The effect of rehabilitation of the knee following anterior cruciate ligament reconstruction with a bone-patellar tendon-bone autograft on synovial fluid based biochemical markers of articular cartilage metabolism

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Introduction: Adverse effects are associated with immobilization of the knee following anterior cruciate ligament (ACL) injury and reconstruction; however, very little is known about how much activity will promote adequate rehabilitation without injuring the healing graft and articular cartilage. Synovial fluid (SF) samples from the knee allow investigation of how biochemical markers of articular cartilage metabolism are altered by ACL injury and subsequent rehabilitation. The primary objective of this investigation was to evaluate markers of articular cartilage matrix synthesis and degradation in the joint fluid of both injured and uninjured knees immediately prior to surgery (baseline) and at postoperative intervals of 6, 12, and 24 months. The primary hypothesis was that after reconstruction of the ACL, there would be a significant increase in the concentrations of the biochemical markers of articular cartilage matrix synthesis and degradation in the SF of the reconstructed knee of subjects who undergo accelerated rehabilitation in comparison to the group that participates in nonaccelerated rehabilitation at each of the follow-up time periods.

Materials and Methods: This was a prospective, randomized, double-blinded clinical study. Forty-two patients who tore their ACL were enrolled and underwent ACL reconstruction with a bone-patellar tendon-bone autograft. Following reconstruction, patients were randomized to undergo accelerated rehabilitation (a 19 week program) or nonaccelerated rehabilitation (a 32 week program) (1). The limits of knee motion, the amount of weight bearing permitted, and the type of rehabilitation activity prescribed were similar for both programs; however, subjects enrolled in the accelerated program performed these activities over a 19 week time period while those in the nonaccelerated program performed the same activities over a 32 week interval. The exercises and time frame over which they were administered were chosen to emphasize a significant difference in the magnitude of strain the healing ACL graft would be exposed to during the rehabilitation period based on prior measurements of ACL biomechanics. At the time of surgery, and 6, 12, and 24 months later, SF samples were collected and stored at -80°C. Commercial assays were used to measure: C-propeptide of Type II procollagen (CPII): a measure of type II collagen synthesis; COL2 3⁄4 C Longmono epitope (C2C): a measure of cleavage of type II collagen by collagenase; and chondroitin sulphate 846 epitope (CS-846): a marker of aggrecan turnover in the SF (IBEX Pharmaceuticals Inc., Montreal, QC). Comparisons between the accelerated and nonaccelerated treatment groups were made with a repeated measures analysis of variance. These analyses included testing for a treatment effect (accelerated vs. nonaccelerated rehabilitation programs), a time effect, and a treatment group-time interaction.

Results: The two rehabilitation programs had a similar effect on articular cartilage metabolism (Figs. 1, 2, 3). There was no difference in levels for CPII and C2C between the accelerated and non-accelerated programs (ANOVA: group p=0.48 for C2C and p=0.15 for CPII; treatment group-time interaction p= 0.31 and 0.16 respectively). Similarly, there was no difference in the level of aggrecan turnover (CS-846) between groups (p=0.45). Levels of CPII, C2C, and CS-846 responded in a similar pattern for both rehabilitation treatments during healing. When data were analyzed as a ratio of injured to uninjured leg, similar results were observed for CS-846 and C2C: The ratio of injured to uninjured CPII was less for the accelerated than nonaccelerated group at the 24 month follow-up interval (0.86 vs. 1.00; p=0.03).

Discussion: This work demonstrated that accelerated rehabilitation results in the same alteration of biomarkers of articular cartilage metabolism as nonaccelerated rehabilitation. This work provides insight into the temporal response of cartilage constituents following ACL injury, reconstruction and rehabilitation and supports the findings of a pilot study by Beynnon et al.(1)

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Fig 1.) Synthesis of type II collagen (CPII) in the injured knee

Fig 2.) Cleavage of type II collagen (C2C) in the injured knee

Fig. 3) Turnover of aggrecan (CS-846) in the injured knee.