Degree of Joint Instability Determines Severity of Cartilage Degeneration in Rabbit Knees

+Tochigi, Y; McKinley, TO; Vaseenon, T; Fredericks, DC; Heiner, AD; Martin, JA; Rudert, MJ; Brown, TD

University of Iowa, Iowa City, IA
E-mail: yuki-tochigi(at)uiowa.edu

PURPOSE: Joint instability associated with an ACL injury is a well-recognized risk factor for post-traumatic OA in the human knee. Therefore, ACL transection (ACL-T) has been employed in several animal models to investigate post-traumatic OA. In ACL-T rabbit models, advanced OA (characterized by deep fibrillation and/or eburnation) predictably develops within 8 weeks of transection. Unfortunately, the severity and rapidity of OA that develops in the rabbit ACL-T model is not optimal for piloting pharma-therapeutic treatments, or for investigating interaction of instability with other pathogenic factors. The goal of this study was to develop a rabbit model of controlled knee instability in which OA develops reproducibly at a more modest level amenable to therapeutic interventions. The hypothesis was that, by inducing a more moderate level of instability in rabbit knees with a partial (rather than total) ACL-T, a reproducible, sub-critical level cartilage degeneration would occur.

METHODS: With institutional approval, sixty New Zealand White rabbits received either total ACL-T (n = 8), partial (medial half) ACL-T (n = 8), or sham surgery (arthrotomy with infra-patellar fat pad resection, n = 7) on their left knees. Eight or sixteen weeks later, these animals (from each group) were subjected to a loading test. Using a custom fixture [1], A-P stability of the knee was quantified in terms of anterior drawer end-point stiffness and neutral-zone length. The joints were then prepared for histo-morphological evaluation. Femoral and tibial surfaces in both medial and lateral compartments were rated individually on the Histological Histochemical Grading Scale (HHGS, 14 points max) [2], by two experienced orthopaedic surgeons. The average of the four surface scores was defined as the whole-joint score. The scores for the most and least affected surface for each joint were also reported. Statistical significance was taken as p < 0.05.

RESULTS: The partial ACL-T knees were more unstable than the control knees, and less unstable than the total ACL-T knees, as indicated by decrease of anterior drawer stiffness and increase of neutral-zone length (Figure 1). In visual inspection at dissection, all partially transected ACLs remained unruptured. Four out of the eight total ACL-T knees were accompanied by a bucket handle tear at the medial meniscus, while none of the partial ACL-T knees had a torn meniscus. Whole-joint average scores of HHGS in the partial and total ACL-T knees were significantly higher than in the control knees (Figures 2, 3). However, degenerative changes observed in those ACL-T knees were relatively mild; single-surface scores higher than 6 points (moderate-to-severe OA) were reported in only five knees (1 partial and 4 total ACL-T knees.) Despite the very controlled experimental setting, there was notable variability as to where surfaces of the joint were most affected. Of the five distinct-OA knees, three were affected most at the medial tibial surface, while the other two were affected most at the lateral or medial femoral surface. Higher degrees of cartilage degeneration occurred with higher degrees of instability (Figure 4), as indicated by statistically significant correlations of the whole-joint HHGS with anterior drawer stiffness and neutral-zone length (correlation coefficients -0.59 and 0.57, respectively).

DISCUSSION: In contrast to many previous studies, cartilage degeneration in the total ACL-T knees at 8 weeks was at a mild to modest level, and severe fibrillation was rarely observed. This may be associated with the surgical technique of the present study, which left both menisci fully intact and intentionally minimized damage to the other surrounding structures. In both the partial and total ACL-T knees, the medial tibial surface was the most degenerated. The total ACL-T knees frequently developed a medial meniscus bucket handle tear. Both of these phenomena are seen in human knees with ACL deficiency. The degree of cartilage degeneration was correlated with the degree of instability, supporting the empirically-plausible (but heretofore unproven) concept that higher degrees of instability lead to higher degrees of cartilage degeneration.

Partial ACL-T caused modest knee instability, and the resulting cartilage degeneration was mild, although significant as compared to sham-surgery control knees. Given that cartilage degeneration in partial ACL-T knees was reproducibly limited to a sub-critical level, this model appears to be a promising tool for future OA research, especially for studies of multiple interacting influences.

Figure 1 Individual specimen’s data in the knee A-P laxity test plotted for the two instability measures. Points at the upper-left corner indicate unstable joints.

Figure 2 Cartilage histology at the medial tibial plateau.

Figure 3 Results of cartilage histology evaluation by HHGS.

Figure 4 Correlations of HHGS with the neutral-zone length.


Acknowledgments: CDC Grant R49 CCR721745-03
NIH Grants 5 P50 AR048939 / P50 AR055533

Poster No. 1115 • 55th Annual Meeting of the Orthopaedic Research Society