KNEE JOINT DISTRACTION INDUCED SHIFT FROM CATABOLIC TO ANABOLIC STATE OCCURS AFTER DISTRACTION PERIOD

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Background: Knee joint distraction (KJD) is a validated joint-preserving treatment strategy for severe osteoarthritis (OA) that provides long-term clinical and structural improvement. Human trials and animal models indicate clear cartilage regeneration from 6 months and onwards post-KJD [1]. Recent work showed that during distraction, the balance between catabolic and anabolic indicators is directed towards catabolism, as indicated by collagen type 2 markers, proteoglycan (PG) turnover and a catabolic transcription profile.

Objectives: To investigate the cartilage changes directly and 10 weeks after joint distraction in order to elucidate the shift from a catabolic to an anabolic cartilage state.

Methods: Knee OA was induced bilaterally in 8 dogs according to the groove model. After 10 weeks of OA induction, all 8 animals were treated with knee joint distraction, employing the left knee as an OA control. After 8 weeks of distraction, 4 dogs were euthanized (KJDdirect) and after 10 weeks of follow-up the 4 remaining dogs (KJD+10). Macroscopic and microscopic cartilage degeneration was assessed using the OARSI canine scoring system. RT-qPCR was used to determine relative expression of aggrecan (ACAN), collagen type II (COL2a1), cartilage oligomeric matrix protein (COMP) and matrix metalloproteinase-3 (MMP3) in the cartilage. PG content was determined by the Alcian Blue assay and the synthesis of PGs was determined using 35SO4 as a tracer, as published before.

Results: Macroscopic cartilage damage of the tibial plateau in the KJDdirect group was higher as compared to the OA control (OARSI score: 1.7±0.2 vs. 0.6±0.3; p < 0.001). For KJD+10 this difference persisted (OARSI score: 1.4±0.6 vs. 0.6±0.3; p = 0.05). Microscopically, an increase in the total OARSI score was seen after 10 weeks post-KJD. This was mainly due to an increase of chondrocyte activity at 10 weeks of follow-up, resulting in an increased subchondrocyte pathology. Remarkably the sub score intensity of proteoglycan staining decreased directly after KJD (indicating a loss of PGs) but increased after 10 weeks of follow-up suggesting a mixed response depending on the time scored.

Cartilage gene expression analysis showed downregulation of COL2a1 (-1.3±0.3), ACAN (-4.4±1.0, p < 0.01) and COMP (-1.7±0.5) in the group compared to OA control suggesting enhanced catabolic activity during KJD. In contrast, after 10 weeks of follow-up the expression of COL2a1 and COMP were increased as compared to the OA control (2.6±1.1 and 2.5±1.2 respectively) as well as compared to the KJDdirect situation (3.2±1.4 and 2.6±2.0). Expression of MMP3 was upregulated directly after KJD (4.1±0.8) and downregulated after 10 weeks of follow-up (-3.3±0.8).

Biochemical analysis of the tibia plateau of the KJDdirect group revealed a lower PG content compared to the OA joint (20.1±10.3 mg/g vs 23.7±1.6 mg/g). At 10 weeks post-KJD this difference in PG content was gone (23.8±6.8 mg/g vs 25.4±7.8 mg/g). The PG synthesis rate directly after KJD appeared significantly lower vs. OA (1.4±0.6 nmol/h.g vs 5.9±4.4 nmol/h.g; p < 0.001). 10 weeks post-KJD this difference was not detected (3.7±1.2 nmol/h.g vs 2.9±0.8 nmol/h.g), and the synthesis rate in the distracted knee was increased compared to directly after distraction (p < 0.01) indicating a shift upon follow-up.

Conclusion: Further in-depth investigation of the material is ongoing and also includes the other joint tissues such as the bone and the synovial tissue. Regardless, these first results on cartilage changes suggest that the shift from a catabolic to an anabolic state occurs within the weeks after joint distraction. As such, the post-distraction period seems to be essential in identifying key-players that support intrinsic cartilage repair.

References:


Disclosure of Interests: Michelle Teunissen: None declared, Jelena Popov-Celeketic: None declared, Katja Coeleveld: None declared, Bjorn Meij: None declared, Floris Latèbre Shareholder of: Co-founder and shareholder of ArthroSave BV, Marianna Tryfonidou: None declared, Simon Mastbergen: None declared

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