

CSAC methodology emerged as the preferred method for recovering extremely small volumes of SF. Furthermore, the results of our pilot *in vitro* COMP analyses suggest that SF-based OA biomarker studies using mice are feasible, effective, and reliable.

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OESTROGEN DEFICIENCY, BUT NOT GLUCOCORTICOID ADMINISTRATION, INDUCES KNEE CARTILAGE LESIONS IN AN EXPERIMENTAL MODEL OF OSTEOPOROSIS IN RABBITS

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Background: The relationship between osteoporosis (OP) and osteoarthritis (OA) is complex and poorly understood. Recent studies suggest that OP could accelerate the progression of established OA, but the influence of OP in healthy cartilage is unknown. Moreover, the pathogenic role of systemic glucocorticoids on cartilage damage is not well defined neither.

Aim: To determine the influence of ovariectomy (OVX) either alone or combined with systemic glucocorticoids administration on healthy cartilage in an experimental model in rabbits.

Methods: Twenty female NZ white rabbits (10 months old; mean weight of 4.3 kg; r: 3.7-6.3) were randomly allocated in three different groups. Seven animals underwent bilateral OVX (OVX group). Low bone mineral content status was induced in 6 animals by OVX and subsequent parenteral methylprednisolone hemisuccinate (MPH) administration (1 mg/kg/d) for 4 weeks to assess the influence of OP on the homeostasis of normal cartilage (OP group). Seven animals were used as controls (Healthy group). To evaluate the bone mass variation, bone mineral density (BMD) was measured by dual energy X-ray absorptiometry (DXA) at both baseline and 6 weeks after OVX (Hologic® QDR-1000) in lumbar spine (L3-L4, LS), global knee (gK) and subchondral bone of the knee (sK). The histopathological cartilage damage at the end of the experimental interventions was evaluated in the medial femoral condyles following the Mankin's system.

Statistical analysis: The difference of the means of the cartilage damage and BMD between groups was calculated using the analysis of the variance (ANOVA). The "post hoc" comparison of the means was studied by the Tukey's test. Correlation between DXA and histological damage was done by Pearson's correlation test (SPSS, vs. 10.0).

Results: Baseline BMD values (mg/cm²) did not show significant differences between groups in any of the anatomical regions analyzed (LS, gK and sK). However, BMD showed a significant decrease in OP rabbits when compared to both OVX and healthy rabbits (p<0.05) (Table 1). A significant negative correlation between BMD at LS and cartilage damage was also demonstrated (p<0.05), but no correlation could be established when BMD was determined at gK and sK.

Group	Mankin score	BMD-LS	BMD-gK	BMD-sK
HEALTHY	0.14 (0.14)	305±13	473±31	642±47
OVX	1.43 (0.30)*	268±37	426±25	578±70
OP (OVX+MPH)	2.42 (0.57)*§	232±40*§	362±86*§	490±97*#

*p<0.05 with respect to healthy group; §non significant differences between OVX and OP; #p<0.05 between OVX and OP. Results are expressed as mean ± SD.

Conclusions: Conclusions: Since isolated OVX induced statistically significant alterations in normal cartilage in our model, oestrogen deficiency might play a direct role in the ethiopathogenesis of OA. The fact that differences in cartilage damage

using the Mankin score were not significant when OVX and OP rabbits were compared, suggests that systemic glucocorticoids do not play any pathogenic role in joint damage.

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EARLY CHANGES OF ARTICULAR CARTILAGE, SYNOVIAL MEMBRANE AND SUBCHONDRAL BONE IN AN EXPERIMENTAL MODEL OF GOAT OSTEOARTHRITIS

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Purpose: Aim of the study was to evaluate the early changes and chronological involvement of articular cartilage, synovial membrane and subchondral bone in an experimental model of goat osteoarthritis (OA).

Methods: OA was induced unilaterally in the right knee joint of nine goats by resection of the anterior cruciate ligament (ACL). Left knee has been considered as control. Three goats have been sacrificed at any time point, one, three and six months, respectively. Plain X-rays of knees have been performed prior to sacrifice. Microradiographic analysis has been carried out to assess volume of subchondral bone, thickness of cortical bone and trabeculae. Histology of synovial membrane was evaluated by ematossilin-eosin staining and the degree of involvement was ranked by using the score system proposed by *Pelletier JP et al.* Safranin staining and *Mankin HJ et al* scoring have been performed to assess cartilage changes.

Results: Analysis of cartilage has shown that ultrastructural changes and decrease of chondrocyte density were present already after one month with progressive reduction of proteoglycan staining which was more marked after six months in the right knee, and the differences with the left knee were statistically significant. After one month, synovial membrane showed a progressive increasing number of layers of the synovial lining and hyperplasia of synovial villi and the differences with the control knee were statistically significant. Also perivascular lymphomonocyte infiltrate was higher in the right knee than in the left knee. Morphometric analysis of subchondral bone detected significant differences between OA and control knee only after 6 months. Volume of cortical bone was increased but volume of trabecular bone was decreased. Also thickness of cortical bone was significantly increased after 6 months in the right knee, whereas no changes in trabeculae thickness was noted.

Conclusions: These findings provided evidence that, at least in our model of OA induced by ACL resection in goats, early signs of OA are detectable both in articular cartilage and synovial membrane. These changes may increase the production of pro-catabolic cytokines and other inflammatory mediators that could play a key role in amplifying the cartilage injury. Involvement of subchondral bone occurs later and always follows cartilage and synovial membrane changes.

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ORALLY ADMINISTERED COLLAGEN HYDROLYSATE HALTS THE PROGRESSION OF OSTEOARTHRITIS IN STR/ort MICE

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Purpose: Experimental investigations on various chondrocyte