Restored Tissue Structural Properties and Knee Joint Laxity: Strong Predictors of Risk of Post-Traumatic Knee Osteoarthritis Following ACL Injury

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Introduction: Anterior cruciate ligament (ACL) reconstruction has been long considered as the gold standard in treatment of ACL injuries. The primary goal of ACL reconstruction is to re-approximate normal joint biomechanics as much as possible. However, patients who have suffered ACL injury are at high risk of developing knee osteoarthritis (OA) within 10-15 years post-injury, even with ACL reconstruction [1]. No study has yet demonstrated that a better graft or surgical technique can result in decreased risk of post-traumatic OA in the human population. Recent validation of a porcine large animal model [2,3] allows for novel testing of hypotheses around the causative relationship between outcomes of ACL repair/reconstruction and potential risk of OA. Previous investigators have hypothesized that the development of OA in a large animal model would be dependent on how well a surgical procedure (repair OR reconstruction) restored normal joint biomechanics. In this study, we hypothesized specifically that the graft (or repaired ACL) yield load and cross sectional area, as well as joint laxity, would be strong predictors of post-traumatic OA risk after an ACL injury.

Methods: Following IACUC approval, 18 adolescent Yucatan mini-pigs (4 months of age) underwent ACL transection. The pigs were randomized into one of three groups: 1) no further treatment (ACL-T), 2) conventional ACL reconstruction (ACL-R) using bone-patellar tendon-bone allograft, or 3) bio-enhanced ACL repair (REPAIR) [3]. Animals were euthanized after 12 months, and both the surgical and contralateral limbs were tested for knee A-P laxity and ACL/graft mechanical properties. Biomechanical testing was performed using a universal testing machine (MTS, Eden Prairie, MN). The A-P knee laxity was measured at 30º of knee flexion through 12 cycles of ±40 N A-P shear force. The capsule and other ligaments were then dissected and ACL/graft size was measured using calipers [3]. Tissue mechanical properties were determined at 30º of knee flexion under a ramping tensile load to failure. Finally, macroscopic cartilage damage was assessed by measuring the area of all visible lesions across the tibiofemoral cartilage using India Ink and calipers [3]. Measurements were conducted by two independent examiners, blind to the treatment, and averaged values were used. Tissue structural properties and joint laxity were normalized to the contralateral intact leg (Surgical-Intact). A general linear model, an ANOVA with post-hoc Bonferroni, and multiple linear regression models were used for statistical analyses. Correlations were classified as poor (<0.4), good (0.4-0.7) and strong (≥0.75) based on determined Pearson’s correlation coefficient (r) [4].

Results: The linear regression model (Figure 1) demonstrated strong correlations between total cartilage lesion area and normalized ACL/graft yield strength in all groups (ACL-R [r=0.99, p<0.0005], REPAIR [r=-0.94, p=0.004], and ACL-T [r=-0.84, p=0.037]). Strong linear correlations were observed between total cartilage lesion area and normalized A-P knee laxity for the reconstructed and repaired groups but not the transected group (ACL-R [r=0.78, p=0.045], REPAIR [r=0.71, p=0.115], and ACL-T [r=0.24, p=0.647]). Finally, good to strong correlations were observed between normalized ACL/graft cross-sectional area and total cartilage area for all groups (ACL-R [r=0.75, p=0.141], REPAIR [r=-0.7, p=0.122], and ACL-T [r=-0.61, p=0.211]). In all cases, the closer that treated knees were to the intact knee in terms of ACL/graft yield load, A-P knee laxity and ACL/graft cross-sectional area, the less cartilage damage was observed. The general linear model showed that treatment type is a significant factor in overall cartilage lesion area (p=0.022). Both ACL-R (74.5±77.6 mm²) and REPAIR (20.9±13.0 mm²) specimens demonstrated less cartilage lesion area compared to the specimens with no treatment (125.9±61.6 mm²). REPAIR resulted in minimum cartilage damage which was statistically significant compared to no treatment (p=0.020). As previously reported [3], both ACL-R (-546.8±269.3 N) and REPAIR (-743.5±411.7 N) resulted in significantly smaller normalized (less variation from intact) ACL yield strength compared to no treatment option (-1310±182.9 N, p=0.035). REPAIR and ACL-R resulted in similar normalized ACL yield loads (p=0.982). Similarly, both ACL-R (0.5±1.3 mm) and REPAIR (1.9±1.9 mm) resulted in smaller normalized A-P knee laxity compared to the specimens with no treatment (3.7±1.8 mm). These changes were only statistically significant between ACL-R and ACL-T groups (p=0.017). While both ACL-R (21.8±27.2 mm²) and REPAIR (1.4±53.4 mm²) resulted in greater ACL/graft cross-sectional area compared to the contralateral intact ACL, the specimens with no treatment (-12.0±32.0 mm²) demonstrated smaller ACL cross-sectional compared to intact. None of these differences were statistically significant.

Discussion: The results reported here support our hypothesis that the restored ACL/graft structural properties, both mechanical and anatomical, are valid predictors of risk of post-traumatic knee OA, regardless of treatment type (no treatment, ACL reconstruction or bio-enhanced ACL repair). With the advent of advanced imaging techniques that are able to accurately predict the mechanical properties and cross sectional area of an ACL graft or repaired ACL [5], these data in a large animal model suggest that in the future we may be able to use this imaging technique to begin to understand which patients are at risk for...
developing knee OA after an ACL injury. Additionally, the restored A-P knee laxity due to surgically recovered tissue properties and function was confirmed to be a strong and valid predictor of knee OA following ACL injury, further supporting our hypothesis. As previously reported [3], both conventional ACL reconstruction and bio-enhanced ACL repair result in reasonable tissue structural properties (yield strength and cross-sectional area) and also improve the abnormal A-P knee laxity which occurs in the porcine knee after ACL transection. In contrast, no treatment of the ACL tear led to significant loss of tissue structural properties and increased knee laxity. Interestingly, although the groups undergoing ACL reconstruction and bio-enhanced ACL repair had similar mechanical properties, the group undergoing bio-enhanced repair showed significantly less knee OA. This may be in fact due to the physiologic recovery of ACL and the preservation of the proprioceptive nerve fibers within the ligament, or to a change in the early inflammatory response to injury caused by the bio-enhanced scaffold within the joint. Further studies are needed to improve our understanding of the mechanisms behind this finding. In summary, the current findings support the hypothesis that the risk of post-traumatic knee OA is a function of how well a surgical procedure (repair OR reconstruction) restores tissue structural properties and normal joint biomechanics.

Significance: A better understanding of associated risk factors (predictors) for post-traumatic knee OA may improve current surgical and rehabilitation strategies, and in turn minimize the risk of knee OA development following ACL injury.

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Figure 1: Linear regression models for predictors of post-traumatic knee OA