THE EFFECT OF ANTI-IGE THERAPY IN KNEE OSTEOARTHRITIS: A PILOT OBSERVATIONAL STUDY

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Osteoarthritis is a whole-joint disease and its pathogenesis remains poorly understood. Recent evidence proposed the importance of the innate immune system as trigger of synovium inflammation following the degeneration of cartilage. Moreover, synovial mast cells (MCs) might be correlated with pain and disability reported by patients. Anti IgE therapy represents a new class of MCs stabilizing agent, licensed for people with asthma and chronic urticaria. Therefore, we studied if the stabilizing effect of anti IgE would improve the pain and disability in patients affected by knee osteoarthritis and atopic disease. This pilot study provides the first evidence that anti IgE treatment induces a short-term clinical improvement supporting the role of MCs in osteoarthritis.
A successful Total Knee Arthroplasty (TKA) requires stability, but rarely in primary TKA, a prosthesis with more constraint than a posterior-stabilizer (PS) is necessary. In patients with severe varus/valgus deformities with incompetent collateral ligaments or in knees that cannot be adequately balanced after ligaments release, a total-stabilizer (TS) prosthesis may be required. The purpose of our retrospective study is to evaluate clinical and radiographic outcomes at short mid-term follow-up in patients treated with a TS TKA. Between January 2013 and August 2016, 36 patients (38 knees) were treated with Stryker Triathlon TS cemented implants. Clinical and radiographic evaluation were performed preoperatively and postoperatively at 1 month, 3 months, 6 months, 1 year and at 1-year intervals thereafter. At final follow-up, 33 patients (35 knees) remained and were included in this study and followed with a mean follow-up of 26.6 months. Clinical evaluation was performed using the Western Ontario and McMaster Universities Arthritis Index (WOMAC score) and the Knee Society rating system that is subdivided into a knee score (KS) that rates only the knee joint itself and a functional score (FS). Knee Score (KS) and Functional Score (FS) increased significantly from a mean pre-operative value of 48 and 45, respectively, to a post-operative value at last follow-up of 86 and 82, respectively. Also WOMAC score improved significantly: the mean pre-operative WOMAC score was 45, while the mean post-operative WOMAC score, at last follow-up, was 19. The difference between pre- and post- operative results was significant at statistical analysis. In our opinion, when the adequately prosthesis balancing isn’t possible, because of primary or secondary severe varus/valgus deformity or severe soft tissues retraction, an available option is to perform a total knee arthroplasty with a total stabilizer polyethylene insert. TS prosthesis gives more stability during the most of ROM and, in addition, Triathlon system provides surgeons the possibility to choose a more constrained implant, than a standard PS one, during surgical procedure saving the bone stock. Our experience with this kind of prosthesis has provided good clinical and radiographic outcomes at a short mid-term follow-up with a low-rate of complications.
IRISIN LEVELS CORRELATE WITH BONE MINERAL DENSITY IN SOCCER PLAYERS

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Irisin, a novel myokine produced in response to physical exercise by skeletal muscle, displays anabolic effect on bone and can improve the bone-loss-induced osteoporosis in hind limb suspended mice. It is well known that muscles positively impact the skeleton and in different sports, including soccer, total body bone mineral density (TB-BMD) is elevated. Therefore, we have investigated the correlation between irisin serum levels and total and bone sub-regional BMD in soccer players never studied before. In this study, Caucasian football players of Bari team have been enrolled. Their sera were collected to measure by ELISA kit irisin levels and by dual-energy X-ray absorptiometry (DEXA) analysis measurements of BMD (g • cm$^{-2}$) in the whole body and different bone sub-regions (head, arms, legs, ribs, dorsal vertebrae, lumbar vertebrae, pelvis) were performed. The BMC (g) was measured in the whole body. By means of Pearson’s (R) and Cohen’s (d) coefficient we investigated the linear association between the irisin serum levels and BMD. In soccer players, we have found a positive correlation between irisin and TB-BMD as demonstrated by the values of Pearson and Cohen’s (d) coefficient. Furthermore, linear association was detected between irisin and BMD of different bone-site such as right arm, lumbar vertebrae and head. A positive trend was also observed analyzing circulating levels of irisin and bone mineral content as well as total Z-score. In conclusion, we have demonstrated the correlation between irisin and total or bone sub-regional BMD in soccer players for the first time, an additional systemic effect of the “sport-hormone” defined myokine.
An attractive method for osteoarthritis (OA) staging is the measurement of biochemical markers in biological fluids, which could reflect dynamic and quantitative changes in joint remodeling and therefore disease progression. Proteome analysis has been recognized as one of the most effective tools to explore biomarkers as it can furnish a wealth of information in both diagnosis and prognosis of diseases. We have recently described an innovative tool for peptidome and lipidome profiling of fluids based on mesoporous aluminosilicate (MPAS) and Matrix-Assisted Laser Desorption/Ionization time-of-flight Mass Spectrometry (MALDI-TOF MS). The aim of this study was to analyze peptide profiles of human synovial fluid in patients with different grade of OA using MALDI-TOF-MS technique in order to identify potential markers of disease progression. Twenty-five patients older than 50 years and affected by primary knee OA diagnosed according to clinical and radiological criteria were enrolled. For each patient a synovial fluid sample was aspirated from the affected knee and analyzed using MALDI-TOF-MS technique. A statistically significant difference in the normalized area of two peaks ($m/z=1865$ and $m/z=2021$) was detected among different stages of OA. The 2 peaks were identified as Complement C3 peptide fragments: C3f and C3f Des-Arg. The expression levels of these two peptides ($m/z=1865$ and 2021) decreased with the progression of OA degrees severity ($\rho_s=-0.434$, $p=0.03$, and $\rho_s=-0.532$, $p=0.006$, respectively). This marker may be a useful tool for assessing the severity of knee OA and it may be a novel target for drug discovery, specifically for the development of disease modifying OA drugs. However further studies are required to clarify the role of C3f in OA pathogenesis.

C3F IS A POTENTIAL TOOL FOR THE STAGING OF OSTEOARTHRITIS

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A reliable and effective technique in case of limb salvage surgery after resection of extensive bone tumors is represented by the implant of modular or custom-made megaprosthesis. Fixation of the residual surrounding soft tissue on the implant represent a challenge for the surgeon and the use of a polyethylene terephthalate (PET) tube over it, also known as Trevira, is currently a common choice for reattachment with good clinical outcomes. We compared fibroblastic cell culture potential over simple titanium coating vs titanium surrounded by Trevira and evaluated cell viability and replication at 24, 48 and 72 h using MTT cell growth assay and scanning electron microscopy to determine if there was any difference in the potential of cell growth associated to the material used. No significant difference was found at different timings in terms of total cell count for cultures over the two materials, but the absolute cell count was slightly higher in the Trevira group in the early time points, reversing the trend at 72 h of incubation. Ninety-four % of the cells analyzed were vital, regardless of the materials involved in the experiment, confirming the biocompatibility of titanium and PET. According to the results shown, we are able to confirm the in vitro safety and efficacy, in terms of newly formed cells extension and adhesion pattern, of using an attachment tube made from Trevira fibers surrounding an oncological megaprosthesis in order to achieve the most anatomical reinsertion of remaining soft tissue following resection.
COMPLICATIONS AND SURVIVAL OF MEGAPROSTHESES AFTER RESECTION OF BONE METASTASES


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Treatment of bone metastases is often palliative, aiming at pain control and stabilization or prevention of pathological fractures. However, a complete resection with healing purposes can be performed in selected cases. The aim of our work was to evaluate the survival of megaprostheses used for reconstruction after bone metastases. Between January 2001 and March 2015, we implanted 169 Megasytem-C® (Waldemar LINK® GmbH & Co. KG, Hamburg, Germany) after bone metastasis resection. Patients, 95 females and 74 males, were operated at an average age of 61 (12-87) years for proximal femoral resection in 135 (79.9%) cases, distal femur in 24 (14.2%), proximal tibia in 6 (3.6%), total femur in 3 (1.8%) and intercalary femur in 1 (0.6%). Mostly, breast cancer metastases (30.8%), kidney (17.8%) and lung (14.2%) were treated. At an average follow-up of 21 (1-150) months, we found a 99.4% overall limb salvage and a 96.1% overall survival rate at 1 year, 92.8% at 2 years, and 86.8% at 5 and 10 years. We found 9 (5.3%) mobilization cases of the proximal femoral implant, 3 needed surgical reduction; 2 (1.2%) cases of aseptic loosening of the prosthetic stem; 2 (1.2%) periprotetic infection cases, one requiring a 2-stage revision. Few literature studies have evaluated the survival of megaprosthetic implant in the treatment of bone metastases. Our data show how in this specific context the rate of complications is significantly lower than expected in general orthopedic orthopedic surgery. The use of modular prostheses is a valid reconstructive strategy after bone metastasis resection in selected patients. The rate of short-term complications is exceptionally low; further studies will have to confirm this in the longer term.
In the last years new surgical techniques are developing to improve prosthesis positioning, increasing clinical and functional results and reducing invasiveness. In this scenario patient-specific instrumentations have been introduced in order to enhance surgical accuracy and ease of implantation. The purpose of this study was to assess the compliance of the pre-operative planning data with bone resections measured intraoperatively and to evaluate prosthesis positioning in patients undergoing total knee arthroplasty (TKA) using an MRI-based pin-guides instrumentation. Thirty consecutive patients (20 women and 10 men) undergoing 30 total knee replacements (20 right- and 10 left-sided knees) were included in this study. The same cemented cruciate ligament sacrificing prosthesis (NexGen LPS, Zimmer, Warsaw, Indiana, USA) was implanted in all patients by a single surgeon using Patient-Specific Instruments (PSI, Zimmer, Warsaw, Indiana, USA). Femoral and tibial bone resections were measured using a manual caliper intra-operatively and compared with the corresponding pre-operative values. Each patient underwent a CT examination following surgery in order to investigate individual component positioning. None of the cases was converted from PSI technique to conventional TKA and adequate femoral and tibial bone cuts were performed without the need for intraoperative adjustments. Two outliers were detected among the intra-operative bone cuts measurements. In all patients the size of femoral and tibial prosthetic components, hypothesized at preoperative planning, was confirmed intra-operatively. Two outliers were detected among post-operative CT measurements as for components positioning. PSI system can assist in obtaining good component positioning with reduction of outliers. Despite the small number of patients, our data demonstrate the validity of this patient-specific pin-guides system in TKA and may support repeatable improvements in surgical accuracy. Level of evidence: IV.
The aim of this study was to evaluate the effect of an in vitro mechanical stimulation by the use of a bioreactor on an engineered tendon for 7 and 14 days and to analyze the effect of the use of different cell sources: tenocytes, dermal fibroblasts or Adipose-Derived Stem Cells (ASCs), isolated from pig tissues. Histology showed a re-organization of the neo-tissue derived from the three cell populations along the direction of the stimulus. At T7, cells morphology was preserved while an increased cellular suffering at T14 was observed for all cell populations. Tenocytes exhibited higher survival than other cells. A stable immunopositivity for collagen type 1 or 3 at both time points was also observed. In conclusion, dermal fibroblasts and ASCs represent an interesting alternative and in vitro culture with mechanical stimuli may enhance the maturation of a tendon-like tissue.
THE ANALYSIS OF DIFFERENT SCAFFOLDS AND THE BENEFIT OF FIBRIN GLUE FOR TENDON TISSUE ENGINEERING AT DIFFERENT CULTURE TIMES

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This study evaluated a tendon substitute model. Tenocytes were isolated from pig Achilles tendon, seeded onto scaffolds (Opocrin 2%, Typeone 3% and Symatese 2%) and studied by histology, immunofluorescence for collagen type 1 and 3 and biochemical analysis to assess cellularity. The permeability of these compounds was evaluated in the presence or absence of fibrin glue. Opocrin 2% was the best choice for cellular distribution within the scaffolds, which were then cultured for T0, T4, T7 and T10 days. Fibrin glue has been strongly supportive for the survival of cells with a significant increase in DNA content at T10 (P<0.05). Moreover, the synthetic activity of fibrin-free scaffolds was always negative. Lastly, a progressive increase in collagen 1 and 3 with fibrin-glue was observed. However, static culture is not sufficient to support long-term cellular activities and at T10 there is still a lack of organized matrix similar to the native tissue.
Main surgical approaches to the hip have been modified during last decades, in an effort to reduce invasiveness of the surgical procedure and allow a faster rehabilitation. Direct anterior approach is the only approach, which does not require muscle detachment, thus theoretically leading to reduced post-operative pain and allows earlier recovery. The aim of this study was to report a comparison between patients operated with direct anterior approach and postero-lateral approach in terms of immediate post-operative and in-hospital records. Pain, operative time, intra- and post-operative complications, blood loss, hospitalization, motor component of the Functional Independence Measure (M-FIM), timed up and go (TUG) test were measured between the two groups and compared. Direct anterior approach showed better results in M-FIM, TUG, hospitalization and blood loss, without any significant difference for intra- and post-operative complications between the 2 groups. This study shows that early post-operative recovery is influenced by the chosen approach. Direct anterior approach showed better outcomes when compared to postero-lateral approach, limited to hospitalization, blood loss, and functional scores. Further comparisons are needed to evaluate direct anterior approach to maintain advantages over postero-lateral approach on longer follow-up period.
Direct anterior approach for THA has gained popularity over the last years. However, concerns have been raised regarding the cosmetic, related to the incision that does not respect the Langer’s skin tension line and may produce hypertrophic scars. The aim of this study was to analyze the preliminary results in 22 young female patients undergoing THA through a minimally invasive direct anterior approach using a modified oblique bikini incision. Clinical evaluations showed an improvement of WOMAC, UCLA and Harris Hip Score at 5-month follow-up. The technique ensured proper implant positioning and showed advantages in terms of complications, transfusion rates, hospital length of stay and functional recovery. From the aesthetic point of view, the expected cosmetic results were obtained. Minimally invasive direct anterior approach using a modified oblique bikini incision represent a viable option for THA, combining both the advantages of a minimal invasive procedure with a better aesthetic appearance.
Direct vertebral rotation (DVR) is widely used to correct the axial deformity in adolescent idiopathic scoliosis (AIS). Indirect rotation techniques may help DVR in order to improve outcome. Vertebral translation technique combined with the use of two differently shaped rods resulted effective in reducing the rib hump deformity. The aim of this study is to describe the technique and evaluate the efficacy of combined DVR and vertebral translation technique on axial deformity correction. Mean follow-up was 2.7 years. Cobb angle, kyphosis angle, apical vertebrae axial rotation angle, SRS-22 questionnaire of 30 AIS patients treated with combined DVR and differently shaped dual rods translation technique were collected and compared preoperatively and postoperatively. At the last follow-up no screw pull-out, nonunion or loss of correction were recorded. The combination of DVR and differently shaped dual rods translation technique in AIS can provide good three-dimensional correction and improvement of patient’s quality of life.
CORRELATION BETWEEN GAMMA GLUTAMYLTRANSFERASE FRACTIONS AND BONE QUALITY

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Gamma-glutamyltransferase (GGT) has been recently identified as a bone-resorbing factor. The aim of this study was to investigate the association between plasma GGT fractions levels and bone quality. Plasma GGT fractions were analysed by gel-filtration chromatography. Bone quality was established quantitatively by two micro-CT derived microarchitectural parameters: the BV/TV (mineralised bone volume/total volume), and the SMI (structure model index) that describes the rod-like (low resistant) or plate-like (high-resistant) shape of bone trabeculae. We enrolled 93 patients hospitalised for elective total hip replacement (group Arthrosis, n=46) or for proximal femoral fracture (group Fracture, n=47). Patients within the first quartile of BV/TV (Q₁, osteoporotic patients, n=6) showed higher levels of b-GGT fraction [median (min-max): 3.37 (1.42–6.81)] compared to patients with normal bone density (fourth quartile Q₄, n=10; 1.40 (0.83–4.36); p=0.0393]. Also, according to SMI, b-GGT value was higher in the subgroup with bone fragility [Q₁, n=8: 1.36 (0.43–4.36); Q₄, n=8: 5.10 (1.4 –7.60); p=0.0117]. In conclusion, patients characterised by fragile bone structure showed specifically higher levels of plasma b-GGT activity thus suggesting fractional GGT analysis as a possible biomarker in the diagnosis of osteoporosis.
USE OF AUTOLOGOUS BONE MARROW CELLS CONCENTRATE ENRICHED WITH PLATELET-FIBRIN ON EXTENSOR MECHANISM ALLOGRAFT RECONSTRUCTION FOR EXTENSOR MECHANISM FAILURE FOLLOWING TOTAL KNEE ARTHROPLASTY

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Allografts techniques remain the best reconstructive strategy for chronic extensor mechanism lesions after total knee arthroplasty (3) but outcomes depend strictly on the host tissue-allograft junctions healing. The purpose of this study is to evaluate if modern techniques of adding autologous bone marrow cells concentrate enriched with platelet-rich fibrin, provide better healing of the allograft. We present the case of an 86 years old patient affected by patellar tendon rupture after TKA. A whole extensor mechanism allograft was performed adding a bone marrow cells concentrate enriched with platelet-rich fibrin on the host tissue-allograft junctions. Preoperatively and at each follow-up the value of Knee Society Score and radiographic consolidation signs were recorded. Radiographic controls showed clear signs of consolidation already at 1 months follow-up and a solid fusion at 3 months. This case report describes a valid method to improve healing using a tissue-construct engineered with stem cells and growth factors.
ONE-STEP CARTILAGE REPAIR WITH MINCED CHONDRAL FRAGMENT ONTO A COMPOSITE SCAFFOLD: AN IN VITRO HUMAN STUDY AT LOW OXYGEN TENSION

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Minced cartilage fragments are a viable cell source for one stage cartilage repair. However, the joint surface is a low oxygen tension microenvironment and little evidence is present in literature regarding the behaviour of cartilage fragments in this peculiar condition. The aim of the study is i) to verify if low oxygen tension could negatively influence chondrocyte outgrowth from cartilage fragments into a Hyaluronic-Acid(HA)/fibrin scaffold and ii) to evaluate its effects on the behaviour of migrating chondrocyte, compared to normoxic condition. A slight decrease in chondrocyte migration and proliferation was observed in low oxygen tension cultures. Conversely, an increase in the expression of SOX9, β-catenin, HIFs, collagen-I and II (p<0.05) in migrating chondrocytes from low oxygen tension cultures was present. Thus, a long term exposure at low oxygen tension seems to improve the chondrocytic phenotype expression of cell outgrowing from cartilage fragments onto a HA/fibrin scaffold.
Bone cement implantation syndrome (BCIS) is a rare form of intraoperative pulmonary embolism (EP) that occurs during cementation. It can be explained by two main theories: the monomer mediated model and the mechanic model. Our goal is to evaluate thromboelastographic changes in patients undergoing surgery for femoral neck fractures. We recruited 32 patients with a femoral neck fracture. The average age was 81.91 years (range 62-95). The patients were divided in two different groups: cemented hip arthroplasty (CC, 13 patients) and other surgical non-cemented techniques (SC, non-cemented hip arthroplasty, osteosynthesis). The coagulation was evaluated by TEG in the early pre-operative (time A) and post-operative (time B), both on native blood and on blood added with Heparinase. We used the $t$-test to compare the differences between the two groups. The coagulation index CI was modified on hypercoagulability by surgery in both groups, but without statistical significance between the two groups ($p>0.05$). R parameter decreases between time A and time B in the same way in both groups ($p>0.05$). Parameter MA had no major variations between time A and B, without statistical significance ($p>0.05$). From our study it is evident that although the surgery would result in a change in the layout of the TEG toward hypercoagulability, this is similar both in cemented and non-cemented surgical interventions for femoral neck fractures in elderly patients. An altered coagulation does not appear to be the cause or a factor in determining the BCIS.
In the last few years, different tissue engineering strategies have been developed for the repair of osteochondral lesions. When the osteochondral scaffold is implanted on the femoral condyle, the meniscus might be affected by the implant and might undergo a progressive degeneration. The aim of our study is to analyze the morphological changes of the meniscus following an osteochondral lesion and the implant of a biphasic scaffold. A critical osteochondral defect was generated in the medial femoral condyle of mature sheep. Three defects were left untreated, the remaining lesions were divided into three groups and treated with a biphasic substituted formed by collagen type I and Wollastonite or Wollastonite/Hydroxyapatite. Animals were sacrificed after 6 months and menisci were isolated and analyzed by arthro-CT, macroscopic evaluation and histology. The results demonstrated that the osteochondral lesion negatively affects meniscus morphology and that the osteochondral substitute only partially mitigates the meniscus degeneration.

HISTOLOGICAL CHANGES OF THE MENISCUS FOLLOWING AN OSTEOCHONDRAL LESION

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THE TREATMENT OF LOW-GRADE SEPTIC NON-UNIONS

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Non-union (or pseudoarthrosis) is defined as a fracture that fails to consolidate after 6 months from the trauma. Current conservative treatments consist of biological (i.e. with calcium, Vitamin D) and mechanical stimulation. Moreover, surgical approaches include the use of endomidollar nail osteosynthesis, compression plates that are often associated with bone grafts. External fixation is a valid surgical alternative especially in case of septic non-unions. Indeed, compression-distraction osteosynthesis results in a significant improvement in bone vascularisation and exerts a powerful osteoinductive stimulus on the non-union site. In this review, we will describe a cohort of patients affected by low-grade septic non-unions and treated with external fixation.
Chronic ulcers of the lower limbs represent a significant social and economic burden. Diabetes is a strong risk factor for development of chronic lesions. Adult stem cells and growth factors derived from the adipose tissue are among the most promising therapeutic strategies for hard to heal wounds. Fat grafts have been used for several decades to treat soft tissue deformities, but despite its excellent characteristics, the outcome was unpredictable, due to partial necrosis and resorption of the graft. Stem cells’ enrichment of these grafts or their injection into the edges of the ulcers have shown encouraging results in various experimental settings. In this pilot study, we compared the standard of care to autologous lipotransfer and stromal vascular fraction (SVF) enriched lipoinjection in 30 patients with diabetic foot ulcers, showing clear superiority of SVF enriched lipoinjection in terms of percentage of reduction of ulcers size and healing time.