Intra-Articular Cellular and Molecular Factors Identified at the Time of Hip Arthroscopy Surgery

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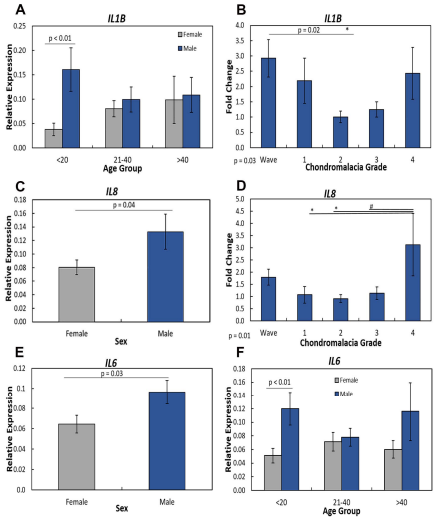
INTRODUCTION:
Femoroacetabular impingement syndrome (FAIS) is a well-known cause of hip pain and dysfunction, and occurs when excess bone forms at the femoral head/neck junction and/or acetabulum resulting in labral injury and cartilage damage and eventual hip osteoarthritis (OA). FAIS can be surgically treated via hip arthroscopy, by repairing the torn labrum and removing impinging bone. Unfortunately, patients with advanced cartilage damage as a sequela of FAIS may be unable to prevent further OA progression. Identification of biomarkers to assess the location on the spectrum of OA as well as to predict the progression of OA after surgical intervention would revolutionize our understanding and treatment of this pathology.
Therefore, the purpose of this study is to examine the molecular environment of the FAIS hip across different age groups, sex, and varying levels of FAIS severity and identify potential biomarkers which suggest critical points of OA progression.
METHODS: This study was approved by the University of Wisconsin-Madison Institutional Review Board (IRB). A total of 90 patients with FAIS were included in the study based on a diagnosis from clinical and radiographic findings. All patients underwent hip arthroscopy where pathological remnants (comprised of capsule, labrum, cartilage, and synovial tissue), were collected and used for QPCR to measure aggrecan (*AGAN*), interleukin 1β (*IL1β*), interleukin 8 (*IL8*), interleukin-6 (*IL6*), matrix metalloproteinase-13 (*MMP13*), collagen type II (C*OL2A1*), a disintegrin and metalloproteinase with thrombospondin motifs-1 (*ADAMTS1*), *ADAMTS5*, cartilage oligomeric matrix protein (*COMP*), and cyclin-dependent kinase inhibitor (*P21*). Genes were selected to identify inflammation (*IL1β*, *IL6, IL8),* ECM anabolism/catabolism (*AGAN,* C*OL2A1*, *MMP13, ADAMTS1, ADAMTS5, COMP)*, and cell senescence (*P21)*. Gene expression was examined based on sex and/or age (< 20 yo, 21-30 yo, and >40 yo) as well as FAIS severity as determined via chondromalacia grade (wave, 1, 2, 3, 4). Age and sex comparisons were analyzed via Student's T-tests. Chondromalacia grade results were analyzed via ANOVA; data that reached significance ($p < 0.05$) were further examined via Tukey's post-hoc analysis.
RESULTS: Results indicate that the inflammatory cytokines *IL1B, IL8,* and *IL6* were differentially expressed. More specifically, *IL1B* expression was significantly greater in males vs. females under the age of 20 yo. (**Fig1A).** Patients with a chondromalacia grade 2 severity expressed significantly lower *IL1B* compared to those with graded as a wave (**Fig. 1B).** *IL8* expression was significantly higher in males vs. females (**Fig. 1C).** Unlike *IL1B,* patients with greater FAIS severity (grade 4) expressed significantly higher levels of *IL8* compared to patients with lower grades of 1, 2, or 3 (**Fig. 1D).** Lastly, *IL6* expression was greater in males than females **(Fig. 1E**), specifically under the age of 20 yo (**Fig. 1F**). No other significant differences were noted with the other genes tested.
DISCUSSION AND CONCLUSION: To our knowledge, this is the first abstract to report the differential expression of inflammatory factors, *IL1B* and *IL8,* based on FAIS severity. Taken together, these markers could help identify the position of FAIS hips on the spectrum of hip OA and lead to an understanding of which hips are susceptible to OA progression. This study also demonstrated that males were more likely to express greater levels of inflammation than females. Lastly, it is interesting to note that the catabolic and anabolic factors tested were not differentially expressed, suggesting that inflammatory markers may identify OA more reliably. Identifying biomarkers that are differentially expressed with FAIS severity, sex, and age may help surgeons better assess patients' current position on the spectrum of OA progression, better indicate the appropriate time to intervene surgically, and better predict future patient-specific outcomes after surgical intervention.


A
IL1B
p < 0.01
Female
Male
Relative Expression
0.25
0.20
0.15
0.10
0.05
0.00
<20
21-40
>40
Age Group
B
IL1B
p = 0.02
*
Fold Change
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
p = 0.03
Wave
1
2
3
4
Chondromalacia Grade
C
IL8
p = 0.04
Relative Expression
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Female
Male
Sex
D
IL8
*
*
#
Fold Change
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
p = 0.01
Wave
1
2
3
4
Chondromalacia Grade
E
IL6
p = 0.03
Relative Expression
0.12
0.1
0.08
0.06
0.04
0.02
0.0
Female
Male
Sex
F
IL6
p < 0.01
Female
Male
Relative Expression
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
<20
21-40
>40
Age Group