The Relationship between Ambulatory Load and Cartilage is Influenced by Age and Gender

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INTRODUCTION

It has been reported that healthy knee cartilage responds positively to ambulatory load, such that regions that experience higher relative load (adduction moment) are relatively thicker (ratio of medial/lateral thickness). Osteoarthritic cartilage, however, responses negatively to ambulatory load. Osteoarthritis (OA) develops as individuals age, with differing risk for men and women, so the positive load response reported in younger male subjects may change with increasing age and is likely also influenced by gender. Understanding the factors affecting this load response relationship can provide important insight into the changes in cartilage with aging. Thus the purpose of this study was to examine the load response relationship described above by testing the following hypotheses: 1) The correlation between the adduction moment and the medial to lateral thickness ratio will improve when age and gender are included in the model, and when subjects are stratified by age. 2) Inter-subject variability due to age and gender can be reduced relative to a single knee analysis by analyzing the left-right difference in adduction moment and medial/lateral cartilage thickness ratio.

METHODS

44 healthy-weight subjects (18 men, avg. age 34±11.1 years, age range 20-59 years, avg. body mass index (BMI) 23±2.4 kg/m²) were bilaterally studied using MRI and gait analysis. All subjects reported no chronic lower body pain and informed consent was obtained per Stanford University IRB guidelines. Two fat-suppressed sagittal plane MRI sequences were used in a 1.5T GE Excite scanner: a 3D spoiled gradient recalled echo (SPGR) sequence to visualize cartilage, and a fast spin echo proton density sequence. Subjects were excluded if the MR images indicated joint injury or early arthritis. Right and left femoral cartilage was segmented by a single observer using the SPGR images and a semi-automated spline algorithm. The segmented images were used to create a 3D thickness map of the femoral cartilage, and the regions corresponding to -15°< anterior, 15-45°< middle, and 45-75°< anterior of knee flexion were identified. The ratio of the average thickness in each region on the median and lateral condyle was calculated for both knees. GAit was analyzed by using 9 optoelectronic cameras and a force plate to capture the kinematic and kinetic data at a self-selected walking speed. Side-side differences between the first peak knee adduction moments and M/L thickness ratios were calculated by subtracting the right knee value from the left and dividing by the average of the two sides. To address hypothesis 1, a linear regression model was calculated for the relationship between the M/L thickness ratio and the first peak knee adduction moment, adding corrections for age and gender. For hypothesis 2, a regression model was created using the left-right differences in adduction moment and M/L thickness ratio. The same analyses were repeated for a subset of subjects younger than the average (30 subjects, 12 men, avg. age 27±3.7 years). A p-value of 0.05 was considered significant.

RESULTS

Hypothesis 1: For all subjects, the relationship between the adduction moment and the M/L thickness ratio for a single knee (left) in the middle region (R²=0.036, p=0.217, Figure 1) improved slightly when the regression included gender and age, but the relationship did not reach significance (R²=0.083, p=0.488). In the younger subset of subjects, however, the relationship was stronger (R²=0.112, p=0.071), and when adjusted for gender, the relationship became significant (R²=0.211, p=0.041). The slope of the regression moment-M/L thickness ratio regression line was higher in the younger subset of subjects (0.0311 and 0.0513 respectively, Figure 1). Hypothesis 2: A significant positive correlation between the difference in peak knee adduction moment and the difference in the M/L thickness ratio in the middle regions was found for all subjects (Figure 2, R²=0.215, p=0.0017), as well as the younger subset (R²=0.317, p=0.0015), and the slope of the regression line was higher in the younger cohort (.288 and .337, respectively). No similar relationships were seen in the anterior or posterior regions.

DISCUSSION

The results support the conclusion that age and gender influence the cartilage response to load, as the correlation between the adduction moment and M/L thickness ratio improved when age and gender were included in the model or when subject age was restricted to a younger cohort (age < 34). The result that the young cohort adjusted for gender had a significant cartilage load response is in agreement with previous work in a young, male cohort. It is also important to note that there was a higher positive cartilage load response in the younger cohort than in all subjects, suggesting that the older group may be approaching a negative load response similar to that reported in OA patients. The regression models using right-left differences show the same trends as those for the single-knee, with a stronger relationship and higher slope in the younger cohort, but overall the relationships are much stronger. This indicates that by conducting an intrasubject analysis, we can eliminate sources of variability in cartilage thickness and adduction moment and detect the same cartilage response to load without adjustment for any subject characteristics. This approach is especially important in studies that analyze a population that comprises both genders and spans different age groups.

SIGNIFICANCE

The results that age and gender influence the cartilage load-response, and that right-left comparisons improve the ability to detect that response, suggest that aging healthy cartilage begins to respond to load in a manner similar to that reported for OA cartilage.

REFERENCES


ACKNOWLEDGEMENTS

Funding was provided by VA #A4861R and the NSF Graduate Fellowship.

Figure 1: The regression relationship between the knee adduction moment and medial/lateral cartilage thickness ratio was dependent on age. All subjects < 59 years (solid red line), younger subjects < 34 years (dashed blue line), and the younger male cohort from Koo et al < 40 years (dash-dot black line).

Figure 2: The relationship between the side-side differences in knee adduction moment and femoral medial/lateral cartilage thickness ratio is stronger than in single-knee analysis.