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The association between radiographic knee osteoarthritis and knee symptoms, function, and quality of life 10-15 years after anterior cruciate ligament reconstruction

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ABSTRACT

Background: There are conflicting results in the literature regarding the association between radiographic knee OA and symptoms and function in subjects with previous anterior cruciate ligament (ACL) reconstruction.

Purpose: To investigate the associations between radiographic tibiofemoral knee OA and knee pain, symptoms, function, and knee-related quality of life (QOL) 10-15 years after ACL reconstruction.

Study design: Cross-sectional study

Material and methods: Two hundred and fifty-eight subjects were consecutively included at the time of ACL reconstruction and followed-up prospectively. **We included the Knee Injury and Osteoarthritis Outcome Score (KOOS) to evaluate knee pain, other symptoms (symptoms), activities of daily living (ADL) and sport and recreation (Sport/Rec), and QOL. The subjects underwent standing radiographs 10-15 years after the ACL reconstruction. The radiographs were graded with the Kellgren and Lawrence (K&L) classification (grade 0-4).**

Results: Two hundred **and** ten subjects (81%) consented to participate at the 10-15 year follow-up. Radiographic knee OA (K&L ≥ grade 2) was detected in 71%, and 24% showed moderate or severe radiographic knee OA (K&L grade 3 and 4) **(25% in the contralateral knee)**. No significant associations were detected between radiographic knee OA (K&L grade ≥2) and pain, function, or QOL, respectively, but subjects with radiographic knee OA showed significantly increased symptoms. Severe radiographic knee OA (K&L grade 4) was significantly associated with more pain, symptoms, impaired **Sport/Rec**, and reduced QOL.

Conclusion: Subjects with radiographic OA showed significantly more symptoms than those without OA, and subjects with severe radiographic knee OA had significantly

more pain, impaired function, and reduced quality of life than those without radiographic knee OA 10-15 years after ACL reconstruction.

INTRODUCTION

Knee osteoarthritis (OA) is considered an important disease in the western world because it may cause knee pain and disability.[1] But in the orthopedic literature OA is usually defined solely based on radiographic abnormalities according to classification criteria defined in atlases.[2-6] In the rheumatologic literature, however, knee OA is defined by radiographic abnormalities in combination with pain or symptoms.[7,8] Bedson et al.[9] reviewed population based observational studies and reported that of subjects with knee pain, between 15-76% had radiographic knee OA.

The association between radiographic knee OA and knee pain, symptoms, or function **has not been consistent**,[10-12] with some studies reporting a weak association.[13] The cut off for defining radiographic knee OA usually includes abnormalities such as one osteophyte **and possible joint space narrowing** [Kellgren and Lawrence (K&L) grade 2], which is in the literature defined as the mildest grade of OA.[2] However, studying the association between pain or function and one osteophyte compared to the association between pain or function and *severe* radiographic findings, such as **definite** joint space narrowing, multiple osteophytes, sclerosis, and bone enlargements may give different results.[12] Neogi et al. [14] **suggested** that radiographic *severity* was strongly associated with knee pain. However, the association between severity of radiographic knee OA and knee pain, symptoms, or function is not thoroughly explored in subjects with previous ACL injury. Furthermore, increased age, female gender and high BMI have **been** shown to be significant risk factors for knee OA[15], and also significantly associated with knee symptoms and function.[16] Few studies, **however**, have adjusted for significant risk factors in the analyses of the association between

radiographic findings and pain, symptoms, or function. **This may cause confliction results**. Ideally, studies should include large populations to enable adjustments for potential confounding factors.

Knee injuries, including anterior cruciate ligament (ACL) ruptur**es** and meniscal injur**ies**, have **been suggested as** important risk factors for the development of knee OA.[17-19] Nevertheless, long term follow-up studies of more than 10 years after ACL injuries are rare, and there are few studies examining the association between radiographic knee OA and knee pain, **other** symptoms, function, or knee-related quality of life (QOL).[20] Furthermore, to our knowledge, no studies with more than 10 years follow-up after ACL reconstruction have examined the association between these variables and radiographic severity. Therefore, the aim of the present study was to investigate the association between radiographic tibiofemoral knee OA using the traditional cutoff for radiographic knee OA (K&L <2 vs. ≥2) and knee pain, symptoms, function, and QOL 10-15 years after ACL reconstruction. Furthermore, the aim was to examine the association between mild, moderate, and severe radiographic knee OA and knee pain, symptoms, function, and QOL, respectively.

MATERIALS AND METHODS

Two hundred and fifty-eight subjects who underwent ACL reconstruction were consecutively included in studies between 1990 and 1997. The subjects were included if they were between 14 and 50 years, had isolated ACL injury or combined with meniscus injury, and/or chondral lesion, and/or medial collateral ligament (MCL) injury **(grade I or II)**.[21-23] The exclusion criteria were injuries **to** the contralateral knee, fractures in both legs the last year before inclusion, and not understanding Norwegian language. The subjects were operated with bone-patellar-tendon-bone (BPTB) autograft or hamstrings tendon (HT) autograft previously described by Aune et al.[21] The chondral lesions, **the MCL injuries** and the meniscal

injuries suffered **prior to or** at the time of **the** ACL injury and the meniscal injuries suffered during **the** follow-up **have retrospectively been extracted from surgeon files of all the subjects included at the 10-15 year follow-up.** The MCL injuries were diagnosed by clinical assessment before the ACL reconstruction.

A supervised rehabilitation program was included postoperatively as a three phase program lasting for 6-9 months.[21,24] The subjects have been followed-up prospectively at 6 months, 1 year, 2 years,[21-23] and 10-15 years[25,26] postoperatively with functional and clinical assessments, but for the aim of this study only the 10-15 year follow-up evaluations were included.

The Regional Committee for Medical and Health Research Ethics in Norway has approved the study and the participants signed an informed consent prior to participating in the study.

Assessments

The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to asses knee pain, symptoms, function, and QOL at the long term follow-up.[27] KOOS is a self-administered questionnaire comprising 5 subscales on pain, other symptoms (symptoms), activities of daily living (ADL) and sport and recreation (**Sport/Rec**), and QOL. The KOOS subscales are organized into categories for each question which are transformed to a 0-100 scale. Zero indicates extreme knee problems and 100 represent no knee problems. KOOS was developed for short and long term follow-up studies and has been validated on several types of injuries to the knee such as ACL and meniscal injuries, and posttraumatic OA.[28,29] **The Tegner activity scale was used to assess the activity level**.[30] **To calculate body mass index (BMI), we used the formula weight (kg)/height(m)^2.**

All the subjects participating at the 10-15 year follow-up went through a radiological assessment of the tibiofemoral joint. The procedure included standing radiographs with the knees flexed in approximately 20° and the feet 5° externally rotated by using a Plexiglas frame (SynaFlexer Inc, **Copenhagen,** Denmark). The frame has been validated for measuring joint space width in patients with knee OA.[31] Radiographs were taken bilaterally from a posteroanterior view.

One radiologist analyzed the radiographs using the K&L classification system.[2,32] The following definitions for each grade were used: grade 0: no changes, grade 1: doubtful narrowing of the joint space and possible osteophytic lipping, grade 2 (mild): 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 (severe): large osteophytes, marked narrowing of the joint space, severe sclerosis and definite deformity of the bone ends.

The radiologist performed intra-rater reliability test for the reading of the radiographs. The intra-rater test w**as** performed with at least 4 weeks interval on 35 radiographs of both knees (n=70). The intra-rater reliability **result** for the x-ray evaluation showed κ=0.77.

Statistical methods

We used linear regression to evaluate the association between radiographic tibiofemoral OA and the KOOS subscales pain, other symptoms, ADL, Sport/Rec, and QOL with adjustment for age, gender, and BMI (SPSS 16.0, SPSS Inc, Chicago, Illinois). First, we evaluated the radiographic OA using a dichotomized radiographic variable: no OA (K&L 0/1 = reference category) vs. OA (K&L grade ≥ 2). Second, we evaluated radiographic OA severity in more detail by dichotomizing each K&L grade still using

K&L grade 0/1 as the reference category: K&L grade 2 vs. 0/1, K&L grade 3 vs. 0/1, and K&L grade 4 vs. 0/1. Standardized beta values, standard errors, 95% confidence intervals (CI), and p-values were given for all regression analyses. We used the Mann Whitney U test for group comparisons of non-parametric data (Tegner), and Kappa (κ) analysis to evaluate the reliability test of the x-ray scores. All tests were two-tailed and we considered a p-value of 0.05 or less as statistically significant.

Table 1. Subject characteristics at the 10-15 year follow-up (n=210)

Variables	**Mean± SD**
Age	39.1 ± 8.7
BMI	26.3 ± 3.6
Time from injury to surgery (months)	24.8 ± 48.7
Time from injury to the 10-15 year follow-up (years)	13.7 ± 4.4
KOOS pain	90 ± 14
KOOS other symptoms	86 ± 16
KOOS activities of daily living	95 ± 10
KOOS sports and recreation	77 ± 24
KOOS knee-related quality of life	75 ± 22
Tegner*	4 (0-9)

SD, standard deviation; BMI, body mass index; KOOS, Knee injury and Osteoarthritis Outcome Score; *__The__ Tegner activity scale is given as median (minimum-maximum).

RESULTS

Two hundred **and** ten subjects participated in the study (81%), 90 females (43%) and 120 males (57%). **Subject characteristics are** presented in Table 1. Of the 210 subjects, 29 (14%) were operated with HT graft, and 181 (86%) with BPTB graft. Isolated ACL injury was detected in 82 subjects (40%) and 128 subjects (60%) had additional meniscal injury, MCL injury or chondral lesion, or a combination of these (Table 2). Eleven subjects had chondral lesions grade 3 (n=5) and grade 4 (n=6). Only 10 (8%) of the total of 121 (100%) subjects with meniscal injuries suffered the meniscal injury during the follow-up period. A total of 137 partial meniscal resections (91%) and 13 sutures (9%) were performed in the 210 subjects

either before the ACL reconstruction (22%), at the time of ACL reconstruction (53%), or during the follow-up period (25%). **The activities performed at the time of injury comprised of pivoting sports in 129 subjects (61%), mainly handball (n=37, 18%), soccer (n=70, 33%), or basket ball (n=9, 4%),** alpine skiing in 46 subjects (22%), and other activities or unknown activity in 23 subjects (11%) and 12 subjects (6%), respectively. No significant difference in median Tegner activity scale was shown between subjects with or without radiographic knee OA. Fourteen subjects (7%) suffered a graft rupture during the follow-up period, and four subjects (2%) suffered a partial graft rupture verified through arthroscopic procedures.

Forty-five subjects (21%) were injured in the contralateral knee during the follow-up period including isolated ACL injuries in 19 subjects (9%), ACL **partial tear** in 1 subject (0.5%), ACL in combination with meniscal injury in 11 subjects (5.5%), and isolated meniscal injury in 14 subjects (7%).

Table 2. Additional injuries at the 10-15 year follow-up (n=210)

Type of injury	Number	%
Isolated **ACL** injury	82	39
Medial meniscus	39	19
Lateral meniscus	19	9
Menisci	26	12
Meniscus and MCL	5	2
Meniscus, MCL, and chondral lesion	3	2
Meniscus and chondral lesion	29	14
Chondral lesion	7	3

MCL, medial collateral ligament.

Seventy-one percent of the subjects had radiographic signs of knee OA according to K&L ≥ grade 2 (Table 3). The corresponding number for the contralateral knee was 25%. Moderate or severe knee OA (K&L≥3) was detected in 24% for the target knee and 6% for the contralateral knee, respectively.

Table 3. Frequency (%) of the Kellgren and Lawrence (K&L) scores for involved and contralateral knee (n=210)

K&L	Involved knee		Contralateral knee	
0	19	(9)	114	(54)
1	42	(20)	43	(21)
2	98	(47)	39	(19)
3	40	(19)	11	(5)
4	11	(5)	3	(1)

Table 4 shows **unadjusted** and adjusted results for the association between each KOOS subscale and radiographic knee OA (K&L <2 vs**.** ≥2). No significant associations were detected, except for symptoms. The adjusted analysis indicated that subjects with radiographic knee OA **at the level of** K&L ≥ grade 2 had on average approximately 6 points lower KOOS other symptoms scores than those without radiographic knee OA.

Table 4. Multiple regression analyses of the association between the Knee injury and Osteoarthritis Outcome subscales and Kellgren and Lawrence (K&L) grade ≥2 vs. grade <2 (n=206)

Dependent variables	K&L <2 vs**.** ≥2	Beta	Standard Error	**95% CI**	P-value
Pain	**Unadjusted**	-4.1	2.2	**-8.4, 0.1**	0.06
	Adjusted	-2.6	2.3	**-7.2, 2.0**	0.26
Other symptoms	**Unadjusted**	-5.9	2.4	**-10.6, -1.3**	0.01
	Adjusted	-5.7	2.5	**-10.7, -0.6**	0.03
Activities of daily lives	**Unadjusted**	-1.6	1.6	**-4.7, 1.4**	0.29
	Adjusted	0.2	1.7	**-3.0, 3,5**	0.89
Sports and recreation	**Unadjusted**	-7.3	3.7	**-14.6, 0.0**	0.05
	Adjusted	-4.6	3.9	**-12.4, 3.1**	0.24
Quality of life	**Unadjusted**	-2.7	3.4	**-9.3, 3.9**	0.42
	Adjusted	-0.9	3.6	**-8.0, 6.2**	0.80

CI, confidence interval. Adjusted for gender, age, and body mass index.

Figure 1 shows the mean values for the KOOS subscales for each K&L grade. No significant associations were detected between the KOOS subscales and mild or moderate radiographic knee OA adjusted for **gender, age, and BMI** (Table 5). Subjects with severe radiographic knee OA had significantly lower values for the KOOS subscales than those without OA.

Table 5. Multiple regression analysis of the association between the KOOS subscales* and the K&L grades

KOOS	Number	K&L grades	Beta	Standard Error	95% CI	p-value
Pain	97	2	**-0.6**	**2.0**	**-4.5, 3.3**	**0.77**
	40	3	**2.6**	**2.6**	**-2.4, 7.8**	**0.30**
	11	4	**-14.3**	**4.3**	**-22.9, -5.8**	**0.001**
Other Symptoms	97	2	**-4.1**	**2.2**	**-8.4, 0.2**	**0.06**
	40	3	**3.9**	**2.9**	**-1.7, 9.5**	**0.17**
	11	4	**-11.6**	**4.9**	**-21.3, -2.1**	**0.02**
ADL	97	2	**-0.4**	**1.4**	**-3.2, 2.4**	**0.80**
	40	3	**3.4**	**1.8**	**-0.2, 7.0**	**0.06**
	11	4	**-7.3**	**3.2**	**-13.4, -1.1**	**0.02**
Sport/Rec	97	2	**-1.1**	**3.4**	**-7.8, 5.5**	**0.74**
	40	3	**3.2**	**4.4**	**-5.4, 11.8**	**0.46**
	11	4	**-20.6**	**7.4**	**-35.2, -6.0**	**0.006**
QOL	97	2	**2.8**	**3.1**	**-3.2, 8.9**	**0.36**
	40	3	**1.2**	**4.0**	**-6.6, 9,1**	**0.76**
	11	4	**-20.7**	**6.6**	**-33.9, -7.5**	**0.002**

KOOS, Knee injury and Osteoarthritis Outcome Score; K&L, Kellgren and Lawrence; CI, confidence interval; ADL, activities of daily living; **Sport/Rec**, function in sports and recreation; QOL, knee related quality of life.*Adjusted for gender, age, and body mass index. K&L grade 0 and 1 constitute the reference category for the independent dichotomous variables (n=60).

DISCUSSION

The results revealed that subjects with radiographic OA had significantly increased symptoms compared to those without radiographic OA. Furthermore, highly significant associations were detected between severe radiographic knee OA and pain, symptoms, ADL, Sport/Rec, and QOL. It has been suggested that a change of 8-10 KOOS points constitues a clinical relevant difference.[28] However 10 points have been arbitrarily set and we suspect that it is difficult to state a common number for a clinical important difference for the different KOOS subscales. Therefore, the significantly increased symptoms for those with mild OA (6 points in mean difference) may be of clinical importance compared to those without radiographic OA. The significantly increased pain, symptoms, and reduced function seen in individuals with ACL reconstruction may be explained by the radiographic abnormalities.

No previous long term studies including subjects with ACL reconstruction have evaluated the relationship between knee symptoms and function and radiographic knee OA using regression analysis. However, previous studies have evaluated the difference in mean values of the KOOS subscales between ACL injured subjects with and without knee OA.[33-36] Lohmander et al.[33] reported significant increased pain and symptoms **in** female soccer players with radiographic knee OA compared to those without radiographic knee OA 12 years after ACL injury in line with our results for symptoms. The mean values for the KOOS subscales were, however, generally lower than those reported in our study. For instance, those with radiographic knee OA had a mean value for pain of 70, compared to 84 in our study. Furthermore, their Sports/Rec and QOL values were 24 and 23 points lower than our results, showing that the female soccer players reported more complaints 12 years after ACL injury compared to our cohort of both males and females. Our results showed no significant differences between females and males for the KOOS subscales. The subjects in the study by Lohmander et al. were younger compared to our cohort. **They were** only female soccer players, they were treated either with ACL reconstruction or non-operatively, and **the study** assessed both patellofemoral and tibiofemoral OA. Inclusion of both patellofemoral and tibiofemoral OA has been **shown** to be more frequently associated with knee pain and impaired function.[12] In addition, a drop-out rate of 35% was reported in the study by Lohmander et al. These differences may explain the more impaired function found in their study. Meunier et al.[34] reported significantly increased pain and symptoms, and impaired function in ADL and **Sport/Rec** in subjects with radiographic OA compared to those without radiographic OA on average 15 years after **the** ACL injury. The mean KOOS subscales scores reported in their study were more similar to those in the present study except for the lower values for **Sport/Rec** (62 vs 75 points), and QOL (63 vs 74 points). Meunier et al. included both subjects with ACL reconstruction and non-operative treatment and subjects with grade 1

radiographic changes were included in the OA group. Our unadjusted results on the association between the KOOS subscales and radiographic OA were not very different from those of Meunier et al. (pain: p=0.06; symptoms: p=0.01; **Sport/Rec**: p=0.05). Furthermore, Neuman et al.[35] studied ACL injured subjects without reconstruction 15 years after the injury and they reported almost identical mean values for the KOOS subscales as found in the present study. These authors detected no significant differences between subjects with or without radiographic knee OA also in line with another follow-up study of male soccer players.[36]

The moderate inter-rater reliability results found for **different radiological classification systems**[5] may be another explanation for the differences in results across studies with respect to the association between radiographic knee OA and pain, symptoms, and function. The different classification systems emphasize to some extent either osteophytes or joint space narrowing which may influence the cutoff for radiographic knee OA.[2,3,37] Common for the above mentioned studies and the present study was the long term follow-up of ACL injured subjects (>10 years), but the studies included different radiological classification systems without attention towards radiographic severity. In the present study we performed regression analysis with adjustment for gender, age, **and** BMI as these factors have **been** shown to influence both the mean KOOS subscale values or the K&L scores.[16,27,38,39] The adjustment for the potential confounding factors did influence the associations, particularly for pain and **Sport/Rec**.

Both biological, psychological, and social factors have **been** shown to influence pain.[40] For instance, psychological factors have been strongly associated with functional impairment and pain after adjustment for radiographic severity in patients with knee OA.[41] Consequently, the lack of association between radiographic knee OA defined by the traditional cutoff and pain or function may be due to a true weak association. **Our** adjusted

analyses showed that there were significant associations between severe radiographic knee OA and all KOOS subscales. **Consequently**, the follow-up studies on subjects with ACL reconstruction should emphasize the self-reported knee pain, symptoms, **including effusion, locking, range of motion, and stiffness**, and function, in addition to severity of radiographic knee OA, more than the prevalence of radiographic knee OA defined with a cutoff.

Our results revealed that those with severe radiographic knee OA had significantly lower values on the KOOS subscales compared to those without OA. However, only 11 subjects had severe radiographic OA, and all these individuals had additional meniscal injury (n=6) or meniscal and chondral injury (n=5). The increased pain and symptoms, and the impaired function in these subjects may be due to the additional injuries and not the radiographic abnormalities. **Meniscal** injury has shown to be the most important risk factor for development of knee OA in subjects with ACL injury,[5] but also for those without ACL injury.[42] Therefore, it is difficult to explain the source**s** of the pain and symptoms in this population. The KOOS other symptoms subscale includes questions related to effusion, locking, range of motion, and stiffness. These factors may be associated with the previous ACL reconstruction and the additional meniscal injuries.[43] In addition, **we detected** no significant association**s** between moderate radiographic knee OA involving multiple osteophytes, definite narrowing of the joint space, and some sclerosis, and the KOOS subscales. Brandt et al.[44] suggested that the synovium and subchondral bone are major sources of joint pain in patients with knee OA, but also that other joint structures, including the menisci and periarticular muscles, may contribute to the knee pain. Nevertheless, it may be reasonable that the increased pain and symptoms, and impaired function detected in our study were due to the **severe** radiographic changes, and not to the additional meniscal injuries suffered several years ago. However, whether the meniscal injuries or the radiographic

abnormalities caused the increased pain and impaired function for those with severe radiographic OA cannot be stated **on the basis of** our data.

The present study has some limitations: A drop-out rate of 19% may have biased the results, but there were no significant differences in gender or age between the study participants and those who dropped out. No data on the patellofemoral joint was available for this study. **There may be a risk of type 2 error in the analyses, therefore, there may be true differences between those with radiographic OA and those without detected with larger sample size.**

This study revealed that only individuals with severe radiographic OA 10-15 years after ACL reconstruction had significantly increased **pain** and reduced function compared to those without knee OA. Future research should perform risk factor analyses to provide **further** evidence for treatment methods to reduce the development or delay the progression of radiographic knee OA, but also **study** treatment methods targeting reducing pain and symptoms and increasing function. Finally, future studies on subjects with ACL injury should include assessment of radiographic severity and the definition of knee OA should involve both radiographic abnormalities and pain or symptoms.

Conclusion

Subjects with radiographic knee OA had significantly increased symptoms compared to those without radiographic OA. Subjects with severe radiographic knee OA had also significantly more pain, impaired function and reduced quality of life compared to those without radiographic knee OA 10-15 years after ACL reconstruction.

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What is already known on this topic

A high prevalence of radiographic knee OA is reported for individuals with ACL reconstruction, but long term self-reported knee function has shown to be good. Conflicting evidence exist on the association between symptoms or function and radiographic knee OA.

What this study adds

This study provides analyses on the association between radiographic severity and knee symptoms and function. This study detected that subjects with *severe* radiographic knee OA had increased symptoms and impaired function compared to those without radiographic knee OA more than 10 years after ACL reconstruction.

Reference List

1 Felson DT. Clinical practice. Osteoarthritis of the knee. N Engl J Med 2006;354:841-848

2 Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494-502

3 Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis Cartilage 2007;15 Suppl A:1-56

4 Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. Knee Surg Sports Traumatol Arthrosc 1993;1:226-234

5 Oiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. Am J Sports Med 2009;37:1434-1443

6 Ahlback S. Osteoarthrosis of the knee. A radiographic investigation. Acta Radiol Diagn (Stockh) 1968;Suppl-72

7 Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986;29:1039-1049

8 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;65:1363-1367

9 Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskelet Disord 2008;2:116

10 Barker K, Lamb SE, Toye F, Jackson S, Barrington S. Association between radiographic joint space narrowing, function, pain and muscle power in severe osteoarthritis of the knee. Clin Rehabil 2004;18:793-800

11 Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27:1513-1517

12 Szebenyi B, Hollander AP, Dieppe P, Quilty B, Duddy J, Clarke S, et al. Associations between pain, function, and radiographic features in osteoarthritis of the knee. Arthritis Rheum 2006;54:230-235

13 Creamer P, Lethbridge-Cejku M, Hochberg MC. Factors associated with functional impairment in symptomatic knee osteoarthritis. Rheumatology (Oxford) 2000;39:490-496

14 Neogi T, Felson D, Niu J, Nevitt M, Lewis CE, Aliabadi P, et al. Association between radiographic features of knee osteoarthritis and pain: results from two cohort studies. BMJ 2009;339:b2844

15 Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med 2000;133:635-646

16 Paradowski PT, Bergman S, Sunden-Lundius A, Lohmander LS, Roos EM. Knee complaints vary with age and gender in the adult population. Population-based reference data for the Knee injury and Osteoarthritis Outcome Score (KOOS). BMC Musculoskelet Disord 2006;7:38

17 Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med 2000;133:321-328

18 Roos EM. Joint injury causes knee osteoarthritis in young adults. Curr Opin Rheumatol 2005;17:195-200

19 Wilder FV, Hall BJ, Barrett JP, Jr., Lemrow NB. History of acute knee injury and osteoarthritis of the knee: a prospective epidemiological assessment. The Clearwater Osteoarthritis Study. Osteoarthritis Cartilage 2002;10:611-616

20 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;35:1756-1769

21 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;29:722-728

22 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;27:1-8

23 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;29:400-412

24 Risberg MA, Holm I, Tjomsland O, Ljunggren AE, Ekeland A. Changes in impairments ans disabilities after anterior cruciate ligament reconstruction. J Orthop Sports Phys Ther 1999;29:400-412

25 Holm I, Oiestad BE, Risberg MA, Aune AK. No difference in knee function or prevalence of osteoarthritis after reconstruction of the anterior cruciate ligament with 4-strand hamstring autograft versus patellar tendon-bone autograft: a randomized study with 10-year follow-up. Am J Sports Med 2010;38:448-454

26 Øiestad BE, Holm I, Aune AK, Gunderson R, Myklebust G, Engebretsen L, Fosdahl M, and Risberg MA. Knee function and prevalence of knee osteoarthritis after anterior cruciate ligament reconstruction. A prospective study with 10-15 years follow-up. Am J Sports Med . 2010.
Ref Type: In Press

27 Roos E.M., Roos H, Ekdahl C., Lohmander LS, Beynnon BD. Knee injury and osteoarthritis outcome score (KOOS) - Development of a self-administered outcome measure. J Orthop Sports Phys 1998;78:88-96

28 Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes 2003;1:64

29 Roos EM, Roos HP, Lohmander LS. WOMAC Osteoarthritis Index--additional dimensions for use in subjects with post-traumatic osteoarthritis of the knee. Western Ontario and MacMaster Universities. Osteoarthritis Cartilage 1999;7:216-221

30 Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop 1985;Sep:43-49

31 Kothari M, Guermazi A, von IG, Miaux Y, Sieffert M, Block JE, et al. Fixed-flexion radiography of the knee provides reproducible joint space width measurements in osteoarthritis. Eur Radiol 2004;14:1568-1573

32 The Atlas of Standard Radiographs of Arthritis. Rheumatology (Oxford) 2005;44 Suppl 4:iv46-iv72

33 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;50:3145-3152

34 Meunier A, Odensten M, Good L. Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: a randomized study with a 15-year follow-up. Scand J Med Sci Sports 2007;17:230-237

35 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;36:1717-1725

36 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;63:269-273

37 Irrgang JJ, Anderson AF, Boland AL, Harner CD, Kurosaka M, Neyret P, et al. Development and validation of the international knee documentation committee subjective knee form. Am J Sports Med 2001;29:600-613

38 Paradowski PT, Englund M, Lohmander LS, Roos EM. The effect of patient characteristics on variability in pain and function over two years in early knee osteoarthritis. Health Qual Life Outcomes 2005;3:59

39 Sharma L, Kapoor D, Issa S. Epidemiology of osteoarthritis: an update. Curr Opin Rheumatol 2006;18:147-156

40 Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet 2005;365:965-973

41 Summers MN, Haley WE, Reveille JD, Alarcon GS. Radiographic assessment and psychologic variables as predictors of pain and functional impairment in osteoarthritis of the knee or hip. Arthritis Rheum 1988;31:204-209

42 Hunter DJ, Zhang YQ, Tu X, Lavalley M, Niu JB, Amin S, et al. Change in joint space width: hyaline articular cartilage loss or alteration in meniscus? Arthritis Rheum 2006;54:2488-2495

43 Kartus J, Movin T, Karlsson J. Donor-site morbidity and anterior knee problems after anterior cruciate ligament reconstruction using autografts
125. Arthroscopy 2001;17:971-980

44 Brandt KD, Dieppe P, Radin EL. Etiopathogenesis of osteoarthritis. Rheum Dis Clin North Am 2008;34:531-559

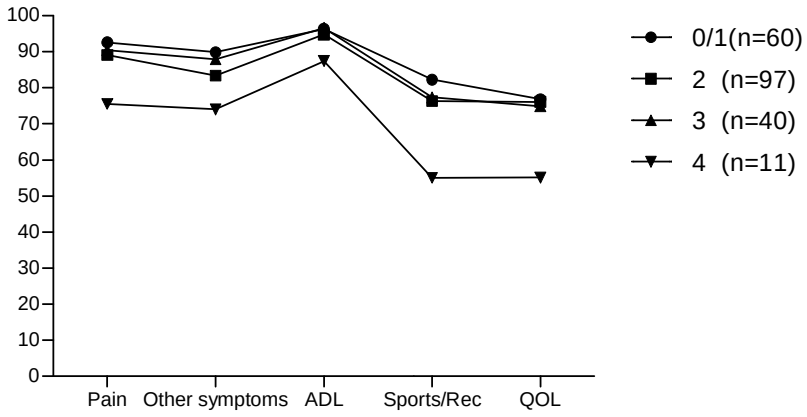

Figure 1. Mean values for the subscales of the Knee injury and Osteoarthritis Outcome Score for each Kellgren and Lawrence grade (0-4)