Evaluation of Partial Transection Versus Synovial Debridement of the ACL as Novel Canine Models for Management of ACL Injuries

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Introduction: Anterior cruciate ligament (ACL) tears are common injuries in athletes. Besides the high morbidity and loss of function associated with ACL trauma, an ACL tear significantly increases the risk of early onset knee osteoarthritis (OA). Most commonly, ACL tears are initially managed by R.I.C.E. (rest, ice, compression and elevation) and non-steroidal anti-inflammatory drugs for weeks to months to prepare the knee for surgical reconstruction or long-term nonsurgical management. While this protocol is considered standard of care, it has not been comprehensively studied and has potential to be detrimental in terms of biologic effects (i.e., inflammatory and degradative mediators) not being fully addressed, which may contribute to the progression of OA. Importantly, the normal ACL is intra-articular, but extra-synovial as it has its own synovial lining. This synovial sheath is a critically important structure for ACL and joint health, and although it is injured in all types of ACL sprains, it has been given little attention with respect to its roles in post-ACL mechanisms of disease or management. One major hurdle for investigating these important clinical questions is a lack of valid, translational animal models for studying them. Canine models have been suggested as valid models for translational research for the human knee. The purpose of this study was to characterize the effects of partial transection versus synovial debridement of the ACL in dogs towards validating novel translational models for subsequent research into acute management of ACL injuries. The clinical questions to be addressed were: 1) is an intact ACL with synovial debridement (exposed ACL) associated with clinically relevant whole-joint inflammation and degradation compared to partial transection of the ACL (partial tear ACL)? and 2) Do the biologic components of ACL injury influence pain, lameness and development of OA?

Methods: Twenty-seven adult hound-mix (mean body weight = 29.0 kg) purpose-bred research dogs were used. Dogs were randomly assigned to one of three ACL-status groups: sham control (intact ACL), exposed ACL and partial tear ACL. For the sham control group, the ACL was only probed (Fig 1A). For the exposed ACL group, the synovial sheath was removed from the ACL to expose it to the joint (i.e., no longer extrasynovial) (Fig 1B). For the partial tear ACL group, a partial transection of the ACL was created (i.e., anterior-medial band transected at its approximate mid-point) (Fig 1C). Orthopedic examination to assess knee comfortable range of motion (CROM), pain, and effusion, and clinical lameness and function assessments were performed on each dog at 1, 2, 3, 5 and 8 weeks after surgery. At 8 weeks post-operatively, histologic scoring of the joint tissues were performed using the OARSI histologic scoring system for canine osteoarthritis, while the histologic scoring system for cruciate ligaments was used for ACL tissue.²,³
**Results:** The partial tear ACL group was associated with significantly \((p<0.05)\) more lameness, pain, effusion and less function and CROM than the sham control group at all-time points after insult. The exposed ACL group had significantly \((p<0.05)\) more effusion and less CROM compared to the sham control group at all post-operative time points. At weeks 1, 3 and 5, the exposed ACL group was associated with significantly \((p<0.05)\) more lameness and pain, and less function than the sham control group. At week 8, the partial tear ACL group had significantly \((p<0.05)\) less function compared to exposed ACL group, and the exposed ACL group was associated with significantly \((p<0.05)\) more pain than the sham control group. No significant differences in function, lameness, pain and CROM were seen within the sham control group over time. In both exposed and partial tear ACL groups, there was more severe (and often significant \([p<0.05]\)) lameness, pain, effusion, and loss of function and CROM over time. Within the sham control group, significantly \((p<0.05)\) more effusion was noted at weeks 1, 2 and 3 than at the pre-operative time point.

The partial tear ACL group was associated with significantly more severe ACL pathology compared to the exposed ACL group \((p<0.001)\) and sham control group \((p<0.001)\) (Fig 2A). The exposed ACL group had higher (more severe) scores for ACL pathology compared to the sham control group, however, this difference was not statistically significant \((p=0.40)\). The partial tear ACL group (Fig 2B,C) had more severe whole-joint pathology compared to the exposed ACL group and sham control group, but only the exposed ACL group was significant \((p<0.05)\). No statistically significant \((p>0.05)\) differences in whole-joint pathology were observed between exposed ACL and sham control groups.

**Discussion:** The most novel findings from this study are the data showing the effects of synovial debridement of the ACL on function of the knee. This new translational model in which we arthroscopically debrided the synovial sheath from the ACL in order to expose it to the articular environment was associated with clinically-relevant detrimental effects on the knee, similar to those reported for grade I ACL sprains. This model was designed to help delineate biologic from biomechanical effects associated with ACL injury in that the ACL’s synovial lining is removed, allowing biochemical interactions between the ACL and all other intra-articular tissues (biology of ACL injury) without significantly affecting the material properties of the ACL (biomechanics of ACL injury). The data suggest that this goal was accomplished based on the significantly detrimental effects of this insult on knee pain, effusion, function, and range of motion, mild effects on ACL histology, and minimal effects on whole-joint pathology. Further research into the long term effects of this insult are needed, but these data suggest that the synovial sheath is a critically important structure for ACL and whole-joint health, and requires increased attention with respect to its roles in post-ACL mechanisms of disease and treatment.

**Significance:** Novel translational models were successfully developed in dogs to evaluate partial transection versus synovial debridement of the ACL. Combined biologic and biomechanical insults to the ACL were associated with clinically relevant functional impairments and whole-joint pathology with the biologic component (ACL synovial sheath debridement) contributing substantially.
Figure 2: ACL and whole-joint pathology (partial tear group). A) ACL (HE), B) synovium (HE), C) femoral condyle (Toluidine blue)

Figure 1: ACL-status groups. A) sham control (intact), B) exposed, C) partial tear

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