Novel Small Animal Model of Hip Osteoarthritis Secondary to an Induced Femoral Head-Neck Deformity: A Platform to Study Mechanism of Hip Osteoarthritis

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INTRODUCTION:

Femoroacetabular impingement (FAI) is a leading cause of hip osteoarthritis (OA). However, the basic biological mechanisms of disease in FAI remain unknown. While the number of surgical procedures to treat hip FAI has grown exponentially in the past decade, there is still a 10-25% failure rate following surgical treatment, with progressive deterioration of the joint leading to OA, suggesting that surgical treatment for hip FAI has outpaced the true understanding of this disease. Animal models can serve as platforms to study the mechanism of disease and the efficacy of potential treatment options. Previously, we have confirmed that we could induce a femoral head neck deformity (FAI type deformity) in immature rabbits by creating a physeal injury to the proximal femoral epiphysis. The aim of this study was to investigate whether the induced head neck deformity results in hip OA.

METHODS:

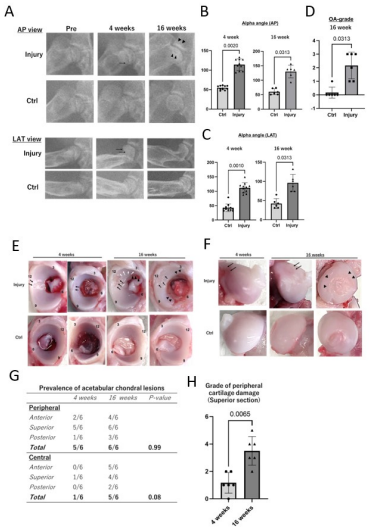
Twenty 6-week-old immature New Zealand White rabbits were used and subjected to right hip surgery. All surgeries were performed as previously reported by performing a 3 × 2 × 6–mm defect in the epiphysis using a 1.6-mm drill bit at the medial third of the epiphysis of the femoral head (FH). Groups were divided in early pre-OA group (4 weeks n=10) and late OA group (3 months n=10). Contralateral hips were served as control (n=20). The alpha angles were used to assess the head-neck deformity, and a semi-quantitative scoring system was used to evaluate the presence and severity of osteoarthritis (Tonnis Score). As a macroscopic evaluation, rabbits were sacrificed at the end of the assigned ambulatory period (pre-oa group 4 weeks or late OA group16 weeks). Both hip joints were dislocated to expose the entire joint and further tissue processing. The acetabular and femoral head chondral lesions were classified using Beck's classification. Osteoarthritis was confirmed using micro computed tomography (μCT). We assessed gene expression for cartilage degeneration, including Col2, Col10, and MMP13 (RT-PCR). The comparison between groups was performed using Mann-Whitney U test. The level of significance was set as *P* value less than 0.05. Data is presented as mean ± standard deviation for parametric test.

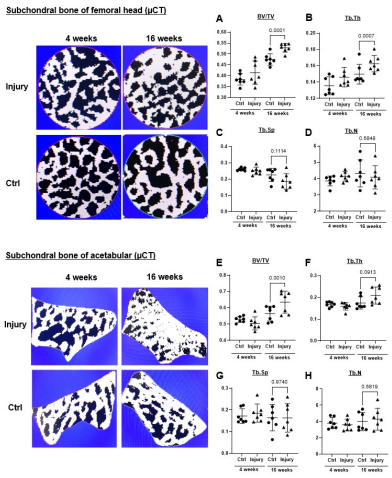
RESULTS:

Radiographs taken at 4 and 16 weeks after surgery demonstrated a femoral head deformity confirmed on AP and lateral hip views (black arrow, Fig 1-A). Femoral head-neck deformity was confirmed with higher alpha angles in both AP and lateral views at 4 weeks (control vs.injured hip, AP-view, 54.9 ± 5.4° vs. 114.3 ± 4.7° p=0.002, lateral-view, 42.7 ± 13.4° vs. 112.0 ± 17.8° p=0.001, Fig. 1-B and 1-C), and 16 weeks after surgery (control vs. injured hip, AP-view, 54.9 ± 5.4° vs. 114.3 ± 14.7° p=0.031, lateral-view, 60.3 ± 10.5° vs. 130.2 ± 21.8° p=0.031, Fig. 1-B and 1-C). Additionally, radiographs at 16 weeks after surgery clearly showed OA changes including bone sclerosis and joint space narrowing (black arrow, Fig 1-B), suggesting progression to hip OA with a Tonnis grade$\geq$ 2 in injured hips (control vs. injured hips : 0.16 ± 0.41 vs. 2.17 ± 0.97, p=0.031, Fig 1-D (Tonnis grade equal or >2 is considered OA). Macroscopic cartilage lesions were observed in the peripheral acetabular area of injured hips at 4 weeks (control vs. injured hip, 0% vs. 83.3%, p=0.015) and 16 weeks after surgery (control vs. injured hip, 0% vs. 100.0%, p=0.002), when compared to control hips (0%, Fig 1-E/F/G). Additionally, more severe cartilage lesions were observed during late stage of disease (16 weeks) (Fig 1-H). Subchondral bone evaluation with μCT confirmed degenerative OA changes in the femoral head and acetabular at 16 weeks. (Fig 2). At 16 weeks, RT-PCR analysis confirmed increase expression of cartilage catabolism with decreased expression of Col2 and increased expression of Col10 (control vs. injured hip, Col2, p=0.043, Col10, p=0.021, Fig. 3) in both femoral head and acetabular cartilage. (control vs. injured hip, Col10, p=0.016, MMP13, p=0.0414, Fig. 3).

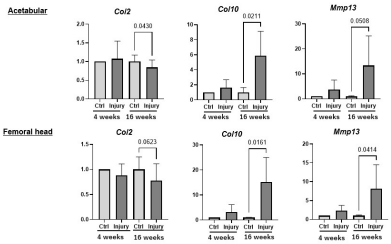
DISCUSSION AND CONCLUSION:

The proposed induced femoral head deformity results in hip OA at 16 weeks. This model has the potential to impact the field, as it will allow, for the first time, to have a low cost, small translational animal model of hip FAI and hip OA. This model could be used as a platform to understand in-depth the mechanisms of hip OA, test interventions, and translate our discoveries to patient care. Mechanical validation to human FAI is ongoing using Finite Element Analysis.


A
AP view
Pre
4 weeks
16 weeks
Injury
Ctrl
LAT view
Injury
Ctrl
B
Alpha angle (AP)
4 week
16 week
0.0020
0.0313
Ctrl
Injury
C
Alpha angle (LAT)
4 week
16 week
0.0010
0.0313
Ctrl
Injury
D
OA-grade
16 week
0.0313
Ctrl
Injury
E
4 weeks
16 weeks
Injury
Ctrl
F
4 weeks
16 weeks
Injury
Ctrl
G
Prevalence of acetabular chondral lesions
4 weeks
16 weeks
P-value
Peripheral
Anterior 2/6 4/6
Superior 5/6 6/6
Posterior 1/6 3/6
Total 5/6 6/6 0.99
Central
Anterior 0/6 5/6
Superior 1/6 4/6
Posterior 0/6 2/6
Total 1/6 5/6 0.08
H
Grade of peripheral cartilage damage (Superior section)
0.0065
4 weeks
16 weeks


Subchondral bone of femoral head (μCT)
4 weeks
16 weeks
Injury
Ctrl
A
BV/TV
0.0001
B
Tb.Th
0.0007
C
Tb.Sp
0.1134
D
Tb.N
0.5848
Ctrl
Injury
4 weeks
16 weeks

Subchondral bone of acetabular (μCT)
4 weeks
16 weeks
Injury
Ctrl
E
BV/TV
0.0010
F
Tb.Th
0.0913
G
Tb.Sp
0.9740
H
Tb.N
0.6619
Ctrl
Injury
4 weeks
16 weeks


Acetabular
Col2
0.0430
Col10
0.0211
Mmp13
0.0508
Femoral head
Col2
0.0623
Col10
0.0161
Mmp13
0.0414
Ctrl
Injury
4 weeks
16 weeks