transforming Growth Factor (TGF) are well known to stimulate new bone formation and regeneration. Unfortunately, the synthesis of these factors is not cost-effective and, the broad application of growth factors is limited by their poor stability in the scaffolds. Instead, it is wise to incorporate osteoinductive nanomaterials such as graphene nanoplatelets into the structures of synthetic scaffolds. In this study, borate-based 13-93B3 bioactive glass scaffolds were prepared by polymer foam replication method and they were coated with graphene-containing poly (ϵ -caprolactone) layer to support the bone repair and regeneration.

Materials and Methods

Effects of graphene concentration (1, 3, 5, 10 wt%) on the healing of rat segmental femur defects were investigated in vivo using male Sprague–Dawley rats. Fabricated porous bioactive glass scaffolds were coated by graphene-containing polycaprolactone solution using dip coating method. The prepared 0, 1, 3, 5 and 10 wt% graphene nanoparticle-containing PCL-coated composite scaffolds were designated as BG, 1G-P-BG, 3G-P-BG, 5G-P-BG and 10G-P-BG, for each group (n: 4) respectively. Histopathological and immunohistochemical (bone morphogenetic protein, BMP-2; smooth muscle actin, SMA and alkaline phosphatase, ALP) examinations were made after 4 and 8 weeks of implantation.

Results

Results showed that after 8-weeks of implantation both cartilage and bone formation were observed in all animal groups. After 4 and 8 weeks of implantation the both osteoblast and osteoclast numbers were significantly higher in the group 4 compared to the control group. Bone formation was significant starting from 1 wt% graphene-coated bioactive glass implanted group and highest amount of bone formation was obtained in group containing 10 wt% graphene ($p < 0.001$). Newly formed vessels expressed this marker and increased vascularization was observed in 8-weeks period compared to the 4-weeks period. In addition, an increase in new vessel formation were observed in graphene-coated scaffold implanted groups compared to the control group. While cartilage tissue was observed in control group, bone formation percentages were significant in graphene-coated scaffold implanted groups. Highest amount of bone formation occurred in group 4 (10 % wt G-C).

Conclusions

Additionally, the presence of graphene nanoplatelets enhanced the BMP-2, SMA and ALP levels compared to the bare bioactive glass scaffolds. It was concluded that pristine graphene-coated bioactive glass scaffolds improve osteointegration and bone formation in rat femur defect when compared to bare bioglass scaffolds.

OC22.3

MATRIX STIFFNESS REGULATES PARACRINE ACTIONS OF MESENCHYMAL STEM CELLS ON MACROPHAGES AND OSTEOBLASTS

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Introduction and Objective

Mesenchymal stem cells (MSC) are attractive candidates for bone regeneration approaches. Benefits of MSC therapy are mainly attributed to paracrine effects via soluble factors, exerting both immunoregulatory and regenerative actions. Encapsulation of MSC in hydrogels prepared with extracellular matrix (ECM) proteins has been proposed as a strategy to enhance their survival and potentiate their function after implantation. Functional activity of MSC can be regulated by the physical and mechanical properties of their microenvironment. In this work, we investigated whether matrix stiffness can modulate the crosstalk between MSC encapsulated in collagen hydrogels with macrophages and osteoblasts.

Materials and Method

Collagen hydrogels with a final collagen concentration of 1.5, 3 and 6 mg/mL loaded with human MSC were prepared. Viscoelastic properties of hydrogels were measured in a controlled stress rheometer. Cell distribution into the hydrogels was examined using confocal microscopy and the levels of the immunomodulatory factors interleukin-6 (IL-6) and prostaglandin E₂ (PGE₂) released by MSC were quantified by immunoassays. To determine the effect of matrix stiffness on the immunomodulatory potential of MSC, human macrophages obtained from healthy blood were cultured in media conditioned by MSC in hydrogels. The involvement of IL-6 and PGE₂ in MSC-mediated immunomodulation was investigated employing neutralizing antibodies. Finally, the influence of soluble factors released by MSC in hydrogels on bone-forming cells was studied using osteoblasts obtained from trabecular bone explants from patients with osteonecrosis of the femoral head during total hip arthroplasty.

Results

MSC loaded in hydrogels containing varying concentrations (1.5, 3 and 6 mg/mL) of collagen were viable. Rheology measurements determined that the hydrogel stiffness increased with increasing collagen concentration. Encapsulation of MSC into hydrogels barely affected their storage modulus values. MSC acquired a three-dimensional (3D) arrangement in all hydrogels and showed a more elongated shape in hydrogels with higher stiffness. The secretion of IL-6 and PGE₂ by MSC in hydrogels increased with increasing matrix stiffness. Media conditioned by MSC encapsulated in stiffer hydrogels decreased TNF- α levels secreted by macrophages to a higher extent than media conditioned by MSC in softer hydrogels. This effect was partially mediated by PGE₂. Finally, our preliminary results indicated that factors released by MSC in hydrogels regulated osteoblast-mediated mineralisation and this effect was dependent on hydrogel stiffness.

Conclusions

Our data indicate that matrix stiffness of collagen hydrogels regulates the production of soluble factors by MSC and their paracrine actions on macrophages and osteoblasts.

OC22.4

LOW-INTENSITY PULSED ULTRASOUND STIMULATION ENHANCES CHONDROGENIC DIFFERENTIATION OF ASCS IN A 3D HYDROGEL

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Introduction

Articular cartilage injuries have a limited potential to heal and, over time, may lead to osteoarthritis, an inflammatory and degenerative joint disease associated with activity-related pain, swelling, and impaired mobility. Regeneration and restoration of the joint tissue functionality remain unmet challenges. Stem cell-based tissue engineering is a promising paradigm to treat cartilage degeneration. In this context, hydrogels have emerged as promising biomaterials, due to their biocompatibility, ability to mimic the tissue extracellular matrix and excellent permeability. Different stimulation strategies have been investigated to guarantee proper conditions for mesenchymal stem cell differentiation into chondrocytes, including growth factors, cell-cell interactions, and biomaterials. An interesting tool to facilitate chondrogenesis is external ultrasound stimulation. In particular, low-intensity pulsed ultrasound (LIPUS) has been demonstrated to have a role in regulating the differentiation of adipose mesenchymal stromal cells (ASCs). However, chondrogenic differentiation of ASCs has been never associated to a precisely measured ultrasound dose. In this study, we aimed to investigate whether dose-controlled LIPUS is able to influence chondrogenic differentiation of ASCs embedded in a 3D hydrogel.

Materials and Methods

Human adipose mesenchymal stromal cells at 2×10^6 cells/mL were embedded in a hydrogel ratio 1:2 (VitroGel RGD®) and exposed to LIPUS stimulation (frequency: 1 MHz, intensity: 250 mW/cm², duty cycle: 20%, pulse repetition frequency: 1 kHz, stimulation time: 5 min) in order to assess its influence on cell differentiation. Hydrogel-loaded ASCs were cultured and differentiated for 2, 7, 10 and 28 days. At each time point cell viability (Live&Dead), metabolic activity (Alamar Blue), cytotoxicity (LDH), gene expression (COL2, aggrecan, SOX9, and COL1), histology and immunohistochemistry (COL2, aggrecan, SOX9, and COL1) were evaluated respect to a non-stimulated control.

Results

Histological analysis evidenced a uniform distribution of ASCs both at the periphery and at the center of the hydrogel. Live & Dead test evidenced that the encapsulated ASCs were viable, with no signs of cytotoxicity. We found that LIPUS induced chondrogenesis of ASCs embedded in the hydrogel, as demonstrated by increased expression of COL2, aggrecan and SOX9 genes and proteins, and decreased expression of COL1 respect to the non-stimulated control.

Conclusions

These results suggest that the LIPUS treatment could be a valuable tool in cartilage tissue engineering, to push the differentiation of ASCs encapsulated in a 3D hydrogel.

OC23 SHOULDER ARTHROPLASTY

K23

SHOULDER PATHOLOGY: FROM ROTATOR CUFF TEARS TO SHOULDER OSTEOARTHRITIS

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The function of the upper extremity is highly dependent on correlated motion of the shoulder. The shoulder can be affected by several diseases. The most common are: rotator cuff tear (RCT), shoulder instability, shoulder osteoarthritis and fractures. Rotator cuff disease is a common disorder. It has a high prevalence rate, causing high direct and indirect costs. The appropriate treatment for RCT is debated. The American Academy Orthopaedic Surgeons guidelines state that surgical repair is an option for patients with chronic, symptomatic full-thickness RCT, but the quality of evidence is unconvincing. Thus, the AAOS recommendations are inconclusive. We are performing a randomized controlled trial to compare surgical and conservative treatment of RCT, in term of functional outcomes, rotator cuff integrity, muscle atrophy and fatty degeneration. Shoulder instability occurs when the head of the upper arm bone is forced out of the shoulder socket. Shoulder instabilities have been classified according to the etiology, the direction of instability, or on combinations thereof. The Thomas and Matsen classification, which is currently the most commonly utilized classification, divides shoulder instability events into the traumatic, unidirectional, Bankart lesion, and surgery (TUBS) and the atraumatic, multidirectional, bilateral, rehabilitation, and capsular shift (AMBRI) categories. The acquired instability overstress surgery (AIOS) category was then added. Surgical procedures for shoulder instability includes arthroscopic capsuloplasty, remplissage, bone block procedure or Latarjet procedure. Reverse total shoulder arthroplasty (RTSA) represents a good solution for the management of patients with osteoarthritis or fracture of the proximal humerus, with associated severe osteoporosis and RC dysfunction.

OC23.1

ENDOPROTHESIS LENGTH AFFECTS STRESS SHIELDING IN PROXIMAL HUMERAL REPLACEMENT FOR TUMOUR EXCISION

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Introduction and Objective

Curative resection of proximal humerus tumours is now possible in this era of limb salvage with endoprosthetic replacement considered as the preferred reconstructive option. However, it has also been linked with mechanical and non-mechanical failures such as stem fracture and aseptic loosening. One of the challenges is to ensure that implants will endure the mechanical strain under physiological loading conditions, especially crucial in long surviving patients. The objective is to investigate the effect of varying prosthesis length on the bone and implant stresses in a reconstructed humerus-prosthesis assembly after tumour resection using finite element (FE) modelling.

Methods

Computed tomography (CT) scans of 10 humeri were processed in Mimics 17 to create three-dimensional (3D) cortical and cancellous solid bone models. Endoprostheses of different lengths manufactured by Stryker were modelled using Solidworks 2020. The FE models were divided into four groups namely group A consisting of the intact humerus and groups B, C and D composed of humerus-prosthesis assemblies with a body length of 40, 100 and 120 mm respectively and were meshed using linear 4-noded tetrahedral elements in 3matic 13. The models were then imported into Abaqus CAE 6.14. Isotropic linear elastic behaviour with an elastic modulus of 13400, 2000 and 208 000 MPa were assigned to the cortical bone, cancellous bone and prosthesis respectively and a Poisson's ratio of 0.3 was assumed for each material. To represent the lifting of heavy objects and twisting motion, a tensile load of 200 N for axial loading and a 5 Nm torsional load for torsional loading was applied separately to the elbow joint surface with the glenohumeral joint fixed and with all contact interfaces defined as fully bonded. A comparative analysis against literature was performed to validate the intact model. Statistical analysis of the peak von Mises stress values collected from predicted stress contour plots was performed using a one-way repeated measure of analysis of variance (with a Bonferroni post hoc test) using SPSS Statistics 26. The average change in stress of the resected models from the intact state were then determined.

Results

The validation of the intact humerus displayed a good agreement with literature values. The peak bone stress occurred distally above the coronoid and olecranon fossa closer to the load application region in the intact and resected bone models with a significant amount of loading borne by the cortical bone, while the peak implant stress occurred at the bone-prosthesis contact interface under both loading conditions. Based on the results obtained, a statistically significant difference ($p = .013$) in implant stress was only seen to occur between groups B and C under tension. Results illustrate initiation of stress shielding with the bone bearing lesser stress with increasing resection length which may eventually lead to implant failure by causing bone resorption according to Wolff's law. The peak implant stress under torsion was 3-5 times the stress under tension. The best biomechanical behaviour was exhibited in Group D, having the least average change in stress from the intact model, 5% and 3.8% under tension and torsion respectively. It can be deduced that the shorter the prosthesis length, the more pronounced the effect on cortical bone remodelling. With the maximum bone and implant stresses obtained being less than their yield strength, it can be concluded that the bone-implant construct is safe from failure.

Conclusions

The developed FE models verified the influence of varying the prosthesis length on the bone and implant stresses and predicted signs of stress shielding in longer endoprostheses. By allowing for 2 cm shortening in the upper extremity and post-surgical scarring, it is beneficial to err towards a shorter endoprosthesis.

OC23.2

PRE-OPERATIVE CT-BASED PLANNING INTEGRATED WITH INTRA-OPERATIVE NAVIGATION IN REVERSE SHOULDER ARTHROPLASTY: DATA ACQUISITION AND ANALYSIS PROTOCOL, AND MID-TERM RESULTS OF NAVIGATED VS CONVENTIONAL SURGERY

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Introduction and Objective

The aim of this study was to evaluate whether CT-based pre-operative planning, integrated with intra-operative navigation could improve glenoid baseplate fixation and positioning by increasing screw length, reducing number of screws required to obtain fixation and increasing the use of augmented baseplate to gain the desired positioning. Reverse total shoulder arthroplasty (RSA) successfully restores shoulder function in different conditions. Glenoid baseplate fixation and positioning seem to be the most important factors influencing RSA survival. When scapular anatomy is distorted (primitive or secondary), optimal baseplate positioning and secure screw purchase can be challenging.

Materials and Methods

Twenty patients who underwent navigated RSA (oct 2018 and feb 2019) were compared retrospectively with twenty patients operated on with a conventional technique. All the procedures were performed by the same surgeon, using the same implant in cases of eccentric osteoarthritis or complete cuff tear. Exclusion criteria were: other diagnosis as proximal humeral fractures, post-traumatic OA previously treated operatively with hardware retention, revision shoulder arthroplasty.

Results

The NAV procedure required mean 11 (range 7-16) minutes more to performed than the conventional procedure. Mean screw length was significantly longer in the navigation group (35.5+4.4 mm vs 29.9+3.6 mm; p . .001). Significant higher rate of optimal fixation using 2 screws only (17 vs 3 cases, p . .019) and higher rate of augmented baseplate usage (13 vs 4 cases, p . .009) was also present in the navigation group. Significant difference there is all in function outcomes, DASH score is 15.7 vs 29.4 and constant scale 78.1 vs 69.8.

Conclusions

The glenoid component positioning in RSA is crucial to prevent failure, loosening and biomechanical mismatch, coverage by the baseplate of the glenoid surface, version, inclination and offset are all essential for implant survival. This study showed how useful 3D CT-based planning helps in identifying the best position of the metaglena and the usefulness of receiving directly in the operation theater real-time feedback on the change in position. This study shows promising results, suggesting that improved baseplate and screw positioning and fixation is possible when computer-assisted implantation is used in RSA comparing to a conventional procedure.

OC23.3

PERIPROSTHETIC INTRAARTICULAR CORTICOSTEROID INJECTION FOLLOWING TOTAL SHOULDER ARTHROPLASTY: IS IT EFFECTIVE AND SAFE?

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Introduction and Objective

Total shoulder replacement is a common elective procedure offered to patients with end stage arthritis. While most patients experience significant pain relief and improved function within months of surgery, some remain unsatisfied because of residual pain or dissatisfaction with their functional status. Among these patients, when laboratory workup eliminates infection as a possibility, corticosteroid injection (CSI) into the joint space, or on the periprosthetic anatomic structures, is a common procedure used for symptom management. However, the efficacy and safety of this procedure has not been previously reported in shoulder literature.

Materials and Methods

A retrospective chart review identified primary TSA patients who subsequently received a CSI into a replaced shoulder from 2011 - 2018 by multiple surgeons. Patients receiving an injection underwent clinical exam, laboratory analysis to rule out infection, and radiographic evaluation prior to CSI. Demographic variables were recorded, and a patient satisfaction survey assessed the efficacy of the injection.

Results

Of the 43 responders, 48.8% remembered the injection. The average time from index arthroplasty to injection was median 16.8 months. Overall, 61.9% reported decreased pain, 28.6% reported increased motion, and 28.6% reported long term decreased swelling. Improvement lasted greater than one month for 42.9% of patients, and overall 52.4% reported improvement (slight to great) in the shoulder following CSI. No patient developed a periprosthetic joint infection (PJI) within 2 years of injection.

Conclusions

This study suggests that certain patients following TSA may benefit from a CSI. However, this should only be performed once clinical, radiographic, and laboratory examination has ruled out conditions unlikely to improve long term from a CSI. Given these findings, further study in a large, prospective trial is warranted to fully evaluate the benefits of CSI following TSA.

OC23.4

ACUTE PAIN MANAGEMENT FOLLOWING ELECTIVE ORTHOPAEDIC SHOULDER SURGERY

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Introduction and Objective

Postoperative pain control in shoulder surgery is challenging even in arthroscopic procedures. Acute postoperative pain can last up to 48hrs despite using multimodal analgesia. Different techniques have been used to control acute pain following shoulder surgery. The most common technique currently used in shoulder surgery at the elective orthopaedic centre in Leeds is a combination of general anaesthetic (GA) and interscalene block (ISB). ISB maybe very effective, however, carries many risks and potential side effects such as brachial plexus injury and paralysis of the vagus and laryngeal recurrent nerves as well as cervical sympathetic nerve and pneumothorax. ISB can also be associated with higher incidence of neurological deficit compared to other peripheral nerve blocks; up to 14% at 10 days in some cases. As such we decided to examine the use of ISB for achieving pain control in our elective unit.

Materials and Methods

A prospective consecutive series of 217 patients undergoing shoulder surgery were studied. These were grouped into 10 groups (table 1). All procedures were arthroscopic apart from shoulder arthroplasty procedures such as hemiarthroplasty and total shoulder replacements (TSRs). The choice of regional anaesthesia was ISB with GA as standard practice. Visual analogue scores (VAS) at 0hrs, 1hr, 2hrs, 4hrs and 6hrs; and total opiates intake were recorded. A one-way single factor ANOVA was used as preferred statistical analytical method to determine whether there is a difference in VAS scores and total opiates intake amongst the groups. Postoperative analgesics were used for pain relief, although these were not standardised.

Table 1: groups of patients according to surgical technique.

Surgical procedure	Number of patients (n)
SAD	30
RSR	20
ASR	10
Hemi	23
Cuff Repair	30
Frozen Shoulder	21
A. stabilisation	23
ACJ fixation	29
D. clavicle excision	19
...	...

Results

In total shoulder replacement group, although the RSR group used more morphine on average compared to the ASR group (Mean morphine intake 6.5mg vs 3mg), this was not statistically significant ($F < F_{crit}$; p value= 0.19). When comparing all the arthroplasty groups, the difference in mean morphine intake was also statistically not significant ($F < F_{crit}$; p value=0.24). However, when comparing all 10 groups' morphine intake there was a statistically significant difference amongst these groups ($F > F_{crit}$; p value=0.03). Interestingly,

there was a statistically significant difference in VAS at 0hrs ($F > F_{crit}$ p value=0.01); 1hrs ($F > F_{crit}$; p value=0.00), and at 6hrs ($F > F_{crit}$; p value=0.02) when comparing all 10 groups.

Conclusions

ISB is an effective technique in achieving pain control in shoulder surgery; however, there are still variations in analgesic needs amongst groups and the use of alternative techniques should be thus explored. A future prospective study looking at acute pain for a longer period of time after shoulder surgery would explore the effectiveness of ISB in achieving pain control consistent with rehabilitation requirements.

OC24 SPINE

K24

AO SPINE GUIDELINE FOR USING OSTEObIOLoGICS IN SPINE DEGENERATION (AO-GO) - Chapter I ACDF

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AO Spine Guideline for Using Osteobiologics in Spine Degeneration project is an international collaborative initiative to identify and evaluate evidence on existing use of osteobiologics in spine degenerative diseases. It aims to formulate clinically relevant and internationally applicable guidelines ensuring evidence-based, safe and effective use of osteobiologics. The current focus is the use of osteobiologics in anterior cervical discectomy and fusion surgeries.

The guideline development is planned in three phases. Phase 1- Evidence synthesis and Recommendation; Phase 2- Guideline with osteobiologics grading and Validation; Phase 3- Guideline dissemination and Development of a clinical decision support tool. The key questions formulating the guidelines for the use of osteobiologics will be addressed in a series of systematic reviews in Phase 1. The evidence synthesized by the systematic reviews will be assessed by Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology, including expert panel discussions to formulate a recommendation. In Phase 2, osteobiologics will be graded based on evidence and the grading will be integrated with the recommendation from Phase 1, and thus formulate a guideline. The guideline will be further validated by prospective clinical studies. In the third phase, dissemination of the proposed guideline and development of a decision support tool is planned.

AO-GO aims to bridge an important gap between quality of evidence and use of osteobiologics in spine fusion surgeries. With a holistic approach the guideline aims to facilitate evidence-based, patient-oriented decision-making process in clinical practice, thus stimulating further evidence-based studies regarding osteobiologics usage in spine surgeries.

OC24.1

SPINAL DEFORMITIES IN PATIENTS WITH PECTUS CARINATUM

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Introduction and Objective

Pectus carinatum is a common congenital anterior chest wall deformity, characterized by outward protrusion of sternum and ribcage resulted from rib cartilage overgrowth. The protrusion may be symmetrical or asymmetrical. Pectus carinatum association with mitral valve diseases, Marfan's syndrome, and scoliosis enforces that poor connective tissue development as possible etiological factor. Despite the coexistence of pectus carinatum and scoliosis has attracted the attention of some researchers, the association between pectus carinatum and the other spinal deformities has not been studied comprehensively. The frequency of spinal deformity in patients with pectus carinatum and the mutual relationships of their subtypes are needed to be studied to determine the epidemiological character of the combined deformity and to plan patient evaluation and management. Our study aimed to investigate the association, define the incidence and evaluate the characteristics between different types of spinal deformities and Pectus carinatum.

Materials and Methods

Radiological and physical examinations were performed for 117 pectus carinatum patients in Marmara university hospital/Turkey in the years between 2006 and 2013. The incidence of spinal deformity was calculated. Spinal deformities were classified as scoliosis, kyphosis, kyphoscoliosis, and spinal asymmetry, whereas pectus carinatum were subdivided into symmetric and asymmetric subgroups. The relationship between spinal deformities and the symmetrical-asymmetric subtype of pectus excavatum was statistically analyzed, Pearson chi-square test was used to compare the association of qualitative data. The significance level was accepted as $p < 0.05$. Lastly, the angular values of the deformities of scoliosis and kyphosis patients were measured using the Cobb method. In this way, the magnitude of the deformity was given as a numerical value.

Results

Spinal deformity was detected in 23 (17 symmetrical PE and 6 asymmetrical PE) of 117 pectus excavatum patients. Scoliosis and kyphosis were seen equally in symmetrical pectus carinatum, whereas scoliosis was seen in 33.3% and kyphosis in 50% in asymmetrical pectus carinatum patients, respectively. However, there were no statistically significant differences in the distribution of scoliosis and kyphosis in patients with symmetrical and asymmetrical PE. Idiopathic scoliosis constituted the most common scoliosis group. Congenital kyphosis was not found in any kyphosis patient. The average Cobb angle of scoliosis patients was 32°, and the mean T2-T12 kyphosis angle of these patients was 55.5°, while the average kyphosis angle of those with kyphosis deformity was 71°.

Conclusions

Patients with Pectus carinatum have a higher incidence of spinal deformities than the normal population. Such high concomitant incidence should be taken under consideration in evaluating and treating patients presenting with either deformity.

OC24.2

EFFICACY OF PERIOPERATIVE HALO-GRAVITY TRACTION IN THE TREATMENT OF SEVERE SPINAL DEFORMITY IN CHILDREN

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Introduction and Objective

The treatment of severe deformities often requiring aggressive techniques such as vertebral resection and osteotomies with high comorbidity. To mitigate this risk, several methods have been used to achieve a partial reduction of stiff curves. The objective of this study was to evaluate and quantify the effectiveness of the Perioperative Halo-Gravity Traction (HGT) in the Treatment of Severe Spinal Deformity in Children.

Materials and Methods

A historical cohort of consecutive children with severe spinal deformity who underwent to a perioperative HGT as a part of the treatment protocol. Minimum follow-up of 2 years. Demographic, clinical and radiological data, including time duration of perioperative HGT and Cobb angle in the coronal and sagittal plane. The radiological variables were measured before the placement of the halo, after placement of the halo, at the end of the period of traction, after surgery and in the final follow-up.

Results

Seventeen males (57%) and twenty females (43%) were included in the final analysis. The mean age was 6.5 years (SD 4.8). The most frequent etiology for the spinal deformity was syndromic (13 patients). The average preoperative Cobb angle was 88° (range, 12-135). HGT was used in 17 cases prior to a primary surgery and in 20 cases prior to a revision surgery. After the HGT, an average correction of 34% of the deformity was achieved ($p < 0.05$). After the surgery this correction improved. At 2-year follow-up there was a correction loss of 20% ($p < 0.05$). There were 3 complications (8.1%): 2 pin infections and cervical subluxation.

Conclusions

The application of HGT in cases of severe rigid deformity is useful allowing a correction of the preoperative deformity of 34%, facilitating surgery. Preoperative HGT seems to be a safe and effective intervention in pediatric patients with high degree deformity.

OC24.3

ARTIFICIAL INTELLIGENCE ACCURATELY DETECTS TRAUMATIC THORACOLUMBAR FRACTURES ON SAGITTAL RADIOGRAPHS

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Introduction and Objective

Up to 30% of thoracolumbar (TL) fractures are missed in the emergency room. Failure to identify these fractures can result in neurological injuries up to 51% of the cases. This article aimed to clarify the incidence and risk factors of traumatic fractures in China. The China National Fracture Study (CNFS). Obtaining sagittal and anteroposterior radiographs of the TL spine are the first diagnostic step when suspecting a traumatic injury. In most cases, CT and/or MRI are needed to confirm the diagnosis. These are time and resource consuming. Thus, reliably detecting vertebral fractures in simple radiographic projections would have a significant impact. We aim to develop and validate a deep learning tool capable of detecting TL fractures on lateral radiographs of the spine. The clinical implementation of this tool is anticipated to reduce the rate of missed vertebral fractures in emergency rooms.

Materials and Methods

We collected sagittal radiographs, CT and MRI scans of the TL spine of 362 patients exhibiting traumatic vertebral fractures. Cases were excluded when CT and/or MRI were not available. The reference standard was set by an expert group of three spine surgeons who conjointly annotated (fracture/no-fracture and AO Classification) the sagittal radiographs of 171 cases. CT and/or MRI were used to confirm the presence and type of the fracture in all cases. 302 cropped vertebral images were labelled "fracture" and 328 "no fracture". After augmentation, this dataset was then used to train, validate, and test deep learning classifiers based on the ResNet18 and VGG16 architectures. To ensure that the model's prediction was based on the correct identification of the fracture zone, an Activation Map analysis was conducted.

Results

Vertebrae T12 to L2 were the most frequently involved, accounting for 48% of the fractures. Accuracies of 88% and 84% were obtained with ResNet18 and VGG16 respectively. The sensitivity was 89% with both architectures but ResNet18 had a significantly higher specificity (88%) compared to VGG16 (79%). The fracture zone used was precisely identified in 81% of the heatmaps.

Conclusions

Our AI model can accurately identify anomalies suggestive of TL vertebral fractures in sagittal radiographs precisely identifying the fracture zone within the vertebral body.

OC24.4

SUCCESSFUL SALVAGE ANTERIOR RETROPERITONEAL APPROACH IN REVISION SURGERY FOR FAILED TRANSFORAMINAL OR POSTERIOR INTERBODY FUSION (TLIF-PLIF). TECHNICAL CONSIDERATION ON CONSECUTIVE 32 CASES

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Introduction and Objective

Posterior and transforaminal lumbar interbody fusion (PLIF, TLIF) represent the most popular techniques in performing an interbody fusion amongst spine surgeons. Pseudarthrosis, cage migration, subsidence or infection can occur, with subsequent failed surgery, persistent pain and patient's bad quality of life. The goal of revision fusion surgery is to correct any previous technical errors avoiding surgical complications. The most safe and effective way is to choose a naive approach to the disc. Therefore, the anterior approach represents a suitable technique as a salvage operation. The aim of this study is to underline the technical advantages of the anterior retroperitoneal approach as a salvage procedure in failed PLIF/TLIF analyzing a series of 32 consecutive patients.

Materials and Methods

We performed a retrospective analysis of patients' data in patients who underwent ALIF as a salvage procedure after failed PLIF/TLIF between April 2014 to December 2019. We recorded all peri-operative data. In all patients the index level was exposed with a minimally invasive anterior retroperitoneal approach.

Results

Thirty-two patients (average age: 46.4 years, median age 46.5, ranging from 21 to 74 years old- 16 male and 16 female) underwent salvage ALIF procedure after failed PLIF/TLIF were included in the study. A minimally invasive anterior retroperitoneal approach to the lumbar spine was performed in all patients. In 6 cases (18.7%) (2 infection and 4 pseudarthrosis after stand-alone IF) only anterior revision surgery was performed. A posterior approach was necessary in 26 cases (81.3%). In most of cases (26/32, 81%) the posterior instrumentation was overpowered by the anterior cage without a previous revision. Three (9%) intraoperative minor complications after anterior approach were recorded: 1 dural tear, 1 ALIF cage subsidence and 1 small peritoneal tear. None vascular injuries occurred. Most of patients (90.6%) experienced an improvement of their clinical condition and at the last follow-up no mechanical complication occurred.

Conclusions

According to our results, we can suggest that a favourable clinical outcome can firstly depend from technical reasons and then from radiological results. The removal of the mobilized cage, the accurate endplate and disc space preparation and the cage implant eliminate the primary source of pain reducing significantly the axial pain, helping to realise an optimal bony surface for fusion and enhancing primary stability. The powerful disc distraction given by the anterior approach allows inserting large and lordotic cages improving the optimal segmental lordosis restoration.

OC25 ROBOTICS, NAVIGATION AND VIRTUAL REALITY

OC25.1

NO DIFFERENCE OF GAIT PARAMETERS IN PATIENTS WITH IMAGE-FREE ROBOTIC-ASSISTED MEDIAL UNICOMPARTMENTAL KNEE ARTHROPLASTY COMPARED TO A CONVENTIONAL TECHNIQUE: A RANDOMIZED CONTROLLED TRIAL

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Introduction and Objective

In recent studies, robotic-assisted surgical techniques for unicompartmental knee arthroplasty (UKA) have demonstrated superior implant positioning and limb alignment compared to a conventional technique. However, the impact of the robotic-assisted technique on clinical and functional outcomes is less clear. The aim of this study was to compare the gait parameters of UKA performed with conventional and image-free robotic-assisted techniques.

Materials and Methods

This prospective, single center study included 66 medial UKA, randomized to a robotic-assisted (n=33) or conventional technique (n=33). Gait analysis was performed on a treadmill at 6 months to identify changes in gait characteristics (walking speed, each degree-of-freedom: flexion–extension, abduction–adduction, internal-external rotation and anterior-posterior displacement). Clinical results were assessed at 6 months using the IKS score and the Forgotten Joint Score. Implants position was assessed on post-operative radiographs.

Results

Post-operatively, the whole gait cycle was not significantly different between groups. In both groups there was a significant improvement in varus deformity between the pre- and post-operative gait cycle. There was no significant difference between the two groups in clinical scores, implant position, revision and complication rates.

Conclusions

No difference of gait parameters could be identified between medial UKA performed with image-free robotic-assisted technique or with conventional technique.

OC25.2

VIRTUAL SURGICAL PLANNING FOR CORRECTING COMPLEX DEFORMITIES OF LONG BONES IN CHILDREN

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Introduction and Objective

Virtual Surgical Planning (VSP) is becoming an increasingly important means of improving skills acquisition, optimizing clinical outcomes, and promoting patient safety in orthopedics and traumatology. Pediatric Orthopedics (PO) often deals with the surgical treatment of congenital or acquired limbs and spine deformities during infancy. The objective is to restore function, improve aesthetics, and ensure proper residual growth of limbs and spine, using osteotomies, bone grafts, age-specific or custom-made hardware and implants.

Materials and Methods

Three-dimensional (3D) digital models were generated from Computed Tomography (CT) scans, using free open-source software, and the surgery was planned and simulated starting from the 3D digital model. 3D printed sterilizable models were fabricated using a low-cost 3D printer, and animations of the operation were generated with the aim to accurately explain the operation to parents. All procedures were successfully planned using our VSP method and the 3D printed models were used during the operation, improving the understanding of the severely abnormal bony anatomy.

Results

The surgery was precisely reproduced according to VSP and the deformities were successfully corrected in eight cases (3 genu varum in Blount disease, 2 coxa vara in pseudo achondroplasia, 1 SCFE, 1 missed Monteggia lesion and 1 post-traumatic forearm malunion deformity). In one case, a focal fibrocartilaginous dysplasia, the intraoperative intentional undersizing of the bone osteotomy produced an incomplete correction of a congenital forearm deformity.

Conclusions

Our study describes the application of a safe, effective, user-friendly, VSP process in PO surgery. We are convinced that our study will stimulate the widespread adoption of this technological innovation in routine clinical practice for the treatment of rare congenital and post-traumatic limb deformities during childhood.

OC25.3

CAN ROBOT-ASSISTED TOTAL KNEE ARTHROPLASTY BE A COST-EFFECTIVE PROCEDURE? A MARKOV-DECISION ANALYSIS

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Introduction and Objective

Total knee arthroplasty (TKA) is a frequently and increasingly performed surgery in the treatment of disabling knee osteoarthritis. The rising number of procedures and related revisions pose an increasing economic burden on health care systems. In an attempt to lower the revision rate due to component malalignment and soft tissue imbalance in TKA, robotic assistance (RA) has been introduced in the operating theatre. The primary objective of this study is to provide the results of a theoretical, preliminary cost-effectiveness analysis of RA TKA.

Materials and Methods

A Markov state-transition model was designed to model the health status of sixty-seven-year-old patients in need of TKA due to primary osteoarthritis over a twenty-year period following their knee joint replacement. Transitional probabilities and independent variables were extracted from existing literature. Patients' state in the transition model was able to change on an annual basis. The main differences between the conventional and RA TKA were the outlier rate in the coronal plane and the cost of the procedure. In RA TKA, it was hypothesized that there were lower revision rates due to a lower outlier rate compared to conventional TKA.

Results

The value attributed to the utility both for primary and revision surgery has the biggest impact on the ICER, followed by the rate of successful primary surgery and the cost of RA-technology. Only 2.18-2.34% of the samples yielded from the probabilistic sensitivity analysis proved to be cost-effective (threshold set at \$50000/QALY). A calculated surgical volume of at least 191-253 cases per robot per year is needed to prove cost-effective taking the predetermined parameter values into account.

Conclusions

Robot-assisted TKA might be a cost-effective procedure compared to conventional TKA if a minimum of 191 cases are performed on a yearly basis, depending on the cost of the robot. The cost-benefit of the robotic TKA surgery is mainly based on a decreased revision rate. This study is based on the assumption that alignment is a predictor of success in total knee arthroplasty. Until there is data confirming the assertion that alignment predicts success robot-assisted surgery cannot be recommended.

OC25.4

INNOVATIVE EDUCATIONAL PATHWAYS IN SPINE SURGERY: ADVANCED VIRTUAL REALITY-BASED TRAINING

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Introduction and Objective

Over the past few years, a reorganization of the educational pathways has been promoted with the purpose of optimizing the acquisition of competences and their assessment, so as to reduce the risks to both health care professionals and end users. Virtual reality (VR) has been repeatedly tested, initially as a positive reinforcement for more traditional educational pathways and, more recently, as their potential substitute. The aim of this study was to demonstrate the potentiality of VR simulation training in spine surgery.

Materials and Methods

The VR simulator reproduced the lateral lumbar access to the spine. The simulation included a tutorial, the preoperative settings, and the surgical session with different levels of procedural complexity. A total of 10 users were recruited for this study: 3 senior surgeons (group A) and 7 orthopedic residents or junior orthopedic surgeons (group B). Each user completed the simulation twice.

Results

The user's age or previous experience with VR technology did not show any relevance. On average, the entire simulation was completed in 24 minutes and 36 seconds. Group B showed an improvement between the 2 attempts in both sessions, the preoperative settings and the surgical simulation. The number of major errors dropped from an average of 5.2 to 1.8 and from an average of 4 (1-6) to 1.4, respectively. The simulation was never interrupted because of technical bugs or adverse effects related to the technology.

Conclusions

VR-based training pathways might promote a high standard of care. Our preliminary experience suggests an effective implementation of the traditional coaching process.

OC26 REGENERATIVE ORTHOPAEDIC

K26

REGENERATIVE MEDICINE FOR OSTEOARTHRITIS

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Osteoarthritis (OA) is the most common type of arthritis and causes a significant deterioration in patients' quality of life. The high prevalence of OA as well as the current lack of disease-modifying drugs led to a rise in regenerative medicine efforts. The hope is that this will provide a treatment modality with the ability to alter the course of OA via structural modifications of damaged articular cartilage (AC). Regenerative therapy in OA starts with the concept that administered cells may engraft to a lesion site and differentiate into chondrocytes. However, recent studies show that cells, particularly when injected in suspension, rapidly undergo apoptosis after exerting a transient paracrine effect. If the injected stem cells do not lead to structural improvements of a diseased joint, the high cost of cell therapy for OA cannot be justified, particularly when compared with other injection therapeutics such as corticosteroids and hyaluronic acid. Long-term survival of implanted cells that offer prolonged paracrine effects or possible engraftment is essential for a successful cell therapy that will offer durable structural improvements. In this talk, the history and current status of regenerative therapy in OA are summarized along with the conceptual strategy and future directions for a successful regenerative therapy that can provide structural modifications in OA.

OC26.1

MANAGEMENT OF GAP NON-UNION TIBIA OF MORE THAN 6 CM WITH 3 RING ILIZAROV FIXATOR FRAME

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Introduction and Objective

Management of gap non-union of the tibia, the major weight bearing bone of the leg remains controversial. The different internal fixation techniques are often weighed down by relatively high complication rates that include fractures which fail to heal (non-union). Minimally invasive techniques with ring fixators and bone transport (distraction osteogenesis) have come into picture as an alternative allowing alignment and stabilization, avoiding a graduated approach. This study was focused on fractures that result in a gap non-union of > 6 cm. Ilizarov technique was employed for management of such non-unions in this case series. The Ilizarov apparatus consists of rings, rods and kirschner wires that encloses the limb as a cylinder and uses kirschner wires to create tension allowing early weight bearing and stimulating bone growth. Ilizarov technique works on the principle of distraction osteogenesis, that is, pulling apart of bone to stimulate new bone growth. Usually, 4-5 rings are used in the setup depending on fracture site and pattern for stable fixation. In this study, we demonstrate effective bone transport and formation of gap non-union more than 6 cm in 10 patients using only 3 rings construct Ilizarov apparatus.

Materials and Methods

This case study was conducted at Dr. D. Y. Patil Medical Hospital, Navi Mumbai, Maharashtra, India. The study involved 10 patients with a non-union or gap > 6 cm after tibial fracture. 3 rings were used in the setup for the treatment of all the patients. Wires were passed percutaneously through the bone using a drill and the projecting ends of the wires were attached to the metal rings and tensioned to increase stability. The outcome of the study was measured using the Oxford Knee scoring system, Functional Mobility Scale, the American Foot and Ankle Score and Visual Analog Scale. Further, follow up of patients was done upto 2 years.

Results

All the patients demonstrated good fixation as was assessed clinically and radiologically. 9 patients had a clinical score of > 65 which implied fair to excellent clinical rating. The patients showed good range of motion and were highly satisfied with the treatment as measured by different scoring parameters.

Conclusions

In this case study, we demonstrate that the Ilizarov technique using 3 rings is equally effective in treating non-unions > 6 cm as when using 4-5 rings. Obtaining good clinical outcome and low complication rate in all 10 patients shows that this modified technique can be employed for patients with such difficulties in the future.

OC26.2

EXOSOMES FROM MECHANICALLY STIMULATED MYOBLASTS PRODUCE DIFFERENTIAL MIRNA CARGO

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Introduction and Objective

Exosomal miRNA have been shown to regulate many myogenic and osteogenic pathways involved in injury repair and healing. It is also known that rehabilitation and exercise can improve muscle mass and bone growth. The mechanisms by which this occurs in vivo are well studied, but the impact exosomes and their associated miRNA cargo have is unclear. With this knowledge and question in mind, we hypothesized that C2C12 myoblasts subjected to in vitro mechanical stimulus ("exercise") would exhibit improved exosome production and differentially expressed miRNA cargo when compared to their static ("unexercised") counterparts.

Materials and Methods

C2C12 myoblasts were cultured using the FlexCell FX-5000TT bioreactor. Two exercise regimens were programmed: 1) low intensity regimen (LIR) (0-15% strain at 0.5 Hz for 24 hours) 2) high intensity interval regimen (HIIR) (12-22% strain at 1 Hz for 10 minutes followed by 50 minutes of rest repeated for 24 hours). Unexercised (static) cells were cultured in parallel. Exosomes were isolated using the Invitrogen Total Exosome Isolation Reagent. The Pierce BCA Protein Assay, System Bioscience's ExoELISA-ULTRA CD81 Kit and, SBI's ExoFlow-ONE EV labeling kit were used to confirm and quantify exosome number and protein concentration. The SBI Exo-NGS service was used to perform miRNA sequencing on isolated exosomes.

Results

All exercise regimens resulted in increased exosome concentrations as determined by CD81 exosome ELISA and flow-cytometry based exosome quantification. The LIR interestingly produced significantly more exosomes than static and HIIR. Within the exosomes from mechanically stimulated cells, 35 miRNAs were found to be differentially expressed when compared to exosomes from unexercised cells. Interestingly, this significance was only found within exosomes from the HIIR group. Specifically, upon investigation 8 of these miRNAs were found to be involved in myogenic and osteogenic proliferation and differentiation. These results correlate with our previous findings that exosomes from exercised cells improve the proliferation and myogenic differentiation of C2C12 myoblasts.

Conclusions

Our results indicate that exercise can be optimized to improve the production and regenerative capacity of exosomes. These results also indicate that exosomes may be intimately involved in systemic health and repair during rehabilitation and exercise. To examine these results in vivo, mouse studies using a crush injury model and exosomes from mechanically stimulated cells are currently planned.

OC26.3

NEW INNOVATIVE TECHNIQUE TO TREAT OSTEOARTHRITIS KNEE WITH CORE DECOMPRESSION AND BMAC WITH POLY ESTER UREA'S STRUCTURAL SCAFFOLD: A PROSPECTIVE CLINICAL STUDY

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Introduction and Objective

Osteoarthritis of the knee joint is common in old age population in every part of world. Pain is the major source of disability in patients with osteoarthritis of the knee joint. Subchondral bone marrow is richly innervated with nociceptive pain fibers and may be a source of pain in patients with symptomatic degenerative joint disease. Current therapy for managing bone marrow oedema is core decompression (CD), combining core decompression and injection of hydroxyapatite cement or autologus chondrocyte supplementtion. But all of this work has been done in femoral head and authors documented good result with minimal complication. There are various studies in literature suggesting treatment to repair BME by restoring support and relieving abnormal stresses with accepted internal fixation and bone stimulating surgical techniques in relieving knee OA pain. In this study, we present efficacy of knee arthroscopy with adjunctive core decompression and supplementation with structural scaffold to improve self-rated visual analog scale (VAS) pain scores, rate of conversion to arthroplasty, and patient satisfaction levels.

Materials and Methods

The study included patients aged between 40 and 75 years old, with pain in the knee for at least six months, associated with high-signal MRI lesion on T2 sequences, on the tibia or femur. Trephine was used as the bone decompression instrument. Trephine has a diameter of 8-10 mm and operation with trephine requires that a cortical incision window be made prior to decompression treatment, thus necessitating strict disinfection. This procedure was done under spinal anesthesia. After diagnostic arthroscopy, decompression was done under C –ARM in desired area on MRI. After decompression, defect was filled with Poly ester urea's scaffold impregnated with BMAC .

Results

Patients were assessed using the visual analog pain scale and the KOOS score, one week before surgery and one, three, six, 12, and 24 weeks after the procedure. MRI images were analyzed Lesions were mapped and measured in the axial, coronal, and sagittal views to plan the injection site and the trajectory of the cannula used for the procedure. Radiographs using anteroposterior, profile, and Rosenberg views of the knee and lower limb were performed to classify the lesion according to the Kellgren-Lawrence classification and to assess lower limb alignment. Evaluation using the KOOS showed a mean total score in the preoperative period of 38.44 points and of 60.7, 59.08, 56.92, 64.40, and 71.36 points at one, three, six, 12, and 24 weeks after surgery, respectively. In the VAS assessment, mean was 7.8 points preoperatively and 2.8, 2.6, 2.5, 1.3, and 0.5 points in the same periods.

Conclusions

Hence it can be Concluded that this new innovative technique has provided significant improvements in the parameters of pain and functional capacity in the short-term assessment.

OC26.4

MICROFRACTURES AND PRP VS MICROFRACTURES, PRP AND ADIPOSE-DERIVED STEM CELLS: ANALYSIS OF CLINICAL OUTCOMES WITH ARTHROSCOPIC SECOND LOOK AND HISTOLOGIC EXAMINATION

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Introduction and Objective

Platelet-Rich-plasma (PRP) has been used in combination with stem cells, from different sources, with encouraging results both in vitro and in vivo in osteochondral defects management. Adipose-derived Stem Cells (ADSCs) represents an ideal resource for their ease of isolation, abundance, proliferation and differentiation properties into different cell lineages. Furthermore, Stem Cells in the adipose tissue are more numerous than from other sources. Aim of this study was to evaluate the potential of ADSCs in enhancing the effect of arthroscopic mesenchymal stimulation combined with infiltration of PRP.

Materials and Methods

The study includes 82 patients. 41 patients were treated with knee arthroscopy, Steadman microfractures technique and intraoperative PRP infiltration, Group A. In the Group B, 41 patients were treated knee arthroscopy, Steadman microfractures and intraoperative infiltration of PRP and ADSCs (Group B). Group A was used as a control group. Inclusion criteria were: Age between 40 and 65 years, Outerbridge grade III-IV chondral lesions, Kellegren-Lawrence Grade I-II. Patient-reported outcome measures (PROMs) evaluated with KOOS, IKDC, VAS, SF-12 were assessed pre-operatively and at 3 weeks, 6 months, 1-year post-operative. 2 patients of Group A and 3 patients of Group B, with indication of Puddu plate removal after high tibial osteotomy (HTO), underwent an arthroscopic second look, after specific informed consent obtained. On this occasion, a bioptic sample was taken from the repair tissue of the chondral lesion previously treated with Steadman microfractures.

Results

PROMs showed statistically significant improvement ($p < 0.05$) with comparable results in both groups. The histological examination of the bioptic samples in Group B showed a repair tissue similar to hyaline cartilage, according to the International Cartilage Repair Society (ICRS) Visual Histological Assessment Scale. In Group A, the repair tissue was fibrocartilaginous

Conclusions

According to the PROMs and the histological results, showing repair tissue after Steadman microfractures qualitatively similar to hyaline cartilage, the combination of ADSCs and PRP could represent an excellent support to the arthroscopic treatment of focal chondral lesions and mild to moderate osteoarthritis.

OC27 TENDON BIOLOGY AND PATHOPHYSIOLOGY

K27

THE FUTURE OF ORTHOBIOLOGICS: FROM THE BENCH-SIDE TO THE BED-SIDE

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Geriatric syndromes could lead individuals to exhibit significant mobility and psychological deficits resulting in significant healthcare costs. Thus, identifying strategies to delay aging, or prevent progressive loss of tissue homeostasis could dramatically restore the function and independence of millions of elderly patients and significantly improve quality of life. One of the fundamental properties of aging is the accumulation of senescent cells and senescence associated secretory phenotypes (SASPs) that needs to be treated in wide range of therapeutics including orthobiologics. Senolytic compounds selectively target and kill senescent cells and inhibit anti-apoptotic pathways that are upregulated in senescent cells thereby inducing apoptotic cell death and abrogating systemic SASP factors. We have also shown that blocking fibrosis with Losartan (TGF- β 1 blocker) can improve musculoskeletal healing and cartilage repair by reducing the amount of fibrosis. Thus, we hypothesize that administration of anti-fibrotic agents will enhance the beneficial effects of orthobiologics. The safety and efficacy of several senolytic and anti-fibrotic agents to delay age-related dysfunction and improve the function of orthobiologics have been demonstrated in a variety of animal models (in vivo). Overall, our innovative approaches target senescent cells (inflammation) and TGF- β 1 (fibrosis) to enhance the clinical efficacy and use of orthobiologics for musculoskeletal repair. We will also discuss ongoing active clinical trials on orthobiologics to aiming at evaluating the safety and efficacy of senolytic agent (Fisetin) and anti-fibrotic agent (Losartan), used independently or in combination, to enhance the beneficial effects of orthobiologics for patients afflicted with musculoskeletal diseases and conditions.

OC27.1

PLATELET-RICH FIBRIN (PRF) ACCELERATES THE HEALING OF ACHILLES TENDON DEFECT BY PROMOTING THE PROLIFERATION AND ACTIVATION OF TENOCYTES VIA FGFR/AKT SIGNALING AND TGF-B/SMAD3 SIGNALING

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Introduction and Objective

Achilles tendon defect is difficult problem for orthopedic surgeon, and therefore the development of new treatments is desirable. Platelet-rich fibrin (PRF), dense fibrin scaffold composed of a fibrin matrix containing many growth factors, is recently used as regenerative medicine preparation. However, few data are available on the usefulness of PRF on Achilles tendon healing after injury. The objective of this study is to examine whether PRF promotes the healing of Achilles tendon defect in vivo and evaluated the effects of PRF on tenocytes in vitro.

Materials and Methods

PRF were prepared from rats according to international guidelines on the literature. To create rat model for Achilles tendon defect, a 4-mm portion of the right Achilles tendon was completely resected, and PRF was placed into the gap in PRF group before sewing the gap with nylon sutures. To assess the histological healing of Achilles tendon defect, Bonar score was calculated using HE, Alcian-blue, and Picosirius-red staining section. Basso, Beattie, Bresnahan (BBB) score was used for the evaluation of motor functional recovery. Biomechanical properties including failure tensile load, ultimate tensile stress, breaking elongation, and elastic modulus were measured. We examined the effects of PRF on tenocytes isolated from rat Achilles tendon in vitro. The number of viable cells were measured by MTS assay, and immunostaining of ki-67 was used for detection of proliferative cells. Migration of tenocytes was evaluated by wound closure assay. Protein or gene expression level of extracellular matrix protein, such as collagen, were evaluated by immunoblotting, immunofluorescence, or PCR. Phosphorylation level of AKT, FGF receptor, or SMAD3 was determined by western blotting. Inhibitory experiments were performed using MK-2206 (AKT inhibitor), FIIN-2 (FGFR inhibitor), SB-431542 (TGF-B receptor inhibitor), or SIS3 (SMAD3 inhibitor). All p values presented are two-sided and p values < 0.05 were considered statistically significant.

Results

In rat Achilles tendon defects, Bonar score was significantly improved in PRF group compared to control group. Collagen deposition at the site of Achilles tendon defect was observed earlier in PRF group. Consistent with the histological findings, BBB score was significantly improved in PRF group. PRF also significantly improved the biomechanical properties of injured Achilles tendon. Furthermore, proliferating tenocytes, labelled by ki-67 were significantly increased in PRF group. These data suggested PRF prompted the healing of Achilles tendon defect. Thus, we further examined the effects of PRF on tenocytes in vitro. PRF significantly increased the number of viable cells, the proliferative cells labelled by ki-67, and migratory ability. Furthermore, PRF significantly increased the protein expression levels of collagen-I, collagen-III, α -SMA, and tenascin-C in tenocytes. Next, we examined the signalling pathway associated with PRF-induced proliferation of tenocytes. PRF increased the phosphorylation level and induced nuclear translocation of AKT, known as key regulator of cell survival. PRF also induced the phosphorylation of FGF receptor. Inhibition of AKT or FGF-receptor completely suppressed the positive effects of PRF on tenocytes. Furthermore, we found that inhibition of FGF receptor partially suppressed the phosphorylation of AKT by PRF. Thus, PRF induced the proliferation of tenocytes via FGFR/AKT axis. We further evaluated the signalling pathway

associated with PRF-induced expression of extracellular matrix. PRF increased the phosphorylation levels of SMAD3 and induced nuclear translocation of SMAD3. Furthermore, inhibition of TGF- β receptor or SMAD3 suppressed increased expression level of extracellular matrix by PRF. Thus, PRF increased expression level of extracellular matrix protein via TGF- β R/SMAD3 axis

Conclusions

PRF promotes tendon healing of the Achilles tendon defect and recovery of exercise performance and biomechanical properties. PRF increases the proliferation ability or protein expression level of extracellular matrix protein in tenocytes via FGFR/AKT or TGF- β R/SMAD3 axis, respectively.

OC27.2

MOLECULAR AND HISTOLOGICAL CHANGES IN RAT ACHILLES TENDONS IN DEPENDENCE OF AGING AND GENETICALLY DETERMINED AEROBIC EXERCISE CAPACITY

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Introduction and Objective

Chronic tendinopathy is a multifactorial disease and a common problem in both, athletes and the general population. Mechanical overload and in addition old age, adiposity, and metabolic disorders are among the risk factors for chronic tendinopathy but their role in the pathogenesis is not yet unequivocally clarified.

Materials and Methods

Achilles tendons of young (10 weeks) and old (100 weeks) female rats bred for high (HCR) and low (LCR) intrinsic aerobic exercise capacity were investigated. Both Achilles tendons of 28 rats were included and groups were young HCR, young LCR, old HCR, and old LCR (n = 7 tendons per group/method). In this rat model, genetically determined aerobic exercise capacity is associated with a certain phenotype as LCR show higher body weight and metabolic dysfunctions in comparison to HCR. Quantitative real-time PCR (qPCR) was used to evaluate alterations in gene expression. For histological analysis, semi-automated image analysis and histological scoring were performed.

Results

Age-related downregulation of tenocyte marker genes (Tenomodulin), genes related to matrix modelling and remodeling (Collagen type 1, Collagen type 3, Elastin, Biglycan, Fibronectin, Tenascin C), and Transforming growth factor beta 3 (Tgfb3) were detected in tendons from HCR and LCR. Furthermore, inflammatory marker Cyclooxygenase 2 (Cox2) was downregulated, while Microsomal prostaglandin E synthase 2 (Ptges2) was upregulated in tendons from old HCR and old LCR. No significant alteration was seen in Interleukin 6 (Il6), Interleukin 1 beta (Il1b), and Tumor necrosis factor alpha (Tnfa). Histological analysis revealed that Achilles tendons of old rats had fewer and more elongated tenocyte nuclei compared to young rats, indicating a reduced metabolic activity. Even though higher content of glycosaminoglycans as a sign of degeneration was found in tendons of old HCR and LCR, no further signs of tendinopathy were detectable in histological evaluation.

Conclusions

Overall, aging seems to play a prominent role in molecular and structural alterations of Achilles tendon tissue, while low intrinsic exercise capacity did not cause any changes. Even though tendinopathy was not present in any of the groups, some of the shown age-related changes correspond to single characteristics of chronic tendon disease. This study gives an insight into tendon aging and its contribution to molecular and cellular changes in Achilles tendon tissue.

OC27.3

THE VACOMYCIN-WRAP HAS NO NEGATIVE EFFECT ON TENDONS AND TENOCYTES

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Introduction and Objective

The rupture of the anterior cruciate ligament is a common sports injury and surgical reconstruction is often required to restore full function of the knee. Hamstring tendons are usually used as autografts. In addition to knee pain and stiffness, infections are feared complications after surgery. Incubation of the autograft in a vancomycin solution until implantation reduced the infection rate by about ten-fold. Recent studies showed no negative effect of vancomycin on the biomechanical properties of porcine tendons. A negative effect of high vancomycin concentrations on chondrocytes and osteoblast is reported, but the effect on tendon and tenocytes is not known.

Materials and Methods

Rat Achilles tendons or isolated tenocytes were incubated with an increasing concentration of vancomycin (0 - 10 mg). Tendons were incubated for 0 - 40 minutes, while tenocytes were incubated for 20 minutes followed by culturing for up to 7 days. Cell viability was assessed with PrestoBlue Assay and live/dead stain. The potential effect of vancomycin on the expression of tendon specific genes and extracellular matrix (ECM) genes was quantified. Possible structural changes of the tendon are analyzed.

Results

Incubation of the tendons or tenocytes with 5 mg vancomycin for 20 minutes (clinical use) had no negative effects on the cell viability in the tendons or the isolated tenocytes, while incubation with the toxic control (ethanol) significantly reduced cell viability. Even twice the concentration and a longer incubation time had no negative effect on the cells in the tendons or the isolated cells. Vancomycin did not affect the expression of Col1a1, Col3a1, and the tenocyte markers mohawk, scleraxis and tenomodulin.

Conclusions

The results showed that clinical practice of wrapping the autograft in vancomycin did not impair the tenocyte viability. The expression of collagens and tenocyte markers was also not affected, neither in the incubated tendons nor in the isolated cells. This indicates that vancomycin had no effect on cell phenotype and the formation of the extracellular matrix, which, in addition to cell viability, is important for the performance of the autograft.

OC27.4

POLYCAPROLACTONE-BASED IMPLANTS FOR TENDON REPAIR PRODUCED BY ELECTROSPINNING

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Introduction and Objective

In the elderly population, chronic rotator cuff tears are often associated with high re-rupture rates after surgical tendon refixation. Implant materials, especially in combination with additives are supposed to positively influence healing outcome. Furthermore, adequate mechanical properties are crucial. In order to realize degradable implants with high specific surface area, polycaprolactone (PCL) was chosen as basic material and processed by electrospinning to achieve a high surface area for growth factor implementation and subsequent cell attachment.

Materials and Methods

PCL (M_n approx. 80,000 g/mol) was used to generate fibre mats by electrospinning (relative collector velocity 8 m/s; flow rate of 4 ml/h). Mechanical analysis was performed according to EN ISO 527-2:2012 with test specimen 1BA (5 mm in diameter). Maximum force at failure (F_{max}) as well as stiffness were evaluated. For preclinical in vivo testing, a coating with CS-g-PCL was performed to increase cellular adhesion and biological integration. Native and TGF- β 3 loaded mats were examined in a chronic rat tendon defect model with dissection of the M. infraspinatus, four week latency and following refixation at the humerus with different PCL-fibre mats (approval Nr. 33.12-42502-04-15/2015). After 8 weeks, rats were finalized and tendon-bone insertions were analyzed biomechanically and via histological methods.

Results

Electrospun PCL-fibre mats ($n = 6$) showed maximum forces of 2.19 ± 0.8 N and a stiffness of 0.38 ± 0.12 N/mm. Native rat infraspinatus tendons showed F_{max} values of 28.4 ± 7.2 N and a stiffness of 11.8 ± 4.9 N/mm. After implantation, F_{max} of the implant-tendon-regenerate was significantly lower in CS-g-PCL - fibre mat groups compared to native control tendons (mean 52 % of native tendon value). Functionalization with TGF- β 3 led to increased F_{max} (78 % of the native tendon value). However, differences were not statistically significant. Histological evaluation revealed no differences between non loaded and TGF- β 3 loaded mats. The implants were strongly disintegrated. Granulation tissue and a high number of foreign body giant cells were present.

Conclusions

Although mechanical properties of fabricated mats were low, loading of the fibre mats influenced the biomechanical outcome of refixed tendons, presumably due to their high potential for binding biological active substances like TGF- β 3. However, in ongoing studies these cell reactions, especially regarding polarization of macrophages and foreign body cells need to be characterized. This research project has been supported by the German Research Foundation "Graded Implants FOR 2180 – tendon- and bone junctions" WE 4262/6-2 and parts were published in J Tissue Eng Regen Med. 2020 Jan;14(1):186-197. doi: 10.1002/term.2985

OC28 HIP ARTHROPLASTY

K28

THE PHYSIOLOGIC POSTOPERATIVE PRESEPSIN LEVELS AFTER PRIMARY TOTAL HIP REPLACEMENT: A PROSPECTIVE OBSERVATIONAL STUDY

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Aim: This study aims to define the normal postoperative presepsin kinetics in patients undergoing primary cementless total hip replacement (THR).

Methods: Patients undergoing primary cementless THR at our Institute were recruited. At enrollment anthropometric data, smoking status, osteoarthritis stage according to Kellgren and Lawrence, Harris Hip Score (HHS), drugs assumption and comorbidities were recorded. All the patients underwent serial blood tests, including complete blood count, presepsin (PS) and C-Reactive Protein (CRP) 24 hours before arthroplasty and at 24-, 48-, 72- and 96-hours postoperatively and at 3-, 6- and 12-months follow-up.

Statistical analysis was performed with SPSS v25.0 (SPSS Inc, Chicago, IL, USA). The Wilcoxon and Kruskal-Wallis tests followed by the Dunn multiple comparison post hoc tests were carried out. Correlations between PS, CRP and TOT were assessed using the Spearman rank correlation coefficient. P values below 0.05 were considered significant.

Results and conclusion: A total of 96 patients were recruited (51 female; 45 male; mean age= 65.74±5.58) were recruited. The mean PS values were: 137.54 pg/ml at baseline, 192.08 pg/ml at 24-hours post-op; 254.85 pg/ml at 48-hours post-op; 259 pg/ml at 72-hours post-op; 248.6 pg/ml at 96-hour post-op; 140.52 pg/ml at 3-months follow-up; 135.55 pg/ml at 6-months follow-up and 130.11 pg/ml at 12-months follow-up. In two patients (2.08%) a soft-tissue infection was observed; in these patients higher levels (>350pg/mL) were recorded at 3-months follow-up.

The lack of a presepsin decrease at 96 hours post-operatively should be a predictive factor of infection.

OC28.1

VALIDATION OF A MOUSE MODEL FOR POST-ARTHROPLASTY HIP HETEROTOPIC OSSIFICATION

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Introduction and Objective

Heterotopic ossification is the formation of extraskeletal mineralized tissue commonly associated with either trauma or surgery. While several mouse models have been developed to better characterize the pathologic progression of HO, no model currently exists to study HO of the hip, the most common location of acquired HO in patients. Owing to the unique biological mechanisms underpinning the formation of HO in different tissues, we sought to develop a model to study the post-surgical HO of the hip.

Materials and Methods

Wild-type mice C57BL/6J mice were used to study the procedure outcomes, while *Pdgfra-CreERT2;mT/mG* and *Scx-GFP* reporter animals were used for the lineage tracing experiments (total n=16 animals, male, 12 weeks old). An anterolateral approach to the hip was performed. Briefly, a 2 cm incision was made centered on the great trochanter and directed proximal to the iliac crest and distally over the lateral shaft of the femur. The joint was then reached following the intermuscular plane between the rectus femoris and gluteus medius muscles. After the joint was exposed, the articular cartilage was removed using a micropower drill with a 1.2 mm reamer. The medius gluteus and superficial fascia were then re-approximated with Vicryl 5-0 suture (Ethicon Inc, Somerville, NJ) and skin was then closed with Ethilon 5-0 suture (Ethicon Inc). Live high resolution XR imaging was performed every 2 wks to assess the skeletal tissues (Faxitron Bioptics, Tucson, AZ). The images were then scored using the Brooker classification. Ex-vivo microCT was conducted using a Skyscan 1275 scanner (Bruker-MicroCT, Kontich, Belgium). 3D reconstruction and analysis was performed using Dragonfly (ORS Inc., Montreal, Canada). For the histological analysis of specimens, Hematoxylin and Eosin (H&E), modified Goldner's Trichrome (GMT) stainings were performed. Reporter activity was assessed using fluorescent imaging.

Results

Substantial periarticular heterotopic bone was seen in all cases. A periosteal reaction and an initial formation of calcified tissue within the soft tissue was apparent starting from 4 wks after surgery. By XR, progressive bone formation was observed within the periosteum and intermuscular planes during the subsequent 8 weeks. Stage 1 HO was observed in 12.5% of cases, stage 2 in 62.5% of cases, and stage 3 HO in 25% of cases. 3D microCT reconstructions of the treated hip joints demonstrated significant de novo heterotopic bone in several location which phenocopy human disease. Heterotopic bone was observed in an intracapsular location, periosteal location involving the iliac bone and proximal femur, and intermuscular locations. Histological analyses further confirmed these findings. To assess the cells which gave rise to HO in this model, an inducible PDGFR α and constitutive *Scx-GFP* reporter mice were used. A dramatic increase in mGFP reporter activity was noted PDGFR α within the HO injury site, including in areas of new cartilage and bone formation. *Scx*-associated reporter activity increased in the soft tissue and periosteal periacetabular areas of injured hips.

Conclusions

HO has a diverse set of pathologies, of which joint associated HO after elective surgery is the most common. Here, we present the first mouse model of hip dislocation and acetabular reaming that mimics elements of human periarticular HO. The diverse locations of HO after acetabular reaming (intracapsular, intermuscular and periosteal) suggests the activation of different and specific HO program after surgery. Such a field effect would be consistent with local trauma and inflammation, which is a well-studied contributor to HO genesis. Not surprisingly, joint-associated HO significantly derives from PDGFR α -expressing cells, which has been shown to similarly give rise to intramuscular and intratendinous HO.

OC28.2

CERAMIC ON CERAMIC BEARING OUTCOMES IN TOTAL HIP ARTHROPLASTY AT A MINIMUM OF 10 YEARS

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Introduction and Objective

Ceramic on Ceramic bearings in Total Hip Arthroplasty (THA) afford a low friction coefficient, low wear rates and extreme hardness. Significant complications include hip squeak, ceramic fracture and poor polyethylene performance in revision procedures due to imbedding of abrasive microscopic ceramic fragments. We report on the results of this bearing at a minimum of 10 years.

Materials and Methods

A single-centre retrospective review of 449 THAs was performed. Primary outcome measures included aseptic revision and all-cause revision rates at a minimum of 10 years post operatively. Evaluation of functionality was performed with WOMAC and SF-36 scores which were performed pre-operatively and at intervals of 6 months, one year, 2 years, 5 years and 10 years post operatively.

Results

There was a 6.2% (n=28) all-cause and 5.3% (n=24) aseptic revision rate for ceramic on ceramic total hip arthroplasty at minimum of 10 years with a mean time to revision 4.8 years (range 2 months - 11.6 years). Notably, there were 2 revisions for ceramic head fracture, one for ceramic liner fracture, 3 for aseptic loosening and 3 revisions for squeaking. Pain of unknown origin was the most common reason for revision. There was an improvement in postoperative WOMAC scores from a mean of 59.8 (range 15-95) pre-operatively to a mean of 15.6 (range 0-78) at 10 years.

Conclusions

This study showed good functional outcomes but high revision rates for CoC THA at a minimum of 10 years. The role for CoC bearings in THA has been called into question in recent years and may continue to decline in popularity, even in younger patients. Further large scale studies are important to assess the long-term outcomes of this bearing surface.

OC28.3

CLINICAL COMPARISON OF TWO DIFFERENT CERAMIC-ON-CERAMIC BRANDS: PURE ALUMINA VERSUS ALUMINA MATRIX COMPOSITE

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Introduction and Objective

Despite pure alumina have shown excellent long-term results in patients undergoing total hip arthroplasty (THA), alumina matrix composites (AMCs) composed of alumina and zirconium oxide are more commonly used. There are no comparative studies between these two different ceramics. We performed a retrospective case-control study to compare results and associated complications between AMC from two manufacturers and those with pure alumina from another manufacturer.

Materials and Methods

480 uncemented THAs with ceramic on ceramic (CoC) bearing surfaces (288 men and 192 women; mean age of 54.1 ± 12.4 years), were implanted from 2010 to 2015. Group 1: 281 THAs with pure alumina; Group 2A: 142 with AMC bearing in a trabecular titanium cup. Group 2B: 57 hips with AMC bearing with a porous-coated cup.

Results

The mean follow-up was 7.3 years. There was one late infection in group 1, eight dislocations, three in group 1 (1.1%), three in group 2A (2.1%), all with a 36 mm femoral head, and two in group 2C (3.5%). Liner malseating was found in one hip in group 1, and in five hips in group 2C, of these, there were four liner fractures (7.0%). Four cups were revised for iliopsoas impingement (three in group 1 and one in group 2B). Two cups were revised for aseptic loosening, one in group 1 and one in group 2A, and four revised femoral stems in group 2A, three for subsidence and another for postoperative periprosthetic B₂ fracture. The mean preoperative Harris Hip Score was 48.6 ± 3.3 in the whole series and 93.9 ± 7.2 at the end of follow-up. The survival rate of revision for any cause was 98.2% (95% Confidence Interval: 96.6-99.8) at ten years for group 1, 95.8% (95% CI: 92.1-99.5) for group 2A, and 91.1% (95% CI: 83.7-98.5) for group 2B (log-rank 0.030).

Conclusions

Outcome of uncemented CoC THA in young patients was satisfactory at mid-term in all three groups. However, liner fractures were frequent in group 2B. All dislocated hips in group 2A had a 36 mm femoral head diameter, and revision due to any cause was less frequent in group 1. Pure alumina CoC THA can be used as a benchmark for comparison with newer CoC THAs.

OC28.4

PREOPERATIVE FACTORS ASSOCIATED TO THE LENGTH OF HOSPITAL STAY AFTER TOTAL HIP ARTHROPLASTY. OUR EXPERIENCE ON 743 CASES

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Introduction and Objective

Several factors contribute to the duration of the hospital stay in patients that undergo to total hip arthroplasty (THA), either subjective or perioperative. However, no definite evidence has been provided on the role of any of these factors on the hospitalization length. The aim of this retrospective investigation is to evaluate the correlation between several preoperative and perioperative factors and the length of hospital stay (LOS) in patients that underwent elective total hip arthroplasty.

Materials and Methods

Medical records of patients that underwent THA since the beginning of 2016 to the end of 2018 were retrospectively screened. Demographics, comorbidities, renal function, whole blood count, and length of post-operative ward stay were retrieved. The association between clinical, biochemical and surgical factors and the length of hospital stay was explored by means of linear regression models.

Results

A total of 743 subjects were included. Retrieved comorbidity included arterial hypertension (47%), dyslipidaemia (20%), chronic kidney disease (CKD) (12%) and diabetes mellitus (9%). The median length of post-operative hospital stay was 4 days (IQR: 2). Variables associated with linear increase of hospitalization length were the estimated Glomerular Filtration Rate (eGFR) (Beta -0.01, 95% CI -0.02, 0), CKD (Beta 0.82, 95% CI 0.29, 1.34), duration of surgery (Beta 0.69, 95% CI 0.44, 0.94). After correction for multiple confounders, the CKD (α -Beta 1.58 95%CI 0.00 - 3.22) and operation time (α -Beta 0.67, 95% CI 0.42, 0.92) were consistently associated with the outcome.

Conclusions

Our analysis demonstrated a significant role played by the eGFR (as an index of renal function) in influencing the length of hospital stay.

OC29 OSTEOARTHRITIS

K29

NOVEL TREATMENT FOR OSTEOARTHRITIS AND INTERVERTEBRAL DISC DISEASE: REGENERATE, RESTORE & RELIEVE

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Osteoarthritis (OA) is a painful and disabling chronic condition that constitutes a major challenge to health care worldwide. There is currently no cure for OA and the analgesic pharmaceuticals available do not offer adequate and sustained pain relief, often being associated with significant undesirable side effects. Another disease associated with degenerating joints is Intervertebral disc degeneration (IVDD) which is a leading cause of chronic back pain and loss of function. It is characterized by the loss of extracellular matrix, specifically proteoglycan and collagen, tissue dehydration, fissure development and loss of disc height, inflammation, endplate sclerosis, cell death and hyperinnervation of nociceptive nerve fibers. The adult human IVD seems incapable of intrinsic repair and there are currently no proven treatments to prevent, stop or even retard disc degeneration. Fusion is currently the most common surgical treatment of symptomatic disc disease. However, radiographic follow-up studies have revealed that many patients develop adjacent segment disc degeneration due to altered spine biomechanics. The development of safe and efficacious disease modifying OA drugs (DMOADs) that treat pain and inflammation in joints will improve our ability to control the disease. In addition, a biologic treatment of IVDD is desirable. This presentation will provide an overview of recent advances and future prospects of a multimodal biologic treatment of OA, and IVDD. We will focus on Link N, a naturally occurring peptide representing the N terminal region of link protein and the first 1-8 residues of Link N (short Link N, sLN) responsible for the biologic therapy in question.

OC29.1

OSSIFICATIONS OF THE ACETABULAR LABRUM: PROBABLY NOT A GOOD SIGN OF OSTEOARTHRITIS OR FEMOROACETABULAR IMPINGEMENT MORPHOLOGY

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Introduction and Objective

To estimate the prevalence of acetabular ossifications in the adult population with asymptomatic, morphologically normal hips at CT and to determine whether the presence of labral ossifications is associated with patient-related (sex, age, BMI), or hip-related parameters (joint space width, and cam- and pincer-type femoroacetabular impingement morphotype).

Materials and Methods

We prospectively included all patients undergoing thoracoabdominal CT over a 3-month period. After exclusion of patients with a clinical history of hip pathology and/or with signs of osteoarthritis on CT, we included a total of 150 hips from 75 patients. We analyzed the presence and the size of labral ossifications around the acetabular rim. The relationships between the size of labral ossifications and patient- and hip-related parameters were tested using multiple regression analysis.

Results

The prevalence of labral ossifications in this population of asymptomatic, non-OA hips was 96% (95%CI=[80.1; 100.0]). The presence of labral ossifications and their size were correlated between right and left hips (Spearman coefficient=0.64 (95%CI=[0.46; 0.79]), $p<0.05$). The size of labral ossifications was significantly associated with age ($p<0.0001$) but not with BMI ($p=0.35$), gender ($p=0.05$), joint space width ($p\geq 0.53$ for all locations) or any of the qualitative or quantitative parameters associated with femoroacetabular morphotype (all $p\geq 0.34$).

Conclusions

Labral ossifications are extremely common in asymptomatic, non-osteoarthritic hips. Their size is not correlated with any patient-, or hip-related parameters except for the age. These findings suggest that the diagnosis of osteoarthritis or femoroacetabular impingement morphotype should not be made based on the sole presence of acetabular labral ossifications.

OC29.2

A NEW WEARABLE TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION DEVICE (ACTITENS®) IS MORE EFFICIENT AND BETTER TOLERATED THAN WEAK OPIOIDS IN THE TREATMENT OF KNEE OSTEOARTHRITIS PAIN

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Introduction and Objective

Knee osteoarthritis (KOA) is a frequent disease for which therapeutic possibilities are limited. In current recommendations, the first-line analgesic is acetaminophen. However, low efficacy of acetaminophen, frequently leads to the use of weak opioids (WO) despite their poor tolerance, especially in elderly patients. The primary objective was to compare the analgesic efficacy and safety of a new wearable transcutaneous electrical nerve stimulation (W-TENS) to weak opioids (WO) in the treatment of moderate to severe, nociceptive, chronic pain in knee osteoarthritis patients.

Materials and Methods

ArthroTENS study is a phase 3, non-inferiority, multicentric, prospective, randomized, single-blinded for primary efficacy outcome, controlled, in 2-parallel groups, clinical study comparing W-TENS versus WO over a 3-month controlled period with an additional, optional, non-controlled, 3-month follow-up for patients in W-TENS group. The co-primary outcome was KOA pain intensity (PI) at month 3 and the number of adverse events (AEs) over 3 months.

Results

The non-inferiority of W-TENS was demonstrated in both the PP and ITT populations. At M3, PI in PP population was 3.87 (2.12) compared to 4.66 (2.37) (delta: -0.79 (0.44); 95% CI (-1.65; 0.08)) in W-TENS and WO groups, respectively. Since the absolute value of the 95% CI of the between-treatments mean PI difference [-1.71, -0.12] was above 0 in ITT set, the planned superiority analysis was performed, demonstrating that W-TENS was significantly superior to WO at M3 (P=0.0124). At M1 and M3, the W-TENS group reached the absolute minimal clinically important difference (MCID) for an analgesic (1.8 (2.1) and 2.1 (2.3), respectively), corresponding to a 20 mm reduction in PI (interquartile range: 15-30) on a 0-100 mm visual analogic scale – i.e. 2 points on a numerical rating scale – which equates to “much better”. Conversely, in the WO group, a 0.5 (1.8) and a 1.1 (2.1) reduction in PI were observed at M1 and M3, respectively, while a 1-point reduction in PI is required to be considered as a “slightly better” improvement. In WO group, AEs were the common systemic AEs reported with WO (nausea, constipation, drowsiness, dizziness, pruritus, vomiting, dry mouth). AEs in W-TENS group were local, such as local cutaneous reaction (erythema). Thirty-nine (70.9%) patients wished to extend W-TENS treatment for 3 additional months. Only one patient discontinued this additional period and results were maintained at M6.

Conclusions

W-TENS was more effective and better tolerated than WO in the treatment of nociceptive KOA chronic pain and could represent an interesting non-pharmacological alternative to WO.

OC29.3

INTERCEPTING OA DISEASE PROGRESSION BY MODULATING EPIGENETIC PROFILE VIA TET1 INHIBITION

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Introduction and Objective

Osteoarthritis (OA) has been associated with many genes and yet the genetic basis for this disease has never formally been established. Recent realization that epigenetic changes could be the underlying pathological mechanisms has helped to explain many complex multifactorial diseases with no clear genetic cause. We therefore asked whether epigenetics could also play a role in OA. We have previously shown that the DNA epigenetic modification, specifically the hydroxymethylation on cytosine (5hmC), undergoes a fivefold increase on OA-associated genes which are activated at OA onset. In this study, we further uncovered a set of 5hmC-mediated gene targets and their mechanistic link to OA progression.

Materials and Methods

We surgically induced OA on 4 to 6 months old Tet1^{-/-} mice (Tet1^{tm1.1Jae}, the Jackson laboratory) and wild-type littermates by performing destabilization of the medial meniscus (DMM) surgery. Joints were collected for histological assessment through blinded grading with the OARSI scoring system. Human articular chondrocytes were harvested from OA cartilage samples obtained during total knee arthroplasty or from grossly normal cartilage pieces obtained during notchplasty or debridement from patients undergoing anterior cruciate ligament (ACL) reconstruction with no history of OA symptoms, under approved Human subjects Institutional Review Board protocols. Bioinformatic analyses of RNA-sequencing and CCGG sequencing (reduced representation 5hmC profiling) were performed to identify TET1 target genes associated with OA progression. Several measurements were used to assess the effect of TET1 ablation on the phenotype of mouse cartilage tissue and human chondrocytes including, histological evaluation, and quantitative bone assessment by micro-CT imaging and multiplex cytokine analyses in the serum of mice in vivo (mouse 39-plex assay) and in the supernatant of human chondrocyte cultures (human 62-plex assay).

Results

We used a mouse model with surgically induced OA and found that OA onset was accompanied by a gain of ~40,000 differentially hydroxymethylated sites prior the notable histological onset of the disease. We additionally revealed that these changes are mediated by the ten-eleven-translocation enzyme 1 (TET1), since Tet1^{-/-} mice lost 98% of 5hmC sites upon OA induction. Remarkably, Tet1^{-/-} mice were protected from OA development including degeneration of the cartilage surface and osteophyte formation. Silencing of TET1 expression in human OA chondrocytes reduced the expression in a set of genes, which may represent the pathological gene targets that exacerbate OA including MMP3 and MMP13 and several inflammatory cytokines. Therefore, our study reveals the unexpected beneficial role of TET1 inhibition in blocking OA progression. In fact, intra-articular injections of a dioxygenases' inhibitor, 2 hydroxyglutarate, on mice after surgical induction of OA stalled disease progression. Furthermore, treatment of human OA chondrocytes with the same inhibitor also phenocopied TET1 loss, implicating a therapeutic potential of TET1 inhibition in OA patients.

Conclusions

Collectively, our study not only demonstrate the role of TET1 in OA; the 5hmC-mediated gene targets acting on multiple OA pathways were identified and can be modulated as therapeutic intervention to treat OA.

OC29.4

IN VITRO EVALUATION OF THE ANTI-OXIDANT AND ANTI-INFLAMMATORY PROPERTIES OF HYALURONIC ACID COMBINED WITH SODIUM SUCCINATE

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Introduction and Objective

Hyaluronic acid (HA) is an effective option for the treatment of osteoarthritis (OA) patients due to several properties such as normalization of the mechanical and rheological properties of the synovial fluid and amelioration of OA symptoms and joints function by promoting cartilage nutrition. Since OA progression is also significantly related to oxidative stress and reactive oxygen species (ROS), sodium succinate (SS) is envisioned as a promising compound for cartilage treatment by providing antioxidant defense able to normalize intracellular metabolism and tissue respiration via mitochondrial mechanism of action. The scope of this study was to investigate on an in vitro inflammatory model the efficacy of Diart[®] product, a combination of HA and SS.

Materials and Methods

Donor-matched chondrocytes and synoviocytes were obtained from KL 3-4 OA patients undergoing total knee replacement. At passage 4, inflammation was promoted with 1 ng/ml IL-1B for 48 hours in absence and presence of Diart[®] at 1:3 dilution rate. Nitric oxide (NO) from cell culture supernatant was measured by Griess reaction. Mitochondrial and cytoplasmic ROS evaluation was assessed by flow cytometry with MitoSox and dichlorodihydrofluorescein diacetate (DCFDA) assays. Gene expression of inflammation/oxidative stress-related transcripts (MMP1/MMP3/INOS/COX2) was evaluated by qRT-PCR using TBP as reference.

Results

NO was detected only in inflamed chondrocytes and Diart[®] was able to abolish its levels. NO was not detected in synoviocytes in all conditions. IL-1B reduced both cytoplasmic (-66%) and mitochondrial (-68%) ROS in chondrocytes, with Diart[®] partially restoring (+40%) mitochondrial levels. In synoviocytes, IL-1B did not alter ROS, with Diart[®] modestly increasing (+27%) mitochondrial levels. Inflammation was able to increase transcript levels of all tested markers, with the exception of INOS in synoviocytes. In chondrocytes, Diart[®] significantly ($p < 0.05$) reduced COX2 (-75%) and MMP1 (-33%). In synoviocytes, Diart[®] significantly reduced COX2 (-77%) and MMP3 (-84%), with MMP1 53% decreased albeit without reaching statistical significance.

Conclusions

Diart[®] biochemical and physiologic properties in the tested in vitro model of inflammation on donor-matched chondrocytes and synoviocytes allowed reducing inflammation and oxidative stress-related markers, prompting the use of this combination as successful strategy to manage OA-related symptoms.

OC30 TRAUMA RESEARCH

K30

THE INTEGRATED EVALUATION WITH FUNCTIONAL, CLINICAL AND PSYCHOLOGICAL TESTS FOR THE RETURN TO SPORT AFTER ACL RECONSTRUCTION

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Barriers to successful return to previous level of activity following Anterior Cruciate Ligament Reconstruction (ACLR) are multifactorial and recent research suggests that athletic performance deficits persist after completion of the rehabilitation course in a large percentage of patients. Thirty soccer athletes (26.9 ± 5.7 years old, male) with ACL injury were surgically treated with all-inside technique and semitendinosus tendon autograft. At 2 years from surgery, they were called back for clinical examination, self-reported psychological scores, and biomechanical outcomes (balance, strength, agility and velocity, and symmetry).

Nonparametric statistical tests have been adopted for group comparisons in terms of age, concomitant presence of meniscus tear, injury on dominant leg, presence of knee laxity, presence of varus/valgus, body sides, and return to different levels of sports. Athletes with lower psychological scores showed lesser values in terms of power, resistance and neuromuscular activity as compared to the ones with good psychological scores that showed, instead, better self-reported outcomes (TLKS, CRSQ) and low fear of reinjury (TSK). In the athletes who had a functional deficit in at least one subtest, a safe return to sports could not have been recommended. Our findings confirmed that demographics, physical function, and psychological factors were related to playing the preinjury level sport at mean 2 years after surgery, supporting the notion that returning to sport after surgery is multifactorial. A strict qualitative and quantitative assessment of athletes' status should be performed at different follow-ups after surgery to guarantee a safe and controlled RTP.

OC30.1

RELIABILITY OF THE LATERAL FEMORAL WALL THICKNESS FOR DETECTING THE POTENTIAL FOR TREATMENT FAILURE AND IMPLANT CHOICE IN PATIENTS WITH TROCHANTERIC HIP FRACTURES; A PROSPECTIVE COHORT STUDY

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Introduction and Objective

Hip fractures represent one of the most challenging injuries in orthopaedic practice due to the associated morbidity, mortality and the financial burden they impose on the health care systems. By many still considered as the gold standard in the management of intertrochanteric fractures, the Dynamic Hip Screw utilizes controlled collapse during weight bearing to stabilize the fracture. Despite being a highly successful device, mechanical failure rate is not uncommon. The most accepted intraoperative indicator for lag screw failure is the tip apex distance (TAD), yet lateral femoral wall thickness (LWT) is another evolving parameter for detecting the potential for lateral wall fracture with subsequent medialization and implant failure. The aim of this study is to determine the mean and cut off levels for LWT that warrant lateral wall fracture and the implications of that on implant failure, revision rates and implant choice.

Materials and Methods

This prospective cohort study included 42 patients with a mean age of 70.43y with intertrochanteric hip fractures treated with DHS fixation by the same consultant surgeon from April 2019 to December 2019. The study sample was calculated based on a confidence level of 90% and margin of error of 5%. Fracture types included in the study are 31A1 and 31A2 based on the AO/OTA classification system. LWT was assessed in all patients preoperatively using Surgimap (Nemaris, NY, USA) software. Patients were divided into two groups according to the post-operative integrity of the lateral femoral wall, where group (A) sustained a lateral femoral wall fracture intraoperatively or within 12 months after the index procedure, while in group (B) the lateral femoral wall remained intact. All patients were regularly followed up radiologically and clinically per the Harris Hip Score (HHS) for a period of 12 months.

Results

At 12 months five patients (12%) suffered a postoperative lateral wall fracture, while in 37 patients (88%) the lateral femoral wall remained intact. The mean preoperative LWT of patients with a postoperative lateral wall fracture was 18.04 mm (SD \pm 1.58) compared to 26.22mm (SD \pm 5.93) in the group without a lateral wall fracture. All patients with post-operative lateral femoral wall fracture belong to 31A2 group, while 78.4% of the patients that did not develop post-operative lateral femoral wall fracture belong to 31A1 group. Eighty percent of patients in group (A) experienced shortening, collapse, shaft medialization and varus deformity. The mean Harris hip score of group (A) was 39.60 at 3 months and 65.67 at 6 months postoperatively, while that of group (B) was 80.75 and 90.65 at 3 and 6 months respectively, denoting a statistically significant difference ($P < 0.001$). Treatment failure meriting a revision surgery was 40 % in group (A) and 8% in group (B) denoting a statistically significant difference ($p < 0.001$). The cut-off point of LWT below which there is a high chance of post-operative lateral wall fracture when fixed with DHS is 19.6mm. This was shown on the receiver operating curve (ROC) by plotting the sensitivity against the 100 % specificity with a set 95% confidence interval 0.721 – 0.954. When lateral wall thickness was at 19.6 mm, the sensitivity was 100% and specificity was 81.8%. The area under the curve (AUC) was 0.838, which was statistically significant ($P = 0.015$).

Conclusions

Preoperative measurement of LWT in elderly patients with intertrochanteric hip fractures is decisive. The cut off point for postoperative lateral wall fracture according to our study is 19.6 mm; hence, intramedullary fixation has to be considered in this situation.

OC30.2

PREVALENCE OF SARCOPENIA IN OLDER SOUTH AFRICAN PATIENTS FOLLOWING SURGERY FOR FRAGILITY FRACTURES OF THE HIP

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Introduction and Objective

Geriatric patients with a fragility fracture of the hip (FFH) are especially prone to sarcopenia with poor functional outcomes and quality of life. We assessed the prevalence of sarcopenia in older South African patients with FFH. Risk factors for sarcopenia were also investigated

Materials and Methods

From August 1 to November 30, 2018, all older patients with FFH were invited to participate. Sarcopenia was diagnosed based on the revised criteria of the European Working Group on Sarcopenia in Older People (EWGSOP2). Handgrip strength (HGS) and muscle strength were assessed. Muscle quantity was determined by dual-energy X-ray absorptiometry. Demographic information was collected, and 25-hydroxyvitamin D (25[OH]D) status was determined.

Results

Of the 100 hip fracture cases, 65 were enrolled, and 52% (34/65) were sarcopenic (women: 62%; men: 38%). HGS accurately identified sarcopenia (sensitivity and specificity: 100%). Patients >80 years of age had a prevalence of sarcopenia twice (18/21 [83%]) that of younger patients (18/44 [36%]). Women with sarcopenia were smaller than those without (weight: $p < 0.001$; height: $p < 0.001$; body mass index: $p = 0.018$). Low 25(OH)D was almost universally present, with median 25(OH)D levels significantly lower in the patients with sarcopenia (27 nmol/L [interquartile range {IQR}: 20–39] vs. 40 nmol/L [IQR: 29–53]). Several risk factors, including advanced age; female sex; a smaller body size, especially among women; limited physical activity; and low 25(OH)D levels, were identified.

Conclusions

The accuracy of HGS testing in this cohort underscores EWGSOP2's recommendation that muscle strength is key to sarcopenia. Further study and follow-up are required to determine the clinical relevance of sarcopenia among FFH patients. The prevalence of sarcopenia in our FFH population is high. Sarcopenia is associated with poor patient outcomes following surgical intervention. Orthopaedic surgeons should therefore be cognisant of the presentation and associated risk of sarcopenia as our patient populations age.

OC30.3

FACTORS ASSOCIATED WITH INCREASED RADIATION EXPOSURE IN PROXIMAL FEMORAL FRACTURES

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Introduction and Objective

When using radiation intraoperatively, a surgeon should aim to maintain the dose as low as reasonably achievable to obtain the diagnostic or therapeutic goal. The UK Health Protection Agency reported mean radiation dose-area-product (DAP) of 4 Gy cm² for hip procedures. We aimed to investigate factors associated with increased radiation exposure in fixation of proximal femur fractures.

Materials and Methods

We assessed 369 neck of femur fractures between April 2019 and April 2020 in one district general hospital. Fractures were classified as extracapsular or intracapsular and into subtypes as per AO classification. Data was collected on type of fractures, implants used, level of surgeon, duration of surgery and DAP. Types of fractures were subclassified as complex (multifragmentary, subtrochanteric and reverse oblique) or simple.

Results

Patients with fractures fixed with DHS, short PFNA, long PFNA and cannulated screws were included. 50% of our patients were fixed with hemiarthroplasty or total hip replacement and were therefore excluded. 184 patients were included in the analysis. There was a significant association of higher DAP with fracture subtype ($P=0.001$), fracture complexity ($P<0.001$), if an additional implant was used ($P=0.001$), if fixation was satisfactory ($P=0.002$) and the operative time ($P<0.001$). DAP was higher in PFNA than DHS and greatest in Long PFNA. There was some evidence of association between the level of the surgeon and DAP, although this was not statistically significant ($P=0.069$) and remained not significant after adjusting for the variables (fracture complexity, fixation or implant used) ($p=0.32$).

Conclusions

Increased radiation in proximal femur fractures is seen in fixation of complex fractures, certain subtypes, the type of implant used and if an additional implant was required. Seniority of surgeon did not result in less radiation exposure even when adjusting for other factors, which is in contrast to other published studies.

OC30.4

RISK OF COMPLICATIONS FOLLOWING SURGICAL FIXATION OF FEMORAL DIAPHYSEAL FRACTURES IN CHILDREN AGED 4 TO 12 YEARS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and Objective

The most common paediatric orthopaedic injury requiring hospital admission is a femoral fracture. There is debate regarding the optimal surgical technique for fixing femoral diaphyseal fractures in children aged 4 to 12 years. The National Institute for Health and Care Excellence (NICE) and the American Academy of Orthopaedic Surgeons (AAOS) have issued relevant guidelines, however, there is limited evidence to support these. The aim of this study was to conduct a systematic review and meta-analysis to compare the complication rate following flexible intramedullary nailing (FIN), plate fixation and external fixation (EF) for traumatic femoral diaphyseal fractures in children aged 4 to 12.

Materials and Methods

We searched MEDLINE, EMBASE and CENTRAL databases for interventional and observational studies. Two independent reviewers screened, assessed quality and extracted data from the identified studies. The primary outcome was the risk of any complication. Secondary outcomes assessed the risk of pre-specified individual complications.

Results

Nine randomised controlled trials (RCTs) and 19 observational studies (six prospective and 13 retrospective) fulfilled the eligibility criteria. Within the RCTs, five analysed FIN (n=161), two analysed plates (n=51) and five analysed EF (n=168). Within the observational studies, 13 analysed FIN (n=610), seven analysed plates (n=214) and six analysed EF (n=153). The overall risk of complications was lower following plate fixation when compared to FIN fixation (RR 0.45, 95% CI 0.28 to 0.73, p=0.001) in the observational studies. The overall risk of complications was higher following EF when compared to FIN fixation in both RCTs (RR 1.94, 95% CI 1.25 to 3.01, p=0.003) and observational studies (RR 1.97, 95% CI 1.50 to 2.58, p<0.001). The overall risk of complications was higher following EF when compared to plate fixation in both RCTs (RR 7.42, 95% CI 1.84 to 29.98, p=0.005) and observational studies (RR 4.39, 95% CI 2.64 to 7.30, p<0.001).

Conclusions

Although NICE and the AAOS recommend FIN for femoral diaphyseal fractures in children aged 4 to 12, this study reports a significantly decreased relative risk of complications when these injuries are managed with plates. Our findings provide valuable information to healthcare professionals who are involved in discussing the risk and benefits of different management options with patients and their families. The overall quality of evidence is low, highlighting the need for a rigorous prospective multicentre randomised trial at low risk of bias due to randomisation and outcome measurement to identify if any fixation technique is superior.

OC31 - ORTHOPAEDIC BIOLOGICAL RESEARCH

OC31.1

CARTILAGE OLIGOMERIC MATRIX PROTEIN LEVEL AS A LABORATORY MARKER FOR OBJECTIVE CLASSIFICATION OF OSTEOARTHRITIS

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Introduction and Objective

The Cartilage Oligomeric Matrix Protein (COMP) is a glycoprotein that is elevated in patients with osteoarthritis. The elevation increases linearly with the radiological grade of osteoarthritis. The objective of this study was to study the levels of COMP in knee osteoarthritis in the Indian population and to correlate (establish ranges) with the specific radiological grade of osteoarthritis (Kellgren and Lawrence grading). Since the radiological classification is subjective, the COMP levels would serve as a more objective way of classifying osteoarthritic joints.

Materials and Methods

We analysed the COMP levels by the Enzyme Linked Immunosorbent Assay (ELISA) method in 100 patients presenting to the outpatient clinic of our hospital, after obtaining due approvals. The radiographs of these patients were classified according to the Kellgren-Lawrence grading by a senior orthopaedic surgeon.

Results

We found a linear correlation with the COMP levels and the radiological classification as established in the previous studies. We were also able to establish a range of COMP levels for each classification stage.

Conclusions

This study would provide means to classify osteoarthritis without the need for radiographs thus minimising radiation to the patient. It would also help us to predict the radiological findings thus serving as a guide for further treatment planning.