Abstract 153 – Figure 1. Significant linear correlations between gene expression normalised to GAPDH and histomorphometric indices in control (CTL) and primary hip osteoarthritic cases (OA) from trabecular bone of the intertrochanteric region. a) β-catenin (CTNNB1) expression increased significantly with OS/BS (%) (r = +0.66, p=0.01). b) CTNNB1 expression increased significantly with OS/BV (mm²/mm³) (r = +0.65, p=0.01). c) Matrix metalloproteinase-25 (MMP25) expression increased significantly with ES/BS (%) (r = +0.49, p=0.03). d) MMP25 expression increased significantly with ES/BV (mm²/mm³) (r = +0.46, p=0.04).

Methods:

Results:

Conclusions:

154

CAN SERUM MARKERS OF BONE METABOLISM PREDICT THE PROGRESSION OF KNEE OA?

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Purpose: Cartilage and bone are affected simultaneously as osteoarthritis progresses, but this relationship is incompletely understood. This study aimed to examine the relationship between serum markers of bone formation and resorption, and change in cartilage quantity over 2 years, and to determine whether ratios of markers of bone formation to resorption provide additional information.

Methods: Change in cartilage volume over 2 years was measured in 117 subjects with symptomatic knee osteoarthritis using MRI. The relationships between change in cartilage volume and baseline levels of serum markers of bone formation (intact N-terminal propeptide of type I procollagen (PINP) and osteocalcin), resorption (N-telopeptide of type I collagen (NTX-I), the C-telopeptide of type I collagen (CTX-I) and the C-telopeptide of type I collagen (ICTP), and ratios of markers of bone formation to resorption were examined.

Results: Individually, lower levels of PINP (p = 0.02), osteocalcin (p = 0.01), NTX-I (p = 0.02), and CTX-I (p = 0.02) were associated with elevated medial cartilage volume loss. No significant associ-
THE EFFECTS OF ENDOMETULLAR IMPLANTS ON THE PERISTEOAL VESSEL STRUCTURES OF THE RAT TibIA

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Purpose: The healing of bones is successfully achieved after intramedullar fracture-fusing techniques after fractures or surgery despite the definite impairment of peri- and endosteal microcirculation. Prostheses used for surgical treatment of hip osteoarthritis also impair endosteal circulation. Based on these observations several authors have proposed that the connection between peri- and endosteal components of the microcirculation is of minimal importance in long canaliculated bones. Alternatively, we hypothesized that the reduced efficacy of the endosteal circulation may be overcome by a compensatory hypertrophy of the periosteal circulation.

To test this presumption, we intended to answer the following questions:
1. To what extent does the impairment of the endosteal circulation modify the density of periosteal vasculature?
2. Is there any impact of drilling the medullar cavity and placement of intramedullar implant on the density of periosteal circulation?
3. Does the implant material influence the changes in periosteal vasculature?

Methods: In female Wistar rats, the medullary cavities of tibias were drilled out with a series of microdrills (after opening the proximal metaphysal cortices of the shin bones) and implants of different material (polyethylene or titanium) were infixed tightly into the moulded cavity. Endomedullary vasculature was injured also by drilling or remained intact in the contralateral tibias. After a 3-months follow up period, the anteromedial and anterolateral surfaces of tibial periostium was evaluated by using an image analyzer computer microscope, and the periosteal microarchitecture was examined with a Cytoscan A/R-type intraval videomicroscope. Vessel density of the anteromedial and anterolateral surfaces of tibial periostium was evaluated by using an image analyzer computer software.

Results: Endomedullary drilling (without implants) did not induce periosteo vascular density changes (total vessel length/examined area). Higher vascular density was observed in the anteromedial and anterolateral periostium (by 40% and 70%, respectively; p<0.001) in bones with polyethylene endomedullary implants as compared to those of the intramedullarily drilled contralateral tibias. With titanium implants, however, the vascular density in the periostium was only 20% higher (ns). A moderate, albeit not significant increase in the ratio of larger diameter vessels in the periostium was seen in response to endomedullar drilling and titanium infixing. In polyethylene implants, however, the direction of changes was opposite as the ratio of large vessels did not increase, but rather decreased by ~20%, suggesting the predominance of smaller-diameter vessels in the periostium.

Conclusions: Surgical damage of the endosteeal vessels itself did not induce significant changes in the vascular structure of the rat periostium. Placement of endomedullar implants, however, induces an enhanced vessel formation in the periostial compartment. The quality of the implant has a strong influence on these structural changes. Specifically, polyethylene brings about a marked increase in periosteo vascular density with a concomitantly increased ratio of small vessels. Our results suggest that the biologically inert endomedullar titanium causes less pronounced compensatory vessel hypertrophy in the periostium as compared to polyethylene. These results can be linked to the lower osteointegrative properties of polyethylene; such material may inhibit the regeneration of the endosteal vessels which is compensated by vascular neogenesis reactions of the periostium.

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PIOGLITAZONE, A PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA AGONIST REDUCES INFLAMMATORY-INDUCED ALTERATION OF BONE STRUCTURE IN RAT ADJUVANT POLYARTHRITIS: EVIDENCE FOR A BONE PROTECTING EFFECT IN INFLAMMATORY CONDITIONS

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Purpose: Rheumatoid arthritis is characterized by synovial hyperplasia, inflammatory infiltration, cartilage destruction and juxta-articular as well as generalized bone demineralization. Since the discovery of their ability to mediate the pleiotropic effects of xenobiotics and fatty acid peroxisome proliferators in rodents, peroxisome proliferators-activated receptors (PPARs) have emerged as key regulator of lipid metabolism in humans. PPARs are members of the nuclear hormone receptor superfamily which behave as ligand-activated transcription factors in response to endogenous fatty acids and eicosanoids or isotype-selective synthetic compounds as fibrates or thiazolidinediones. In this last decade, increased evidence has shown a role of their three isotypes in inflammatory modulation. We and others demonstrated previously that PPAR gamma agonists reduced the severity of experimental polyarthritis and the overall bone loss. In the present study, we investigated the effect of pioglitazone on inflammatory-induced demineralization and bone microarchitecture in arthritic rats, and the possible contribution of the osteoclastogenesis mediators RANKL and IL-17.

Methods: Lewis rats were sensitized by an intra-dermal injection of 1 mg of complete Freund’s adjuvant (CFA) at the basis of the tail and were treated orally for 21 days with 30 mg/kg/d pioglitazone, or with vehicle only. Arthritis severity was evaluated by clinical scoring and histological examination. Bone mineral density (BMD) of three regions of interest (lumbar spine, right and left femurs) was measured by dual-energy X-ray absorpsiometry (DEXA) before sensitization and at day 20. Micro-computed tomography (micro-CT) analysis of femur was performed to measure mean cortical height at three different points. Bone volume fraction (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N) and trabecular separation (Tb.Sp) were calculated. Circulating levels of soluble RANKL, and IL-17 were determined using commercially available immunoassays.

Results: Treatment with pioglitazone, beyond its ability to reduce arthritis severity, revealed a major protecting effect on bone erosion, as supported by the histological grading of ankle joints. Pioglitazone was effective in preventing bone resorption in arthritic animals as: i) BMD values in all ROIs of treated animals were significantly higher compared to BMD values of vehicle-treated controls, ii) femoral cortical bone thickness was preserved markedly.