Ovariectomy and High Fat Diet Results in Diminished Bone and Cartilage Content in the Murine Hip

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Introduction:
Arthroscopic hip surgery is rapidly emerging as one of the most popular disciplines in orthopaedics; recent studies have reported 15% growth annually. The most common indication for the procedure is femoroacetabular impingement (FAI), and its use has proven itself as an effective and durable treatment with consistent improvements in patient reported outcomes (PROs). However, recent studies have suggested that women, especially those over the age of 45, may have a more unpredictable level of improvement after hip arthroscopy compared to their younger or male counterparts. These findings suggest that the lack of estrogen may drive some of the early changes in the development of hip pathology and furthermore may account for the poorer PROs observed following hip arthroscopy. In addition, patients with obesity also demonstrate poorer outcomes after hip arthroscopy, a growing concern given its increasing prevalence.

Method:
Sixteen-week-old female C57BL/6 mice underwent ovariectomy (OVX) or sham (SHA) procedure. At 20 weeks of age, mice were placed on a low fat (LD: 10% kcal) or high fat diet (HFD: 60% kcal). At 32 weeks of age the mice were sacrificed, one hip was disarticulated and the femur was cleaned of soft tissue attachments. Serum was collected for metabolic parameters. Micro-computed tomography (μCT) and histomorphometric analysis were performed on the femurs using AMIRA 3D software and Osteomeasure, respectively, to determine cortical and trabecular bone volume, subchondral bone area and cartilage volume.

Two-way ANOVA with a post hoc analysis was performed to determine the effects of diet, ovariectomy and their interaction. Differences are considered significant when p<0.05.

Results:
- Twenty weeks of high fat diet is sufficient to induce a metabolic syndrome-like phenotype in female mice.
- Ovariectomy at 16 weeks of age is sufficient to induce changes in bone content in the murine hip at maturity.
- Ovariectomy-induced loss in cortical and trabecular bone content within the femoral head (15% and 16%, respectively).
- High fat diet alone did not affect bone content, however there was a further loss of cortical bone content in the setting of concurrent ovariectomy.

Discussion:
The present study is the first to demonstrate the pathological changes that occur in the hip joint in response to estrogen deprivation and high fat diet. Ovariectomy appears to induce a more significant effect on hip joint pathology than exposure to a high fat diet. Ovariectomy resulted in a reduction of both cortical and trabecular bone volume in the femoral head to a similar extent as previously demonstrated in other animal models. Furthermore, the loss of femoral head cartilage and subchondral bone content are pathological changes consistent with the development of early osteoarthritis. The reduction in bone quantity and quality, could account for the poorer outcomes observed in older female patients following hip arthroscopy. Furthermore, others that have demonstrated that women have increased joint mobility in the hip compared with their male counterparts, resulting in an increased translational and shear vector during joint motion; a finding that highlights the difference between the sexes and hip joint mechanics. Thus, the combination of metabolically impaired articular cartilage and subchondral bone, as well as increased translational arthrokinematics, likely results in accelerated joint degeneration. The data presented here suggest the utility of using the murine hip in future experimental models examining pathological changes in the hip joint. Moreover, conclusions drawn from these data support the need for further study as to the influence of metabolic factors on hip joint deterioration and its relationship to hip pain.

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