Øiestad, B. E., Holm, I., Aune, A. K., Gunderson, R., Myklebust, G., Engebretsen, L., Fosdahl, M. A., Risberg, M. A. (2010). Knee function and prevalence of knee osteoarthritis after anterior cruciate ligament reconstruction: a prospective study with 10 to 15 years of follow-up. *American Journal of Sports Medicine, 38*, 2201-2210.

Dette er siste tekst-versjon av artikkelen, og den kan inneholde ubetydelige forskjeller fra forlagets pdf-versjon. Forlagets pdf-versjon finner du på ajs.sagepub.com: <u>http://dx.doi.org/10.1177/0363546510373876</u>

This is the final text version of the article, and it may contain insignificant differences from the journal's pdf version. The original publication is available at ajs.sagepub.com: <u>http://dx.doi.org/10.1177/0363546510373876</u>

Knee function and prevalence of knee osteoarthritis after anterior cruciate ligament reconstruction. A prospective study with 10-15 years follow-up

Britt Elin Øiestad^{1,7}, Inger Holm^{2,6}, Arne Kristian Aune³, Ragnhild Gunderson⁴, Grethe Myklebust⁵, Lars Engebretsen^{6,7}, Merete Aarsland Fosdahl², May Arna Risberg^{1, 5,7}

¹Norwegian research centre for Active Rehabilitation (NAR)
² Department of Rehabilitation, Oslo University Hospital Rikshospitalet
³Drammen Private Hospital
⁴Department of Radiology, Oslo University Hospital Rikshospitalet
⁵Department of Sport Medicine, Norwegian School of Sport Sciences
⁶Faculty of Medicine, University of Oslo
⁷Department of Orthopaedics, Oslo University Hospital Ullevaal

Corresponding author: Britt Elin Øiestad Hjelp 24 NIMI Ullevaal Pb. 3843 Ullevål stadion 0805 Oslo Norway Telephone: 0047-92803089 Fax: 0047-23265667

Acknowledgement This study was funded by the South-Eastern Norway Regional Health Authority through the Osteoarthritis Research Group.

Abstract

Background: Few prospective long term studies of more than 10 years have reported changes in knee function and radiological outcomes after anterior cruciate ligament (ACL) reconstruction.

Purpose: To examine changes in knee function from 6 month to 10-15 years after ACL reconstruction, and to compare knee function outcomes over time for subjects with isolated ACL injury to those with combined ACL and meniscal injury and/or chondral lesion and/or medial collateral ligament (MCL) injury. Furthermore, the aim was to compare the prevalence of radiographic and symptomatic radiographic knee OA between subjects with isolated ACL injuries to those with combined ACL and meniscal and/or chondral lesions 10-15 years after ACL reconstruction.

Study design: Prospective cohort study.

Methods: Follow-up evaluations were performed on 221 subjects at 6 months, 1 year, 2 years, and 10-15 years after ACL reconstruction with bone-patellar-tendon-bone (BPTB) autograft. Outcome measurements were: KT-1000 arthrometer, Lachman and pivot shift tests, Cincinnati knee score, isokinetic muscle strength tests, hop tests, visual analogue scale (VAS) for pain, Tegner activity scale, and the Kellgren and Lawrence (K&L) classification.

Results: One hundred and eighty-one subjects (82%) were evaluated at the 10-15 year follow-up. A significant improvement over time was revealed for all prospective outcomes of knee function. No significant differences in knee function over time were detected between the isolated and combined injury groups. Subjects with combined injury had significantly higher prevalence of radiographic knee OA compared to those with isolated injury (80% and 62%) (p=.008), but no significant group differences were shown for symptomatic radiographic knee OA (46% and 32%) (p=.053).

Conclusion: An overall improvement in knee function outcomes was detected from 6 months to 10-15 years after ACL reconstruction for both individuals with isolated and combined ACL injury, but significantly higher prevalence of radiographic knee OA was found for individuals with combined injuries.

Keywords: ACL reconstruction, knee function, knee osteoarthritis, isolated and combined injury, long term follow-up

INTRODUCTION

Anterior cruciate ligament (ACL) injuries are common in young athletic individuals. The treatment method often includes ACL reconstruction with the aim of restoring the mechanical stability of the knee joint and re-establishing knee function.⁵² Studies have shown that subjects with ACL reconstruction have good clinical outcomes and knee function more than 10 years after surgery, however, few prospective studies have included evaluation of self-reported knee function, muscle strength, and hop tests over time for more than 10 years.^{2, 43, 27} Furthermore, the reported prevalence of radiographic knee OA has varied from less than 10% to more than 90%.^{12, 14, 18, 27, 30, 54} A recent systematic review by our group showed that studies with the highest methodological quality reported up to 13% radiographic tibiofemoral OA for isolated ACL injuries, and between 21% and 48% for subjects with combined ACL and meniscal injuries, more than 10 years after the injury.³⁵ The long term follow-up studies of subjects with ACL injuries in orthopaedic journals usually only report radiographic knee OA. However, symptomatic radiographic knee OA should also be studied.⁴²

Several factors may influence the development of knee OA in individuals with ACL reconstruction. Meniscal tears with subsequent partial resections, as well as chondral lesions at the time of the ACL injury have shown to increase the prevalence of radiographic knee OA.^{29, 51} However, less is known about the influence of additional injuries in patients with symptomatic radiographic OA. Despite the growing number of studies that have reported long term consequences of ACL injuries,^{23, 25, 28, 31, 32, 40, 55} little knowledge exists on the long term functional and radiological outcomes for subgroups of subjects with isolated injuries compared to those with combined injuries. The existing studies are heterogeneous due to differences in study populations, treatment procedures, and radiological methods. In addition, a majority of the existing studies have demonstrated methodological weaknesses, such as retrospective study design, small sample sizes, and high drop-out rates.³⁵ Thus, there is a need for prospective studies of subjects with ACL injuries that report functional and radiological outcomes. Therefore, the aim of the present study was to examine changes in knee function from 6 month to 10-15 years after ACL reconstruction, and to compare knee function over time for subjects with isolated ACL injury to those with combined ACL and meniscal injury and/or chondral lesion and/or medial collateral ligament (MCL) injury. Furthermore, the aim was to compare the prevalence of radiographic and symptomatic radiographic knee OA between subjects with isolated ACL injuries and those with combined ACL and meniscal and/or chondral lesions and/or MCL injury 10-15 years after ACL reconstruction.

MATERIALS AND METHODS

Two hundred and twenty-one subjects scheduled for ACL reconstruction were included consecutively in studies from 1990 to 1997.^{7, 46, 47} The inclusion criteria were: age between 15 and 50 years; isolated ACL injury or combined with meniscal injury, MCL injury, or chondral lesion. The exclusion criteria were: other major injuries to the lower extremities less than 1 year before surgery, and cruciate ligament injuries to the contralateral knee. Follow-up evaluations were performed at 6 months, 1 year, 2 years, and 10-15 years postoperatively.

Arthroscopy was used to verify all the ACL ruptures and chondral lesions, and the additional meniscal injuries up to 10-15 years. The subjects were asked at the 10-15 year follow-up if they had suffered any re-injuries after the ACL reconstruction, or if they had gone through any surgical procedures after the ACL reconstruction. Surgical files were collected for all subjects that reported re-injuries. The surgeon files for all the

included patients from the index operation and for re-injuries have thoroughly been read to extract data on additional injuries and ACL graft ruptures. The MCL injuries were diagnosed by clinical assessment before surgery.

The combined injury group presented in this study consisted of subjects with ACL injury and meniscal injury suffered at the time of ACL reconstruction or during followup, either isolated or in combination with chondral lesion, or MCL injury. Subjects with chondral lesion (grade III and IV) at the femur condyle or at the tibia plateau, but with no meniscal injury, were included in the combined injury group. The isolated injury group involved subjects with isolated ACL injury from the index operation to the 10-15 year follow-up, as well as those with MCL injury reported to be healed at the time of ACL reconstruction.

The study was approved by the Regional Ethical Committee and The Data Inspectorate in Norway. All subjects signed an informed written consent, and could withdraw from participation in the study at any time point.

Surgical method

The subjects were reconstructed with bone-patellar-tendon-bone autograft (BPTB), either with mini-open or arthroscopic procedure.⁷ The arthroscopic procedure has previously been described by Aune et al.⁷: A 10-mm BPTB graft was harvested and trimmed to pass through a 9-mm diameter cannula. A guide wire was drilled using a drill guide (Linvatec Corp., Largo, Florida) from the medial side of the tibial tubercle (45°) to the tibial shaft, and advanced to the preserved ligament stump in the posterior portion of the ACL footprint. A femoral aimer with 7-mm offset (Linvatec Copr., Largo, Florida) was used (with the knee flexed) through the tibial tunnel and positioned at the 11-or 1o'clock (right or left knee, respectively). The graft was fixed with 7×25-mm titanium femoral and tibial interference screws (Linvatec Corp., Largo, Florida) and tensioned to 20 pounds while the knee was cycled to allow stress relaxation.⁷ Meniscal tears were treated with partial meniscectomy, or sutured, or left untreated. The MCL injuries were sutured (grade III) or left surgically untreated (grade I and II). No treatment of the chondral lesions were performed except for shaving or removing loose edges.

Rehabilitation

A rehabilitation program was included for all the subjects and described in previously published studies.^{7, 47, 48} Rehabilitation exercises involved: stationary bicycling and exercises with partial weight-bearing (2-6 weeks postoperatively); exercises with full weight-bearing, functional activities, muscle strength and neuromuscular training (6-9 weeks post-operatively), and muscle strength and neuromuscular training, and running after 9 weeks postoperatively.^{7, 47, 48}

Assessments

The KT-1000 arthrometer (MEDmetric Corp., San Diego, California) using the manual maximum force test was included at all follow-ups to test anterior-posterior displacement of the tibia relative to the femur. The Lachman test¹⁵ and the pivot shift test²⁶ were included at the 10-15 year follow-up. Weight was measured on all the follow-ups and body mass index (BMI) was calculated (kg/m²).

The Cincinnati knee score (6-100 points) was used to evaluate knee function at all follow-ups.^{34,8} The questionnaire evaluates pain, swelling, giving way, general activity level, walking, stair climbing, running, jumping, and pivoting activities, and has previously been validated and used in other outcome studies.^{44, 46} A score of 100 represents normal knee function.

Muscle strength tests were performed using the Cybex 6000 (Cybex Lumex Inc, Ronkonkoma, NY, USA) at all follow-ups. Isokinetic concentric knee flexion (hamstrings muscle strength) and extension (quadriceps muscle strength) were tested in a range from 0 to 90 degrees of knee flexion at 60 °/sec and 240 °/sec with respectively 5 and 30 repetitions. Total work (TW) in Joule (J) and index in percent [(injured/uninjured) x 100] were recorded.

The triple jump test for distance and the stair hop test previously tested for reliability and validity by our group, were performed at all follow-ups and reported as index [(injured/uninjured) x 100].^{33, 45}

A visual analogue scale (VAS)⁴¹ was used to measure knee pain at rest and during or right after physical activities at the 10-15 year follow-up. The subjects made a mark on a 10 cm line from no pain (0) to worst pain (10). Data on return to sports after the ACL reconstruction was collected by asking the subjects at the 10-15 year follow-up: "Did you return to sport after the ACL reconstruction?" We did not collect data on time of return to sports. The Tegner activity scale was included at the 10-15 year follow-up.⁵³

Subjects with bilateral injuries suffered during follow-up were excluded from the analyses for knee joint laxity tests, the Cincinnati knee score, the muscle strength tests, and hop tests for all assessments.

Radiographs were included at the 10-15 year follow-up using the SynaFlexer frame (Synarc, Inc, Copenhagen, Denmark) to examine radiographic tibiofemoral knee OA. This frame placed the knees in approximately 20° of flexion and the feet positioned in 5° of external rotation. A 10° caudal x-ray beam ensured alignment of the beam corresponding to the medial tibial plateau.²⁴ The radiographs were taken bilaterally from a posteroanterior view. The radiographs were read according to the Kellgren and Lawrence (K&L) classification^{1, 21}, including grade 0: no changes, grade 1: doubtful narrowing of the joint space and possible osteophytic lipping, grade 2: definite osteophytes and possible narrowing of the joint space, grade 3: moderate multiple osteophytes, definite narrowing of the joint space, and some sclerosis, and possible deformity of the bone ends, grade 4: large osteophytes, marked narrowing of the joint space, severe sclerosis and definite deformity of the bone ends. Grade \geq 2 was used to define OA.⁵⁰

A question developed for estimating the prevalence of symptomatic knee OA was included⁴⁹: "During the past 4 weeks, have you had knee pain in the injured knee?" Those who answered yes to this question combined with K&L grade ≥ 2 was considered to have symptomatic radiographic knee OA.³⁸

All the radiographs were read by one radiologist. We included intra-rater reliability tests for the radiologist with at least a four week interval. Inter-rater reliability test was also performed including the radiologist and one orthopaedic surgeon on 35 radiographs for both knees (n=70), with functional and self-administered outcomes unknown to the readers. Blinding of the reconstructed knee on the x-rays was not possible, due to the visible screws in the surgically treated knee.

Statistical methods

Statistical Package for Social Sciences (SPSS 16.0, SPSS Inc, Chicago, Illinois) was used for all statistical analyses. All variables were tested for normality using the Kolmogorov-Smirnov test. Analysis of variance (ANOVA) (mixed between-within subject model) and Bonferroni post hoc test were used to test changes over time between and within groups for all the prospective outcome measurements. The Friedman test was used to measure changes between specific time points for the Cincinnati knee score. Student's t-tests were used for group comparisons when normality was accepted (age, BMI, time between injury and surgery) and Mann-Whitney U test was used when normality was rejected (VAS, Tegner). Chi-square test was used for group comparisons of two categorical variables (differences in gender, return to sports, and OA for the isolated and combined groups, respectively). Kappa statistic was performed to determine intra-rater and inter-rater reliability of the reading of the radiographs. A p-value of <.05 was considered statistical significant.

RESULTS

One hundred and eighty-one subjects (82%) consented to participate at the 10-15 year follow-up, with a mean follow-up time of 12.4 (±1.2 years) (Figure 1). Subject characteristics are presented in Table 1. The activities performed at the time of injury were team handball, soccer or basketball (61%), alpine skiing (21%), and other physical activities (12%). Activity data at the time of injury were missing for eleven subjects (6%). One hundred and twenty-one subjects (67%) returned to sport after the rehabilitation period was finished: 50 subjects returned to soccer (28%), 25 subjects to team handball (14%), 8 subjects returned to basket ball (4%), 9 returned to other ball sports (5%), 22 returned to alpine skiing (12%), and 7 returned to other sport activities (4%). No significant differences between the isolated and combined groups were detected for those who returned to sport or not, or type of return to sport activities.

Thirty-seven subjects (20%) were injured in the contralateral knee during the follow-up: 15 isolated ACL injuries (8%), 11 combined ACL and meniscal injuries (6%), and 11 meniscal injuries (6%).

Additional injuries

Isolated injuries were detected in 69 subjects (38%) and combined injuries were detected in 112 subjects (62%) (Table 2). Eight of the 106 subjects (7%) suffered meniscal injuries during the follow-up period. A total of 127 partial meniscal meniscectomies were performed in 106 subjects: 28 (22%) before; 69 (54%) during. and 30 (24%) after the ACL reconstruction. Meniscal sutures were performed in 8 subjects (8%), and no meniscal treatment in 8 subjects (8%). Chondral lesions at the time of surgery were reported in 37 subjects (20%). Nine subjects (3%) had fullthickness chondral lesions localized at femur (n=5); at femur and tibia (n=2), or at patella (n=2). One of the 37 subjects had superficial chondral lesion at the patella, but no meniscal injury, and was therefore included in the isolated injury group. Nine subjects suffered a MCL injury in whom 4 were sutured, and 5 were not surgically treated. According to the surgical files, 2 of the subjects had a healed MCL injury at the time of the ACL reconstruction, and were therefore included in the isolated group. Shaving of chondral lesions and removing loose edges were performed in 7 subjects (4%). Other surgical procedures performed during the follow-up included: osteotomy (n=1), removed scar tissue (n=12), removed screws (n=3), and arthroscopies (n=14).

Fifteen subjects (8%) had an ACL graft re-injury during the follow-up; 9 isolated ACL graft ruptures, 2 ACL graft ruptures combined with meniscal injury, and 4 partial ACL graft ruptures. One subject suffered a second ACL graft rupture. All the ACL graft ruptures were reconstructed. The mean time from the ACL reconstruction to reoperations of the ACL graft ruptures or meniscal injuries was 57±47 months.

Knee function outcomes

A significantly increased knee joint laxity (KT-1000 manual maximum test) was revealed from 6 months to 10-15 years for the whole cohort (p<.001). But there were no significant differences in knee joint laxity (KT-1000) over time for the subjects with isolated injuries (Table 3). No significant differences for the Lachman or Pivot shift tests were found for the isolated and combined injury groups (Table 4).

A significantly improved Cincinnati knee score was detected from 6 months to 10-15 years for the whole cohort (p<.001). No significant group differences were shown over time (Table 3; Figure 2).

A significant improvement in quadriceps and hamstrings muscle strength (J and %) and hop tests (%) was detected over time for all the measurements, but no group differences were found (Table 3; Figure 3 and 4).

No significant differences were found between the groups for VAS pain at rest (isolated group: 0.5±0.9 and combined group: 0.8±1.5), or pain during activity (isolated group: 1.5±1.8 and combined group: 2.1±2.2) at the 10-15 year follow-up.

Radiological outcome

Radiographs were performed on 181 subjects 10-15 years after ACL reconstruction (Table 5). K&L grade ≥ 2 was detected in 74% of the subjects (n=133), including 47% grade 2. Symptomatic radiographic knee OA was revealed in 41% of the subjects (n=74). The combined injury group revealed significantly higher prevalence of radiographic knee OA compared to the isolated injury group (80% and 62%) (p=.008), but no significant group differences were detected between isolated injury group (n=22) compared to combined injury group (n=52) for symptomatic radiographic OA (46% and 32%) (p=.053). Seven of the 9 subjects with full-thickness chondral lesions at the time of surgery had K&L grade 3 or 4. Six of the 9 subjects with full-thickness chondral lesions had symptomatic radiographic knee OA. The intra-rater and inter-rater reliability tests revealed a Kappa of 0.77 and 0.57, respectively.

DISCUSSION

Significantly improved knee function was detected from 6 months to 10-15 years in individuals with isolated and combined ACL injury. No significant differences in knee function over time were detected between the isolated and the combined injury group. But subjects with combined injuries revealed a significantly higher prevalence of radiographic knee OA than those with isolated ACL injuries (80% and 62%) (p=.008). A similar trend was shown for symptomatic radiographic knee OA, but the result was not significant (46% and 32%)(p=.053).

Normal, or nearly normal knee joint laxity (grade 0 and 1) were found in over 80%, 10-15 years after ACL reconstruction. These results corresponded to the results of previous long term follow-up studies of ACL injured subjects.^{16, 25, 40} The Cincinnati knee scores showed improved mean scores over time, but no significant group differences were revealed. To our knowledge, no other studies with more than 10 years follow-up on ACL reconstructed subjects have evaluated knee function over time using self-reported outcome such as the Cincinnati knee score. However, even though the mean scores over time was >80 points; more than 30% revealed mean values less than 80 points for both the isolated injury group and the combined injury group. This may indicate that a majority of the subjects revealed good knee function corresponding to normative data for other similar outcomes measures^{4, 6}, but it also revealed that 30% of the subjects have function over time.

The muscle strength deficits between the injured and uninjured knees were on average less than 10% both at the 2 year and the 10-15 year follow-up. Sixty percent of the subjects in the isolated group, but only 38% in the combined group showed quadriceps index values >90% at the 10-15 years follow-up. This indicated that more subjects with isolated injury had normal index values than those with combined injuries (p=0.012). Ageberg et al.² reported isokinetic index values between 94-102%, 1 year, 3 years, and 15 years after ACL injury, and 77% showed index values above 90%.² The study by Ageberg et al. included non-surgically treated patients in whom 33% had additional meniscal injury, and they excluded subjects with re-injuries. Quadriceps weakness has been among the neuromuscular deficiencies seen after ACL injuries.³⁷ Our cohort showed significantly increased absolute muscle strength values from the 6 month to the 2 year follow-up, but decreased absolute muscle strength values from 2 years to 10-15 years. The significantly decreased absolute muscle strength values detected from 2 to 10-15 years may be explained by increased age³⁹ and reduced activity level. The median Tegner score of 4 at the 10-15 year follow-up, was lower compared to the median score of 6 reported for individuals with normal knees with a mean age of 41 years.¹¹ Other studies with more than 10 years follow-up have reported Tegner scores between 4 to 6.^{22, 30, 54, 57} The differences in activity level reported in these studies may be due to different study populations. The reduced activity level compared to the normative data presented by Briggs et al.¹¹ revealed that subjects with knee injuries seem to modify their activity level. The reduced muscle strength seen at the 10-15 year follow-up may also be due to other factors associated with impaired muscle function such as arthrogenic muscle inhibition or activation failure.⁹ Impaired muscle function has been seen in subjects who have undergone joint surgery, but also individuals with knee OA.9, 13

A high prevalence of radiographic knee OA (74%), particularly mild radiographic knee OA (47%) was detected in the present study. Long term follow-up studies by Lohmander et al.²⁸ and von Porat et al.⁵⁵ evaluating soccer players have also reported high prevalence of knee OA (69% and 59%, respectively) in subjects with ACL injuries combined with meniscal injuries. Lebel et al.²⁵ retrospectively examined 98 subjects with BPTB autograft, and found a prevalence of knee OA of 13.6% in subjects with isolated injuries and 21.5% for subjects with combined injuries.¹⁷ Other prospective studies have found a low prevalence of radiographic knee OA (1%-11%) in subjects who have undergone ACL reconstruction.^{40,14} The above mentioned studies are discussed in a systematic review by Øiestad et al.³⁵ (see in particular Appendix 2). The variation in the reported prevalence may be explained by different study designs, different ACL populations, or different surgical procedures. Our study population seemed to have more additional injuries (62%) compared to the above mentioned studies which may explain the higher prevalence of radiographic knee OA in our study. However, in our cohort, not only subjects with combined injury, but also subjects with isolated injuries revealed a high prevalence of radiographic knee OA compared to other studies.^{25, 40, 56} Nevertheless, among those with isolated injuries, only 10% had moderate and none had severe radiographic knee OA (K&L grade 3 and 4). The corresponding numbers for the combined injury group were 27% with moderate and 10% with severe radiographic knee OA. Thus, the prevalence of moderate and severe radiographic OA was higher for those with combined injuries. Nevertheless, the ACL reconstruction did not seem to prevent the development of mild OA. More studies exploring non-operative treatment compared to reconstructive surgery are needed in order to detect and explain eventually differences in the prevalence of knee OA between these two treatment strategies.

The variation in reported radiographic knee OA may also as previously reported be explained by the use of different radiological classification systems.^{5, 19, 21, 35} For instance, K&L grade 2 involves osteophytes and possible JSN, whereas both the IKDC classification and the Ahlbäck classification involve mainly JSN for defining knee OA. The K&L classification involves JSN as a criterion for grade 3 and 4, but not necessarily for grade 2. Thus, comparing results from studies that have included osteophytes to define knee OA to studies that have emphasized JSN to define knee OA may be cautiously done. If we compare results for K&L grade \geq 3 to the IKDC grade \geq C and Ahlbäck grade \geq 1, our results on radiographic knee OA for subjects with isolated ACL injuries (10%) can be compared to the results by Lebel et al.²⁵ (13.6%). The corresponding numbers for combined injuries were 37% in our study and 21.5% in the study by Lebel et al.

Symptomatic radiographic knee OA was revealed in 41% of the subjects corresponding to a similar study reporting 46% symptomatic radiographic knee OA in soccer players.²⁸ Knee pain may be derived from other conditions than OA, for instance, anterior knee pain has been associated with the BPTB procedure.¹⁰ The proportion of symptomatic OA may therefore have been overestimated.

The prevalence of radiographic knee OA in the uninjured contralateral knee was 15%, including 12% K&L grade 2 and 3% grade 3 in line the results from similar studies^{14, 28, 31, 54} The contralateral knee is often used as control knee to avoid the costs of including a healthy control group, but may not be optimal due to also altered joint loading in the uninjured knee and previously reported neuromuscular bilateral alterations and cross-over effects seen after ACL injuries.^{3, 36} However, by introducing the contralateral knees as a control group, perfectly matching of age, BMI, activity level, and genetic risk factors have been included.

The present study is the first to compare prospective long term data on knee function for subjects with isolated to those with combined injury. The study had a high follow-up rate (82%), and a relatively large study cohort compared to the existing literature.³⁵ However, some limitations need to be addressed: Radiographic evaluation was only performed at the 10-15 year follow-up, thus we have no data on the onset of knee OA. In addition, the inter-rater reliability data showed moderate results. The time span from the ACL injury to surgery showed a mean time of 28 month (range 0-278) giving a wide variation in time from the ACL injury to the 10-15 years follow-up. The retrospectively collected data on additional injuries may have underestimated the number of additional injuries. Furthermore, we had no prospective data on activity level or return to sport (only retrospectively collected). A recently published study by Keays et al.²⁰ found no significant association between type of postoperative sport and OA in subjects with ACL reconstruction, but this should be further explored in future prospective studies. Future studies should also assess the correlation between knee function and knee OA, and furthermore, explore risk factors for development of knee OA. Finally, these relative young retired athletes should be followed longer than 10-15 years to examine the consequences of the high prevalence of mild knee OA, but also to assess what characterize those subjects that function well and do not develop knee OA more than 10 years after ACL reconstruction.

CONCLUSION

Individuals with ACL injury revealed a significantly improved knee function from 6 months to 10-15 years after ACL reconstruction, with no significant differences found between individuals with isolated compared to those with combined injury over time. Subjects with combined injuries had significantly higher prevalence of radiographic knee OA compared to those with isolated ACL injuries 10-15 years after ACL reconstruction (80% and 62%), but no significant differences between groups for symptomatic radiographic knee OA was detected. This study showed that individuals with an ACL reconstruction seem to restore and maintain good, but not normal knee function in the majority of the individuals with isolated and combined injuries more than 10 years after the ACL reconstruction.

Reference List

- (1) The Atlas of Standard Radiographs of Arthritis. *Rheumatology (Oxford)* 2005 December;44 Suppl 4:iv46-iv72.
- (2) Ageberg E, Pettersson A, Friden T. 15-Year Follow-up of Neuromuscular Function in Patients With Unilateral Nonreconstructed Anterior Cruciate Ligament Injury Initially Treated With Rehabilitation and Activity Modification: A Longitudinal Prospective Study. *Am J Sports Med* 2007 August 17.
- (3) Ageberg E, Thomee R, Neeter C, Silbernagel KG, Roos EM. Muscle strength and functional performance in patients with anterior cruciate ligament injury treated with training and surgical reconstruction or training only: a two to five-year followup. *Arthritis Rheum* 2008 December 15;59(12):1773-9.
- (4) Agel J, LaPrade RF. Assessment of differences between the modified Cincinnati and International Knee Documentation Committee patient outcome scores: a prospective study. *Am J Sports Med* 2009 November;37(11):2151-7.
- (5) Ahlback S. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968;Suppl-72.
- (6) Anderson AF, Irrgang JJ, Kocher MS, Mann BJ, Harrast JJ. The International Knee Documentation Committee Subjective Knee Evaluation Form: normative data. *Am J Sports Med* 2006 January;34(1):128-35.
- (7) Aune AK, Holm I, Risberg MA, Jensen HK, Steen H. Four-strand hamstring tendon autograft compared with patellar tendon-bone autograft for anterior cruciate ligament reconstruction. A randomized study with two-year follow-up. *Am J Sports Med* 2001 November;29(6):722-8.
- (8) Barber-Westin SD, Noyes FR, McCloskey JW. Rigorous statistical reliability, validity, and responsiveness testing of the Cincinnati knee rating system in 350 subjects with uninjured, injured, or anterior cruciate ligament-reconstructed knees. *Am J Sports Med* 1999 July;27(4):402-16.
- (9) Bennell KL, Hunt MA, Wrigley TV, Lim BW, Hinman RS. Role of muscle in the genesis and management of knee osteoarthritis. *Rheum Dis Clin North Am* 2008 August;34(3):731-54.
- (10) Biau DJ, Katsahian S, Kartus J et al. Patellar tendon versus hamstring tendon autografts for reconstructing the anterior cruciate ligament: a meta-analysis based on individual patient data. *Am J Sports Med* 2009 December;37(12):2470-8.
- (11) Briggs KK, Steadman JR, Hay CJ, Hines SL. Lysholm score and Tegner activity level in individuals with normal knees. *Am J Sports Med* 2009 May;37(5):898-901.
- (12) Cohen M, Amaro JT, Ejnisman B et al. Anterior cruciate ligament reconstruction after 10 to 15 years: association between meniscectomy and osteoarthrosis. *Arthroscopy* 2007 June;23(6):629-34.

- (13) Diracoglu D, Baskent A, Yagci I, Ozcakar L, Aydin R. Isokinetic strength measurements in early knee osteoarthritis. *Acta Reumatol Port* 2009 January;34(1):72-7.
- (14) Drogset JO, Grontvedt T, Robak OR, Molster A, Viset AT, Engebretsen L. A sixteenyear follow-up of three operative techniques for the treatment of acute ruptures of the anterior cruciate ligament. *J Bone Joint Surg Am* 2006 May;88(5):944-52.
- (15) Gurtler RA, Stine R, Torg JS. Lachman test revisited. *Contemp Orthop* 1990 February;20(2):145-54.
- (16) Hanypsiak BT, Spindler KP, Rothrock CR et al. Twelve-year follow-up on anterior cruciate ligament reconstruction: long-term outcomes of prospectively studied osseous and articular injuries. *Am J Sports Med* 2008 April;36(4):671-7.
- (17) Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. *Knee Surg Sports Traumatol Arthrosc* 1993;1(3-4):226-34.
- (18) Hertel P, Behrend H, Cierpinski T, Musahl V, Widjaja G. ACL reconstruction using bone-patellar tendon-bone press-fit fixation: 10-year clinical results 110. *Knee Surg Sports Traumatol Arthrosc* 2005 May;13(4):248-55.
- (19) Irrgang JJ, Snyder-Mackler L, Wainner RS, Fu FH, Harner CD. Development of a patient-reported measure of function of the knee. *J Bone Joint Surg Am* 1998 August;80(8):1132-45.
- (20) Keays SL, Newcombe PA, Bullock-Saxton JE, Bullock MI, Keays AC. Factors Involved in the Development of Osteoarthritis Following Anterior Cruciate Ligament Surgery. Am J Sports Med 2010 January 5.
- (21) Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis* 1957 December;16(4):494-502.
- (22) Kessler MA, Behrend H, Henz S, Stutz G, Rukavina A, Kuster MS. Function, osteoarthritis and activity after ACL-rupture: 11 years follow-up results of conservative versus reconstructive treatment. *Knee Surg Sports Traumatol Arthrosc* 2008 February 22.
- (23) Kostogiannis I, Ageberg E, Neuman P, Dahlberg L, Friden T, Roos H. Activity level and subjective knee function 15 years after anterior cruciate ligament injury: a prospective, longitudinal study of nonreconstructed patients. *Am J Sports Med* 2007 July;35(7):1135-43.
- (24) Kothari M, Guermazi A, von IG et al. Fixed-flexion radiography of the knee provides reproducible joint space width measurements in osteoarthritis. *Eur Radiol* 2004 September;14(9):1568-73.
- (25) Lebel B, Hulet C, Galaud B, Burdin G, Locker B, Vielpeau C. Arthroscopic reconstruction of the anterior cruciate ligament using bone-patellar tendon-bone autograft: a minimum 10-year follow-up. *Am J Sports Med* 2008 July;36(7):1275-82.

- (26) Leitze Z, Losee RE, Jokl P, Johnson TR, Feagin JA. Implications of the pivot shift in the ACL-deficient knee. *Clin Orthop Relat Res* 2005 July;(436):229-36.
- (27) Lohmander LS, Englund PM, Dahl LL, Roos EM. The Long-term Consequence of Anterior Cruciate Ligament and Meniscus Injuries: Osteoarthritis. *Am J Sports Med* 2007 August 29;35(10):1756-69.
- (28) Lohmander LS, Ostenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum* 2004 October;50(10):3145-52.
- (29) Louboutin H, Debarge R, Richou J et al. Osteoarthritis in patients with anterior cruciate ligament rupture: A review of risk factors. *Knee* 2008 December 19.
- (30) Marcacci M, Zaffagnini S, Giordano G, Iacono F, Presti ML. Anterior cruciate ligament reconstruction associated with extra-articular tenodesis: A prospective clinical and radiographic evaluation with 10- to 13-year follow-up. *Am J Sports Med* 2009 April;37(4):707-14.
- (31) Meunier A, Odensten M, Good L. Long-term results after primary repair or nonsurgical treatment of anterior cruciate ligament rupture: a randomized study with a 15year follow-up. *Scand J Med Sci Sports* 2007 June;17(3):230-7.
- (32) Neuman P, Englund M, Kostogiannis I, Friden T, Roos H, Dahlberg LE. Prevalence of tibiofemoral osteoarthritis 15 years after nonoperative treatment of anterior cruciate ligament injury: a prospective cohort study. *Am J Sports Med* 2008 September;36(9):1717-25.
- (33) Noyes FR, Barber SD, Mangine RE. Abnormal lower limb symmetry determined by function hop tests after anterior cruciate ligament rupture. *Am J Sports Med* 1991;19(5):513-8.
- (34) Noyes FR, Barber SD, Mooar LA. A rational for assessing sports activity levels and limitations in knee disorders. *Clin Orthop* 1989;Sep(246):238-49.
- (35) Oiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. *Am J Sports Med* 2009 July;37(7):1434-43.
- (36) Palmieri-Smith RM, Thomas AC. A neuromuscular mechanism of posttraumatic osteoarthritis associated with ACL injury. *Exerc Sport Sci Rev* 2009 July;37(3):147-53.
- (37) Palmieri-Smith RM, Thomas AC, Wojtys EM. Maximizing quadriceps strength after ACL reconstruction. *Clin Sports Med* 2008 July;27(3):405-ix.
- (38) Peat G, Thomas E, Duncan R, Wood L, Hay E, Croft P. Clinical classification criteria for knee osteoarthritis: performance in the general population and primary care. *Ann Rheum Dis* 2006 October;65(10):1363-7.

- (39) Phillips BA, Lo SK, Mastaglia FL. Isokinetic and isometric torque values using a Kin-Com dynamometer in normal subjects aged 20 to 69 years. *Isokinetic Exc Sci* 2000;(8):147-59.
- (40) Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med* 2007 April;35(4):564-74.
- (41) Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 1983;17(1):45-56.
- (42) Radin EL. Who gets osteoarthritis and why? J Rheumatol Suppl 2004 April;70:10-5.
- (43) Risberg MA, Ekeland A. Assessment of functional tests after anterior cruciate ligament surgery. *J Orthop Sports Phys Ther* 1994;19(4):212-7.
- (44) Risberg MA, Holm I. The Long-term Effect of 2 Postoperative Rehabilitation Programs After Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Clinical Trial With 2 Years of Follow-Up. Am J Sports Med 2009 June 25.
- (45) Risberg MA, Holm I, Ekeland A. Reliability of functional knee tests in normal athletes. *Scand J Med Sci Sports* 1995;5:24-8.
- (46) Risberg MA, Holm I, Steen H, Beynnon BD. Sensitivity to changes over time for the IKDC form, the Lysholm score, and the Cincinnati knee score. A prospective study of 120 ACL reconstructed patients with 2 years follow-up. *Knee Surg Sports Traumatol Arthrosc* 1999;(7):152-9.
- (47) Risberg MA, Holm I, Steen H, Eriksson J, Ekeland A. The effect of knee bracing after anterior cruciate ligament reconstruction. A prospective, randomized study with two years' follow-up. *Am J Sports Med* 1999;27(1):1-8.
- (48) Risberg MA, Holm I, Tjomsland O, Ljunggren E, Ekeland A. Prospective study of changes in impairments and disabilities after anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 1999 July;29(7):400-12.
- (49) Roux CH, Saraux A, Mazieres B et al. Screening for hip and knee osteoarthritis in the general population: predictive value of a questionnaire and prevalence estimates. *Ann Rheum Dis* 2008 October;67(10):1406-11.
- (50) Schiphof D, Boers M, Bierma-Zeinstra SM. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. *Ann Rheum Dis* 2008 July;67(7):1034-6.
- (51) Shelbourne KD, Gray T. Minimum 10-year results after anterior cruciate ligament reconstruction: how the loss of normal knee motion compounds other factors related to the development of osteoarthritis after surgery. *Am J Sports Med* 2009 March;37(3):471-80.
- (52) Tashman S, Kopf S, Fu FH. The Kinematic Basis of ACL Reconstruction. *Oper Tech Sports Med* 2008 July 1;16(3):116-8.

- (53) Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop* 1985;Sep(198):43-9.
- (54) van der Hart CP, van den Bekerom MP, Patt TW. The occurrence of osteoarthritis at a minimum of ten years after reconstruction of the anterior cruciate ligament. *J Orthop Surg* 2008;3:24.
- (55) von Porat A., Roos EM, Roos H. High prevalence of osteoarthritis 14 years after an anterior cruciate ligament tear in male soccer players: a study of radiographic and patient relevant outcomes. *Ann Rheum Dis* 2004 March;63(3):269-73.
- (56) Wu WH, Hackett T, Richmond JC. Effects of meniscal and articular surface status on knee stability, function, and symptoms after anterior cruciate ligament reconstruction: a long-term prospective study. *Am J Sports Med* 2002 November;30(6):845-50.
- (57) Yamaguchi S, Sasho T, Tsuchiya A, Wada Y, Moriya H. Long term results of anterior cruciate ligament reconstruction with iliotibial tract: 6-, 13-, and 24-year longitudinal follow-up. *Knee Surg Sports Traumatol Arthrosc* 2006 November;14(11):1094-100.

Variables	All	Isolated	Combined	p-
				value
Age (years)	39.5 (8.6)	37.5 (8.2)	40.7 (8.7)	.02
Females, number (%)	76 (43)	36 (47)	40 (53)	
Males, number (%)	105 (57)	33 (31)	72 (69)	.03
Time between injury and surgery (months)	28 (52)	7.1 (10.7)	42.4 (63)	<.001
VAS at rest (mm) (0-10)	0.7 (1.3)	0.5 (0.9)	0.8 (1.5)	.23
VAS during or after activity (mm) (0-10)	1.8 (2.1)	1.5 (1.8)	2.1 (2.2)	.07
Tegner, median (min-max) (0-10)	4 (1-9)	4 (1-9)	4 (1-9)	.72

Table 1. Subject characteristics at the 10-15 year follow-up (n=181)

Values are given as mean (SD, standard deviation) unless otherwise stated; VAS, visual analogue scale.

Table 2. Frequencies (%) of additional injuries at the 10-15 year follow-up

$\operatorname{AII}\left(\operatorname{II}=101\right)$	Unilateral injury (n=144)
69 (38)	58 (40)
38 (21)	28 (19)
20 (11)	16 (11)
14 (8)	13 (9)
4 (2)	2 (2)
27 (15)	18 (13)
3 (2)	3 (2)
6 (3)	6 (4)
1	69 (38) 38 (21) 20 (11) 14 (8) 4 (2) 27 (15) 3 (2) 6 (3)

MCL, medial collateral ligament.

		6 months	1 year	2 years	10-15 years	Between group
				-	·	differences
Variable	Type of injury	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	p-value
Body mass index	Isolated (n=41)	23.2±3.2	23.1±2.3	23.1±2.3	25.2±3.0 ^{abc}	0.105
	Combined (n=81)	23.7±3.1	23.8±2.9	23.9±3.0	$26.8\pm4.0^{\text{abc}}$	
KT-1000, Manual maximum (mm)	Isolated (n=43)	2.7±2.8	3.1±2.3	3.5 ± 2.4	2.8±2.7	0.502
	Combined (n=69)	2.3±2.9	2.7±3.0	3.1 ± 3.1^{a}	2.7 ± 3.4	
Cincinnati knee score (6-100)	Isolated (n=41)	79±12	85 ± 12^{a}	87 ± 12^{ab}	85±15ª	0.169
	Combined (n=69)	77±13	81±13 ^a	85 ± 13^{ab}	82±16 ^a	
Hamstrings muscle strength (J) (60°/sec)	Isolated (n=33)	466±151	531 ± 148^{a}	535 ± 147^{a}	482 ± 149^{bc}	0.448
	Combined (n=59)	493±166	561 ± 165^{a}	580 ± 176^{a}	481 ± 172^{bc}	
Hamstrings muscle strength (J)(240°/sec)	Isolated (n=33)	1386±395	1449±383	1470±454	1321 ± 417^{bc}	0.733
	Combined (n=58)	1454±555	1470±543	1542±577	1300 ± 492^{abc}	
Quadriceps muscle strength (J) (60°/sec)	Isolated (n=33)	594±237	711 ± 234^{a}	791 ± 234^{ab}	749 ± 220^{a}	0.843
	Combined (n=59)	596±219	736±208ª	815 ± 216^{ab}	733±223 ^{ac}	
Quadriceps muscle strength (J)(240°/sec)	Isolated (n=33)	1796±623	1988±623 ^a	2099±662 ^a	2076 ± 603^{a}	0.580
	Combined (n=59)	1829±672	2035±632 ^a	2237 ± 657^{ab}	2154 ± 714^{a}	
Triple jump test (%)	Isolated (n=32)	95±6	95±4	98±3	99 ± 5^{ab}	0.176
	Combined (n=54)	92±6	95±5ª	98 ± 4^{ab}	98 ± 14^{a}	
Stair hop test (%)	Isolated (n=28)	82±14	93±16 ^a	96 ± 8^{a}	102 ± 16^{a}	0.665
	Combined (n=50)	82±20	91±11 ^a	94±7 ^a	103 ± 15^{abc}	

Table 3. Prospective outcomes from 6 months to 10-15 years (n=144)

J, Joules; ^aSignificantly different from 6 months; ^bSignificantly different from 1 year; ^cSignificantly different from 2 years (p<.05).

Table 4. Knee joint laxity tests in subjects with unilateral ACL injury 10-15 years after ACL reconstruction (n=144)

	Number	Grade 0 (%)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)
Lachman Isolated	58	16 (28)	32 (55)	10 (17)	0 (0)
Combined	86	30 (35)	43 (50)	12 (14)	1(1)
Pivot shift Isolated	58	34 (59)	14 (24)	9 (16)	1(1)
Combined	86	60 (70)	19 (22)	6 (7)	1 (1)

The side-to-side difference for the Lachman test was graded as either grade 0 (normal), grade 1 (<5 mm difference), grade 2 (6-10 mm difference), or grade 3 (>10 mm difference). The pivot shift test was graded as grade 0 (normal), grade 1+ ("slip"), grade 2+ ("jump"), and grade 3+ ("transient lock").

Score	Injured	Uninjured	Injured	Injured	Uninjured	Uninjured	Uninjured	Uninjured	Knee pain
	(n=181)	(n=181)	Isolated	Combined	Without	With	Isolated	Combined	(n=97/181)
			injury	injury	injury	injury	injury*	injury*	
			(n=69)	(n=112)	(n=144)	(n=37)	(n=69)	(n=112)	
0	15 (8)	98 (54)	10 (15)	5 (5)	92 (64)	7 (16)	47 (68)	51 (46)	7 (4)
1	33 (18)	38 (21)	16 (23)	17 (15)	31 (21)	6 (19)	12 (17)	26 (23)	16 (9)
2	84 (47)	31 (17)	36 (52)	48 (43)	17 (12)	14 (38)	7 (10)	24 (21)	49 (27)
3	38 (21)	11 (6)	7 (10)	31 (27)	4 (3)	7 (19)	2 (3)	9 (8)	18 (10)
4	11 (6)	3 (2)	0 (0)	11 (10)	0 (0)	3 (8)	1 (2)	2 (2)	7 (4)

Table 5. Kellgren and Lawrence and knee pain scores given as frequencies (%) at the 10-15 year follow-up

*Isolated or combined injury in the target knee.



Figure 1. Flow-chart of the subjects included in the 10-15 year follow-up study



Figure 2. Cincinnati knee scores for the isolated and the combined injury groups at 6 months, 1 year, 2 years, and 10-15 years after ACL reconstruction. No group differences were detected over time. ^aSignificantly different from 6 months; ^bSignificantly different from 1 year (p<.05).



Figure 3. Quadriceps strength index given for the isolated group and the combined group at 6 months, 1 year, 2 years, and 10-15 years after ACL reconstruction. No group differences were detected over time. ^aSignificantly different from 6 months; ^bSignificantly different from 1 year (p<.05).



Figure 4. Hamstrings strength index given for the isolated and the combined injury groups at 6 months, 1 year, 2 years, and 10-15 years after ACL reconstruction. No group differences were detected over time. ^aSignificantly different from 6 months (p<.05).