coordinate system, to fully account for the position of the tibia relative to the femur while acquiring data.

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DOES SUBCHONDRAL SCLEROSIS PROTECT PROGRESSION OF JOINT SPACE NARROWING IN PATIENTS WITH VARUS KNEE OSTEOARTHRITIS?

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**Purpose:** Abnormal medial loading in varus knee osteoarthritis (OA) results in decreased cartilage thickness, osteophyte ingrowth and subchondral bone sclerosis in the medial femoral and tibial condyles. Some studies have shown that higher bone mineral density (BMD) is protective for knee OA progression. Also, BMD is not necessarily associated with decreased cartilage thickness of knee OA. In addition, the relationship between BMD and knee OA may differ by measurement site of BMD and severity of knee OA. We hypothesized that subchondral bone sclerosis might protect decreased cartilage thickness in knee OA. The aim of this study was to assess the relationship between joint space narrowing and BMD of the knee condyles in patients with varus knee OA.

**Methods:** This study involved 192 women with varus knee OA at our institution. All patients underwent knee radiograph, dual energy x-ray absorptiometry at lumbar spine, proximal femur and knee condyles. The femorotibial angle (FTA) was defined as the lateral angle between the axis of the femoral and tibial shafts. The joint space narrowing angle (JSNA) was defined as the angle between the tangents to the femoral condyles and the tibial plateau marginal line, and was used as an indicator of medial joint space narrowing. Medial and lateral condyles BMD at the femur and the tibia were measured. BMD of the femoral and medial condyles was used as the indicator of subchondral sclerosis. According to the Kellgren & Lawrence grading system, 11 knees were grade 0, 51 knees were grade 1, 51 knees were grade 2, 47 knees were grade 3. According to the FTA and JSNA, mean BMD of the femoral and tibial shafts was correlated with JSNA and FTA.

**Results:** The protective effect might be associated with reducing the risk of joint space narrowing. Our cross-sectional results showed that the increase in subchondral bone sclerosis in the medial femoral and tibial condyles might protect the decrease of cartilage thickness in patients with varus knee OA.

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DELAY IN OSTEOARTHRITIC CHANGE IN A LOX-1 KNOCKOUT MOUSE MODEL OF OSTEOARTHRITIS

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**Purpose:** LOX-1, a vascular endothelial cell receptor for oxidized low-density lipoprotein (ox-LDL), is reportedly involved in the progression of knee osteoarthritis (OA); however, the underlying mechanism has not been well established. In the present study, we established a mouse model of OA through destabilization of the meniscus (DMM) to investigate the role of LOX-1 in the pathogenesis of OA progression.

**Methods:** In this study, we used 9-week-old LOX-1−/− and LOX-1+/− mice. The mice underwent DMM at the right knee (DMM side) as well as a skin incision along with placement of a joint capsule on the contralateral knee (sham-operation side). Samples were obtained from both the knee joints at 4 and 8 weeks after surgery. Safranin staining was performed for each section to assess the osteoarthritic change. Cartilage degeneration, osteophyte formation were assessed by using a scoring system. Moreover, the expression levels of LOX-1 and ox-LDL were assessed in each sample by immunostaining.

**Results:** On the DMM side, osteophyte formation and cartilage degeneration were significantly suppressed in LOX-1−/− mice at 8 weeks after surgery. However, no significant difference in osteophyte formation or cartilage degeneration was noted on the sham-operation side at both 4 and 8 weeks. OA progression was only slightly observed among these mice. Expression was observed cartilage cells, the formation of osteophytes section. Moreover, the expression levels of LOX-1 and ox-LDL in LOX-1−/− mice were found to be increased from 4 weeks to 8 weeks after surgery.

**Conclusions:** Thus, we believe that LOX-1 may play an important role in the pathogenesis of OA progression. Moreover, we suggest that LOX-1 could be used as a potential target for the prevention and treatment of OA progression.

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CARTILAGE MINERALIZATION AND CELL DEATH WITHIN EXPERIMENTAL OSTEOARTHRITIS

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**Purpose:** Osteoarthritis (OA) is characterized by the progressive loss of articular cartilage (AC), accompanied by altered subchondral bone remodeling. In addition calcium deposits have been related to AC degeneration and have been observed in late stages of OA. However, the role of those deposits, whether they induce OA pathogenesis or they appear as a consequence of such process, is still unknown. Therefore the main aim of our research was to determine mineralization markers and cell death in AC.

**Methods:** Knee articular cartilage samples from OA and normal tissue from patients were studied. Macroscopic and microscopic observations, alkaline phosphatase staining for light and electron microscopy (bright and dark fields), TUNEL technique, electron diffraction (EDS), and x-ray microanalyses were performed. In addition we studied the kinetics of expression and tissue localization of osteopontin (OPN), a mineralization biomarker, and calcium deposits in samples from (normal, sham) and osteoarthritic cartilage studied in a rat model. Immunohistochemical and western blot assays for OPN, as well as Alizarin red staining for calcium deposits performed in the superficial, middle, and deep zones of AC were analyzed.

**Results:** Chondrocytes from patients displayed a morphology of apoptosis and showed abundant alkaline phosphatase (ALP)-rich matrix vesicles (MV) budding from the plasma membrane with hydroxyapatite microcrystals on their surface. Farther from the cells hydroxyapatite crystals were detected on the MV surface and increased as they approached the subchondral bone. The concentration of Ca and P in rat and human cartilage increased inside the ALP-rich MV in relation to the proximity to subchondral bone. In the subchondral bone the ratio Ca/P varied from 3.936 to 0.974. In normal tissue the ratio was very homogeneous (maximum 1.973, minimum 1.781).

**Conclusions:** In situ, apoptotic chondrocytes correlate with factor known to be involved in the calcification of the extracellular matrix. This suggests that apoptosis is involved in the abnormal calcification of OA cartilage, and consequently in the altered remodeling of the subchondral bone. In addition, the expression and localization of OPN and calcium deposits during OA pathogenesis suggests that the pathological AC mineralization starts in the superficial zone during OA pathogenesis, which correlates with an increased expression of apoptotic cell death markers found mainly in chondrocytes from S2 in early stages of OA.

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IDENTIFYING THE EARLIEST HISTOPATHOLOGICAL CHANGES IN KNEE OSTEOARTHRITIS

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