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Title: Does Extended Preoperative Rehabilitation Influence Outcomes 2 Years after ACL Reconstruction?
A Comparative Effectiveness Study between MOON and Delaware-Oslo ACL Cohorts

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Abstract:

Background: Rehabilitation prior to anterior cruciate ligament (ACL) reconstruction (ACLR) is effective at improving post-surgical outcomes, at least in the short-term. Less is known about the effects of pre-operative rehabilitation on functional outcomes and return to sport rates 2 years after reconstruction.

Purpose: The purpose of this study was to compare functional outcomes 2 years after ACLR in a cohort that underwent additional pre-operative rehabilitation including progressive strengthening and neuromuscular training after impairments were resolved compared to a non-experimental cohort. We hypothesized that the cohort treated with extended pre-operative rehabilitation would have superior functional outcomes 2 years after ACLR.

Study Design: Cohort Study

Methods: This study compared outcomes after ACL rupture in an international cohort (Delaware-Oslo ACL Cohort, DOC) treated with extended pre-operative rehabilitation including neuromuscular training to data from the Multicenter Orthopedic Outcomes Network cohort (MOON), which did not undergo extended pre-operative rehabilitation. Inclusion and exclusion criteria from the DOC were applied to the MOON database to extract a homogeneous sample for comparison. Subjects achieved a quiet knee prior to ACLR and post-operative rehabilitation followed each cohort's respective criterion-based protocol. Subjects completed International Knee Documentation Committee Subjective Knee Form (IKDC) and Knee Injury and Osteoarthritis Outcome Score (KOOS) at enrollment and again 2 years after ACLR. Return to sport rates were calculated for each cohort at 2 years.

Results: After adjusting for baseline IKDC and KOOS scores, the DOC showed significant and clinically meaningful differences in IKDC and KOOS scores 2 years after ACLR. The DOC had a significantly higher ($p < .001$) percentage of patients returning to pre-injury sports (72%) compared to MOON (63%).

Conclusion: The cohort treated with additional pre-operative rehabilitation consisting of progressive strengthening and neuromuscular training followed by a criterion-based post-operative rehabilitation program had greater functional outcomes and return to sport rates 2 years after ACLR. Prehabilitation should be considered as an addition to the standard of care to maximize functional outcomes after ACLR.

Clinical Relevance: Progressive rehabilitation prior to ACLR should be considered as an addition to the standard of care to maximize functional outcomes after ACLR.

Key Terms: Knee, Return to Sport, Rehabilitation, Prehabilitation, ACL reconstruction, Outcomes

What is known about the subject: Rehabilitation prior to ACLR has not been robustly studied but has shown promise with better outcomes up to 2 years after surgery. Previous work, however, has not compared those with similar post-operative rehabilitation protocols.

What this study adds to existing knowledge: This study compared two cohorts that employed criterion based rehabilitation progressions supported in the literature after surgery. The MOON cohort was designed as a benchmark for outcomes in the United States. This study confirms that pre-operative rehab leads to superior outcomes and return to sports rates after ACLR.

Introduction:

Early anterior cruciate ligament (ACL) reconstruction (ACLR) remains the gold standard of treatment for active individuals with ACL ruptures in the United States,^{20,22} with up to 175,000 reconstructions being performed annually.²⁸ Goals for ACLR include restoring primary passive restraint, returning to pre-injury activity and previous level of function, and preserving long-term knee joint health.^{20,22} Reconstruction, however, does not guarantee return to previous activity or functional levels, or prevention of post-traumatic knee osteoarthritis.^{9,10,20}

Large multicenter orthopedic registries have been developed and implemented to track outcomes after ACLR in the United States and abroad. The Multicenter Orthopedic Outcomes Network (MOON) registry pools data together from 7 orthopedic centers across the United States.²⁷ These centers are all highly active in orthopedic and sports clinical treatment and research, with unified pre-operative milestones to undergo ACLR, and a single criterion-based post-operative protocol with objective return to sport criteria.^{27,30} The MOON cohort can serve as the benchmark or usual care for comparative effectiveness studies to compare ACLR outcomes.²⁷

Rehabilitation prior to surgery, termed pre-operative rehabilitation, is the physical preparation for a period of immobility and reduced activity due to surgery. Few studies have explored the effects of prehabilitation on outcomes after ACLR.¹² Shaarani and colleagues completed a randomized controlled trial that found a 6 week pre-operative rehabilitation program led to improved functional performance and self-reported function up to 12 weeks after reconstruction.²⁵ The addition of neuromuscular training to pre-operative rehabilitation is another attempt to improve outcomes after ACL injury.^{5,6,13,14} Specifically, perturbation training, has been studied in conjunction with a pre-operative rehabilitation program⁸ and is currently under investigation for its use after surgery.²⁹ Grindem and colleagues compared functional outcome measures 2 years after ACLR in the Norwegian half of our cohort to usual

care as benchmarked by the Norwegian Knee Ligament Registry (NKLK).¹¹ There were statistically significant and clinically meaningfully better outcomes in the Delaware-Oslo ACL Cohort (DOC) as evidenced by higher Knee Injury and Osteoarthritis Outcome (KOOS) Scores. The limitation of this study, however, is the rehabilitation in the NKLK was not standardized. The question remains how the progressive preoperative rehabilitation that includes neuromuscular training affects outcomes after ACLR when both cohorts receive otherwise similar care.

The purpose of this study was to compare functional outcomes 2 years after ACLR in a cohort that underwent additional pre-operative rehabilitation including progressive strengthening and neuromuscular training after impairments were resolved compared to a non-experimental reference group (MOON ACL cohort). We hypothesized that the cohort treated with extended pre-operative rehabilitation would have superior functional outcomes 2 years after ACLR. The implications of this research could lead to changes in the standards of care prior to undergoing reconstruction after ACL injury.

Methods:

This is a cohort study comparing outcomes in an international cohort (Delaware-Oslo ACL Cohort, DOC) treated with extended pre-operative rehabilitation including neuromuscular training with data from a non-experimental cohort (MOON ACL consortium). Outcomes of interest include pre- and post-operative International Knee Documentation Committee subjective knee form (IKDC)² scores, as well as KOOS²⁴ scores and return to pre-injury sports (RTS) rates. Eighty-four subjects from the Norwegian arm of the Delaware-Oslo ACL cohort were previously included in the comparison to the NKLK by Grindem and colleagues described above.¹¹

Subjects

The Delaware-Oslo ACL cohort is an ongoing international prospective collaboration evaluating the effects of neuromuscular training after ACL injury and reconstruction. This collaboration includes 150 subjects from the University of Delaware in the United States, and 150 subjects from the Norwegian Research Center for Active Rehabilitation, Norwegian School Sport Sciences in Oslo, Norway. Subjects were enrolled at both centers between 2007 and 2012. Subjects were included if they had a unilateral primary ACL rupture within 7 months of enrollment, and participated in level I or II sports (IKDC activity classification) greater than 50 hours per year prior to injury.⁴ Subjects were excluded if they had a concomitant grade III ligamentous injury, a full thickness articular cartilage lesion larger than 1 cm², a symptomatic meniscal tear, a potentially repairable meniscal tear, or a history of previous injury or surgery of the uninvolved knee. All subjects underwent initial impairment resolution (little to no swelling or pain, full range of motion, 70% quadriceps strength index) followed by progressive strengthening and neuromuscular training called perturbation training, as previously described by Eitzen.⁸ Following completion of these additional training sessions, subjects selected to undergo ACLR or remain non-operatively managed. While all subjects were followed, only the subjects who underwent ACLR are included in this analysis. Those from the DOC who did not immediately undergo reconstruction following training continued on a home exercise program, if needed, for maintenance until reconstruction was performed. All subjects after ACLR underwent a criterion-based post-operative rehabilitation protocol with strict RTS criteria.¹ The University of Delaware Institutional Review Board and Region Ethics Committee for South East Norway approved all aspects of this study, and written informed consent was obtained for all subjects prior to enrollment.

The MOON cohort consists of subjects enrolled between 2002 and 2008 from 7 orthopedic/sports medicine centers around the United States. Subjects were included if they were scheduled to undergo a unilateral ACLR and were between the ages of 10 and 85 years. Subjects were

enrolled at time of presentation to the orthopedic surgeon, and followed prospectively after surgery. This cohort is intended to be community-based, with all ages, activity levels, injury history, and concomitant injury included.²⁷ All subjects after ACLR underwent a criterion-based post-operative rehabilitation protocol with strict RTS criteria.³⁰ Institutional Review Board approval was obtained from all participating centers and written informed consent was obtained for all subjects prior to enrollment.

For this study, inclusion and exclusion criteria from the DOC were applied to the MOON cohort and only those who met the criteria for DOC described above were included. MOON data were extracted based on these criteria and de-identified data were provided for analysis. Subjects whose imaging revealed a potentially repairable meniscal injury were excluded from enrollment in the DOC. During reconstruction, however, 11% of subjects from the DOC had concomitant meniscal repair despite initial presentation on imaging, and therefore, we included those with concomitant meniscal repair from the MOON dataset. Surgical variables recorded included graft type, concomitant meniscal procedures and articular cartilage pathology. (Figure 1.)

Criteria for Reconstruction

Both cohorts used guidelines to determine when athletes were ready to undergo ACLR. The recommendations for the DOC subjects to undergo ACLR were little to no knee joint effusion, symmetrical knee range of motion, no obvious gait impairments and a minimum of 70% quadriceps strength index (quiet knee). MOON preoperative guidelines included no obvious gait impairments, knee range of motion from 0-120, minimal knee joint effusion, and the ability to complete 20 straight leg raises without a lag.

Rehabilitation

Postoperative rehabilitation for the DOC subjects followed a rigorous criterion-based protocol. Objective clinical criteria, such as pain, range of motion, quadriceps strength and activation, and

changes in knee joint effusion are used to monitor and determine progression through the different phases of postoperative rehabilitation. These criteria, in addition to functional performance testing and patient reported outcomes, are utilized in determining return to sport readiness for athletes. Subjects were followed for repeated testing at time-points of 6, 12, and 24 months following reconstruction. If subjects were not maintaining strength or functional levels required to return to sport, counseling was provided. The respective rehabilitation protocols can be found in the appendix.

The MOON cohort subjects followed a unified postoperative protocol regardless of at which location their surgery or rehabilitation was performed. This protocol is criterion-based, utilizing measures of pain, range of motion, functional strength, and movement quality to progress patients through the phases of rehabilitation. Return to sport readiness was determined by a combination of objective measures (functional performance testing, patient reported outcomes) and subjective measures (movement quality and confidence). Beyond those return to sport criteria, the MOON protocol also recommended isokinetic strength testing, vertical jump, and deceleration testing.

Outcome Measures

Subjects completed the IKDC and KOOS pre-operatively and again 2 years after ACLR. The IKDC is a valid and reliable measure commonly used in the ACL population.^{2,15} The minimal clinically important difference (MCID) for the IKDC is 11.5.¹⁵ The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a valid and reliable outcome measure commonly used in the ACL injured population to assess outcomes in knee pain, knee symptoms, knee function in daily activity, knee function in sporting activity, and knee related quality of life.^{23,24} The proposed MCID for each subscale is 10 points.²³

At enrollment, each subject was asked to report their primary sporting activity prior to injury. At 2 year follow-up, subjects were asked to name their primary sport currently (MOON) or if they had

returned to their pre-injury sport (DOC). Subjects were considered to have returned to sport if they were participating in their pre-injury sport 2 years after ACLR.

Statistical Analysis

Group differences were analyzed using chi square for nominal variables and t tests for continuous variables. To account for differences in baseline IKDC, a one-way analysis of covariance was used to compare 2 year IKDC scores between groups with baseline IKDC scores as a covariate. To account for differences in baseline KOOS, a one-way analysis of covariance was used to compare 2 year KOOS scores between groups with baseline KOOS scores as a covariate for each subscale. Because differences were found between groups in the proportion of concomitant meniscal surgery, analysis of variance was used to assess the interaction of group and meniscal surgery on 2 year IKDC scores. Because differences were found between groups in proportion of graft types used for ACLR, analysis of variance was used to assess the interaction of group and graft type on 2 year IKDC scores. All statistical analyses were performed using PASW version 23 (SPSS, Inc, IBM Company, Chicago, Illinois).

Results

Subjects who underwent ACLR from the DOC (n=192) and 1,995 subjects who met the DOC inclusion criteria were included from MOON. There were no differences between groups in age, sex, or body mass index (Figure 2). Baseline Marx scores were available in the MOON cohort (12.78 ± 4) but not the DOC. Surgical demographics revealed a higher proportion of patellar tendon autografts ($p = .001$) in the MOON cohort, and a higher proportion of hamstring autografts ($p = .006$) in the DOC cohort. There was also a significantly higher proportion of concomitant meniscal surgery performed ($p = 0.029$) in the MOON cohort (Figure 3). There were no significant group by meniscal procedure ($p = .345$) or group by graft type ($p = .073$) interactions on 2 year IKDC scores. The DOC cohort had significantly higher baseline IKDC scores compared to the MOON cohort (70 ± 13 ; 50 ± 17 ; $p < .001$), which also exceeded the MCID

(Figure 4). The DOC significantly improved from baseline to post-training (after prehab) in IKDC scores (70 ± 13 ; 77 ± 13 ; $p < .001$). Two years after reconstruction, 148 subjects for the DOC and 1994 subjects from MOON completed the IKDC. Controlling for baseline IKDC scores, the DOC cohort continued to have significantly higher IKDC scores at 2 years after ACLR (84 ± 25 ; 71 ± 32 ; $p < .001$), again exceeding the MCID (Figure 5). Post-hoc power analysis revealed the ability to detect a difference of 2 points on the IKDC between groups. Baseline KOOS scores were available for 1991 subjects in the MOON cohort and 58 subjects in the DOC. The DOC had significantly higher baseline KOOS scores than the MOON cohort across all subscales: pain (84 ± 11 ; 73 ± 17 ; $p < .001$), symptom (75 ± 14 ; 67 ± 18 ; $p < .001$), ADLs (93 ± 7 ; 82 ± 17 ; $p < .001$), sports/recreation (66 ± 19 ; 48 ± 29 ; $p < .001$), and quality of life (51 ± 19 ; 37 ± 20 ; $p < .001$). The DOC cohort, after controlling for baseline KOOS scores, continued to have higher and clinically meaningful differences in scores at 2 years on the pain (94 ± 10 ; 78 ± 33 ; $p = .004$), symptom (89 ± 12 ; 72 ± 32 ; $p < .001$), ADLs (98 ± 5 ; 82 ± 34 ; $p = .006$), sports/recreation (85 ± 18 ; 70 ± 33 ; $p < .001$), and quality of life (76 ± 20 ; 64 ± 32 ; $p = .072$) subscales of the KOOS (Figure 6). Return to sport rates were significantly higher in the DOC cohort (72%) compared to the MOON cohort (63%) ($p < .001$).

Discussion

The purpose of this study was to compare functional outcomes 2 years after ACLR in the DOC that underwent additional progressive pre-operative rehabilitation including neuromuscular training compared to the MOON ACL cohort. The primary findings of this study are the DOC had significantly higher and clinically meaningful patient-reported function, and higher RTS rates, 2 years after ACLR. Grindem¹¹ and colleagues found this pre-operative rehabilitation led to higher KOOS scores 2 years after reconstruction compared to the patients in the NKLR, however, the NKLR post operative rehabilitation was not standardized. Conversely, the subjects in the MOON cohort received specified post-operative care at facilities that were part of large orthopedic and sports medicine research centers, which allowed for a more homogeneous comparison between cohorts. This study did not determine what the optimal

pre-operative rehabilitation program is, and did not differentiate which aspect of a program is most important (i.e. progressive strengthening, neuromuscular training), but does suggest giving patients additional rehabilitation beyond a quiet knee (full range of motion and quadriceps activation, little to no pain or joint effusion) before surgery may lead to meaningful improved outcomes 2 years after ACLR.

Pre-operative IKDC scores were higher in the DOC and may have been related to differences in the timing of baseline testing between cohorts. The baseline testing may have occurred prior to impairment resolution in the MOON cohort, however, the MOON protocol called for impairments to be resolved prior to undergoing reconstruction.³⁰ Both cohorts had to achieve minimum criteria before surgery, ensuring that neither cohort had substantial impairments going into reconstruction. Several studies have shown pre-operative muscle performance maximization and ROM deficit minimization related to optimized post-operative outcomes.^{7,16,18,21} This is also consistent with previously published findings that pre-operative outcome scores significantly predict post-operative outcome scores.²⁶ Eitzen and colleagues found a 5 week pre-operative program can lead to improved functional outcomes after ACLR.⁸ Our overall findings are consistent with both Eitzen and Grindem in that progressive pre-operative rehabilitation is an important factor to maximize post-operative outcomes.

While each cohort used a different rehabilitation protocol for pre and post-operative rehabilitation, both protocols utilized a criterion-based approach. Criterion-based rehabilitation protocols utilizing tissue healing timeframes, factors associated with outcomes, and expert opinion are considered the most evidence-based protocols to our current knowledge. Both of the protocols used have been published and are considered standards of care after ACL injury.^{1,30} The primary difference between the post-operative protocols is the DOC protocol used primarily objective criteria and the MOON cohort used a mixture of objective and subjective criteria for program advancement. Patients in the DOC also underwent structured follow-up testing at 6 months and 1 year after ACLR, which may have benefited them in terms of progressing home exercise programs or providing counseling and/or

consultation on current functional status. While differences between graft type and meniscal procedure proportions between cohorts also have the potential to influence outcome scores at 2 years, our analysis of graft type and meniscal procedure on IKDC scores suggest that differences in proportions of surgical variables between cohorts did not have an effect on the outcome scores.

The DOC had a significantly higher RTS rate 2 years after ACLR compared to the MOON cohort. The MOON cohort return to pre-injury sport rate of 63% is consistent with the Ardern meta-analysis that reported 65% return to pre-injury sports.³ The DOC RTS percentage rate of 72% exceeded both MOON and that reported by Ardern. Objective return to sport criteria were used in both cohorts to determine individual readiness to return sport among patients. There is currently no consensus on specific RTS criteria, however, the use of clinical, functional performance, and patient-reported outcome measures have been suggested as the current standards after ACLR.¹⁷ The DOC criteria used higher cutoff scores than the MOON criteria, which ensured higher symmetry between limbs prior to clearance for RTS. Functional performance symmetry restoration is needed to maximize patient-reported functional recovery,¹⁹ and may also explain some of the variation in 2 year outcomes scores between cohorts.

A limitation of our study is that comparing two separate cohorts does not allow for a true cause and effect evaluation of extended pre-operative rehabilitation to post-operative outcomes. There also were some differences in the post-operative rehabilitation programs, graft types, and the return to sport criteria that may have affected the outcomes. The strengths of this study are the large sizes of the cohorts, and the application of similar inclusion and exclusion criteria to both cohorts for a homogeneous comparison, and the use of criterion-based post-operative protocols. Future studies should use the randomized control trial study design to better assess the value of preoperative rehabilitation after ACL rupture.

Conclusion

The cohort treated with pre-operative rehabilitation consisting of progressive strengthening and neuromuscular training had higher functional outcomes and return to sport rates compared to the benchmark cohort that also used criterion-based post-operative rehabilitation program 2 years after ACLR. The standard of care in the United States is to achieve a quiet knee (little to no pain and effusion, full range of motion and good quadriceps activation) prior to undergoing reconstruction. While achieving a quiet knee prior to surgery may thwart surgical complications such as arthrofibrosis, it may not be enough to maximize functional outcomes even with rigorous post-op rehabilitation. Progressive pre-operative rehabilitation prior to ACLR should be considered as an addition to the standard of care to maximize functional outcomes after ACLR.

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Figure Legends

- Figure 1 Testing timeline differences between cohorts
- Figure 2 Baseline Demographics between Cohorts
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- Figure 5 IKDC scores 2 years after ACLR
- Figure 6 KOOS subscale scores 2 years after ACLR

Figure 1

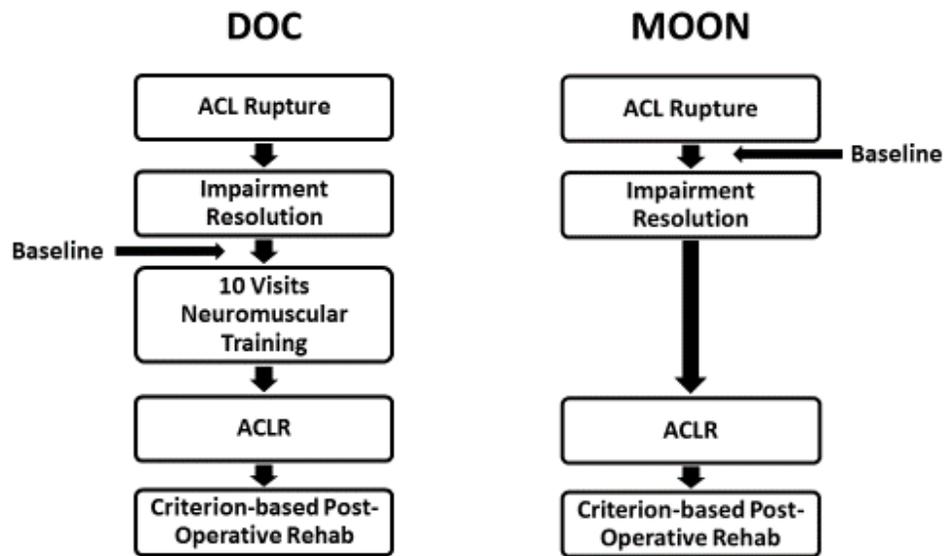


Figure 2. Baseline demographics between cohorts

	Delaware-Oslo (n=192)	MOON (n=1995)	P Value
Age	24.7 ± 9	24.3 ± 10	.612
Sex	55% men	54% men	.144
BMI	24.5 ± 4	25 ± 4	.231
Time from injury to enrollment	1.9 ± 1 months	< 6 months	

Key: Continuous variables are listed as mean ± standard deviation; categorical variables are listed as frequencies (percentages); DOC – Delaware-Oslo Cohort; MOON – Multicenter Orthopaedics Outcome Network; BMI – body mass index.

Figure 3. Surgical demographics between cohorts

	DOC n=192	MOON n=1995	P-Value
Patellar Tendon Autograft	21%	48%	.001
Hamstring Autograft	51%	36%	.006
Soft-tissue Allograft	28%	16%	.005
No Meniscal Procedure	60%	46%	.029
Meniscal Excision	18%	28%	.017
Meniscal Repair	11%	14%	.301
Meniscal Trephination	2%	2%	1.00
Combination of Meniscal Procedures	9%	11%	.433
Time from ACLR to 2 yr	2.1 ± .02 yrs	2.4 ± 0.4 yrs	.532

Figure 4

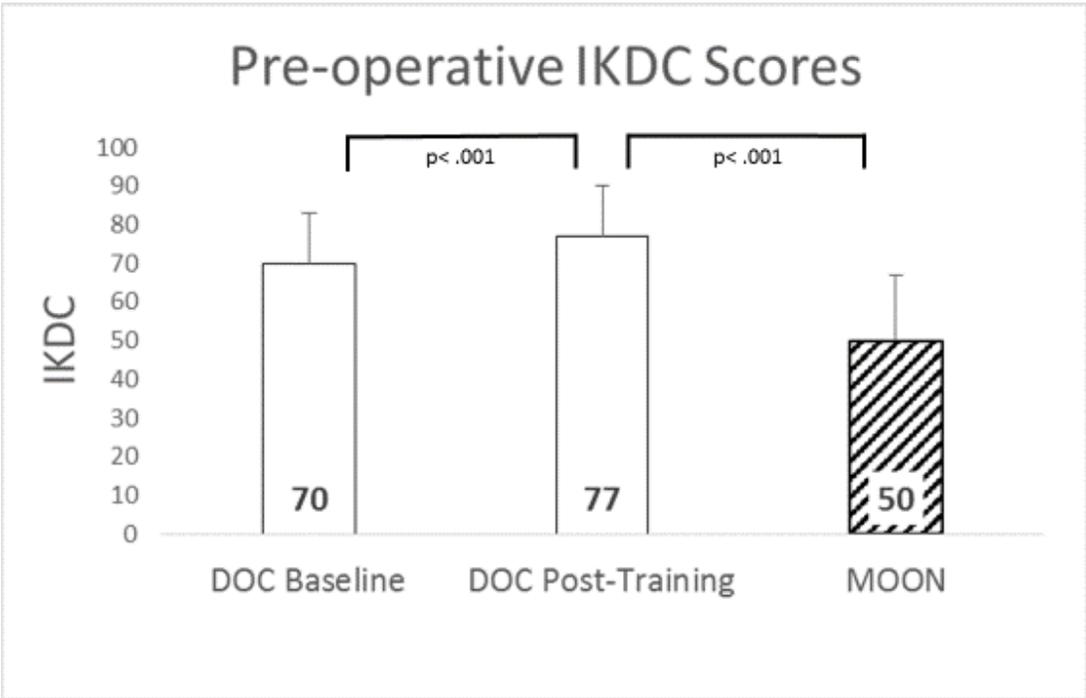


Figure 5

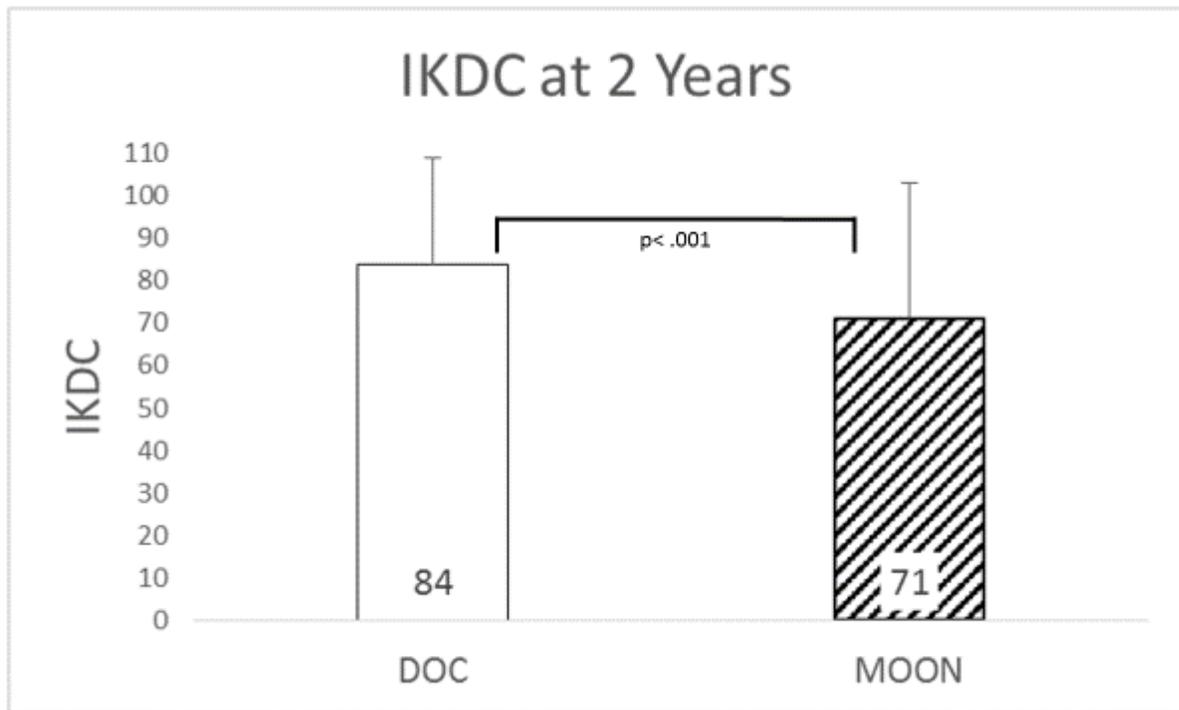
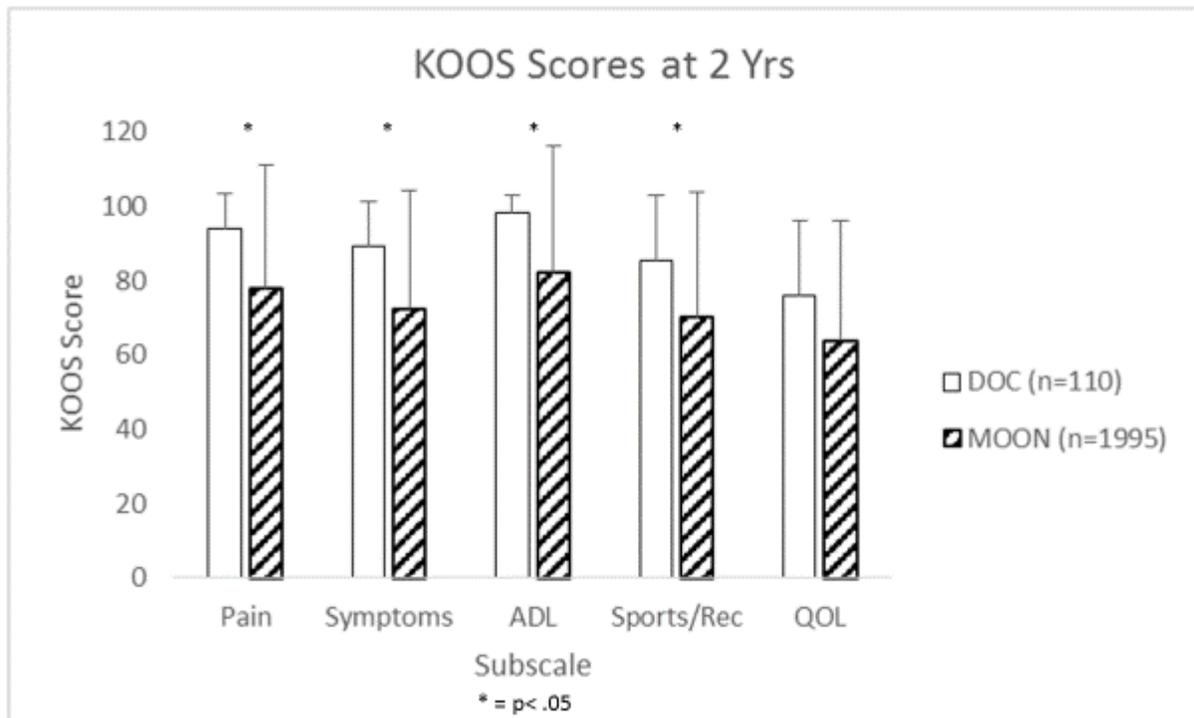


Figure 6



Appendix:

Extended Pre-operative Rehabilitation Program: This 5 week program consists of 10 physical therapy sessions, following the achievement of a quiet knee, which emphasizes progressive quadriceps strengthening and neuromuscular training in the form of perturbation training. The quadriceps strengthening program consists of both open and closed chain exercises, with progression guided by the use of soreness rules (table re-print of soreness rules). Perturbation training utilizes balance and stability exercises performed with a rockerboard, rollerboard, and stationary platform. A perturbation of the surface was created by the therapist with a variety of forces and torques applied to the involved limb in various directions and amplitudes but within a controlled and progressive manner. Progression of perturbation training was according to guidelines established by the University of Delaware (reprint of appendix B from JOSPT article).