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Changes in knee osteoarthritis, symptoms and function after anterior cruciate ligament reconstruction

-A 20-year prospective follow-up study-

Abstract

Background: Progression of tibiofemoral (TF) and patellofemoral (PF) osteoarthritis (OA), and changes in knee function more than 15 years after ACLR, are not well known.
Purpose: To examine progression of knee OA and changes in symptoms and function in isolated and combined injuries from 15 to 20 years after ACLR.
Study design: Prospective cohort study.
Methods: Two hundred and ten subjects with ACLR was prospectively followed and at the 15 and 20-year follow-up, radiographs were obtained and the Kellgren and Lawrence (K&L) classification system was used. Symptoms and function were evaluated using the Knee injury and Osteoarthritis Outcome Score (KOOS) and isokinetic quadriceps and hamstring muscle strength tests.
Results: One hundred and sixty eight subjects returned for the 20-year follow-up (80%) with a mean age: 45 (±9) years, BMI: 27 (±4), and median (range) Tegner activity level: 4 (0-9). The prevalence of radiographic TF and PF OA at the 20-year follow-up was 42% and 21%, respectively. Those with combined ACL injuries had significantly higher prevalence of radiographic TF OA compared to those with isolated ACL injury ($p<0.0001$). There was a 13% increase in radiographic TF OA ($p=0.001$) and an eight percent increase in PF OA ($p=0.015$) from the 15 to 20-year follow-up. A significant deterioration in knee symptoms and function was observed in four of the KOOS subscales ($p\leq0.01$), not for KOOS QoL ($p=0.14$), as well as for quadriceps muscle strength and hamstring muscle strength ($p<0.0001$).
Conclusion: The prevalence of radiographic TF and PF OA was 42% and 21%, respectively. A significantly higher prevalence of TF OA was found for those with combined injuries compared to isolated ACL injury. The majority of the subjects were stable radiographically over the 5 years. There was a statistically significant deterioration in symptoms and function, but the mean changes were of questionable clinical importance.

Clinical relevance: The majority of individuals with ACLR who have become middle-aged are radiographically stable over 5 years, although the prevalence of TF OA was 42% at the 20-year follow-up. There was significantly higher number of subjects with radiographic TF and PF OA in those with combined injuries compared to those with isolated ACL injury.

What is known about the subject: There is an increased risk of tibiofemoral osteoarthritis long term after ACL reconstruction, and those with combined injuries seem to have a significantly higher risk of developing knee osteoarthritis.

What this study adds to existing knowledge:

- One of very few studies with 20 years outcome on both radiographic measurements, patient reported outcome measures, as well as quadriceps and hamstring muscle strength data in patients that have been followed prospectively
- Prevalence data on patellofemoral knee osteoarthritis after ACL reconstruction
- Progression over time for tibiofemoral and patellofemoral osteoarthritis, as well as symptomatic and functional changes in ACL reconstructed individuals who have become middle-aged
- The ACL reconstructed population should be recognized as a heterogeneous group treated accordingly
- These new data suggests implementation of preventive strategies targeting those with combined injuries: 1) early after ACL injury to prevent additional injuries 2) reducing symptoms and improving function to reduce progression of symptomatic osteoarthritis

INTRODUCTION

There is an increased risk of knee osteoarthritis (OA) after anterior cruciate ligament (ACL) injury and reconstruction (ACLR), in particular those with additional meniscus injury.[2,19,30,35,55] A systematic review showed that more than 10 years after ACL reconstruction, up to 50% had developed radiographic tibiofemoral (TF) OA[35], but we lack knowledge on the prevalence of patellofemoral (PF) OA in this population.[8,37] The incidence of knee OA increases with age, with the elderly most commonly affected. However, posttraumatic knee OA typically develops in young to middle-aged adults, affecting quality of life as early as the 4th decade of life.[14] However, the rate of progression of both TF and PF OA in these middle-aged individuals has, to our knowledge, not been thoroughly addressed.

Although knee OA has been reported to be a painful and disabling disease in the elderly [18,26], we lack knowledge on changes in symptoms and function over time in middle-aged individuals with posttraumatic knee OA.[36,38,54]

We have prospectively followed a cohort of ACLR subjects and have previously reported a high prevalence of TF and PF OA 15 years after ACLR.[36,37] Furthermore, significantly higher prevalence of knee OA was reported in those with combined injuries (meniscus injury) compared to those with isolated ACL injury[36,37]. However, longitudinal studies are needed to better understand whether early radiographic changes in the knee joint continue to progress over time, if these changes also follow a decline in lower extremity muscle strength and function, and evaluate if these changes are different in those with combined compared to those with isolated ACL injury. Accordingly, the objective of this study was to continue to follow our prospective cohort of ACLR subjects to: 1) examine the prevalence of both TF and PF OA up to 20 years after ACLR; 2) determine progression of radiographic and symptomatic TF and PF OA in those with combined and isolated ACL injury from 15 to 20 years after ACLR; and 3) to evaluate changes in patient-reported outcomes (PROs) as well as quadriceps and hamstring muscle strength between 15 and 20 years after ACLR. We hypothesized that radiographic and symptomatic knee OA as well as patient reported outcomes and muscle strength would deteriorate significantly from 15 to 20 years after ACLR.

MATERIALS AND METHODS

Two hundred and ten ACLR subjects were eligible for the 20-year follow-up based on our prospective cohort that we have followed since the time of ACLR.[3,20,46] The subjects (in total 258) were included from 1990 to 1996 and followed prospectively 6 months, 1 year, 2 years, 10-15 years[36,37] (herein called the 15-year follow-up) and for this study, up to 20 years after ACLR (herein called the 20-year follow-up). Hence, to address the specific aims of this study related to changes in TF and PF OA and changes in knee symptoms and function, only those subjects who attended the 15-year follow-up (which included radiographic assessment), were eligible for inclusion in this 20-year follow-up (n=210) (Figure 1). In this study, the involved knee at inclusion (baseline) was defined as the involved knee throughout the whole study.

The Regional Ethical Committee and The Data Inspectorate in Norway approved the study, and all subjects signed informed consent, and could withdraw from the study at any time.

Surgical Method and Rehabilitation

The majority of subjects underwent an ACLR using a bone-patellar-tendon-bone (BPTB) autograft (n=181, 86%) previously described by Aune et al.[3] and also previously described in the 15 year follow-up.[36] The graft was positioned at the 11-or 1-o'clock (right or left knee, respectively) and fixed with titanium femoral and tibial interference screws (Linvatec Corp., Largo, Florida) tensioned to 20 pounds while the knee was cycled to allow stress relaxation.[3] The remaining 14% (n=29) underwent a quadrupled hamstring tendon autograft looped over a

5-mm polyester tape (Endotape, Smith & Nephew Endoscopy, Andover, Massachusetts) and with a titanium button (Endo-Button, Smith & Nephew) placed into the holder on the GRAFTMASTER (Smith & Nephew). We have previously reported no significant differences between the BPTB group and the quadrupled-hamstring tendon-autograft group with regard to radiographic knee OA[20]. Hence, we continued to include both surgical techniques in our further analysis for this 20-year follow-up. The structured rehabilitation programs these individuals completed have been described previously in the 2-year follow-up studies.[3,45,46,46]

Radiographic Assessment

Standing radiographs of the TF joint were taken bilaterally with a Synaflexer Frame (Synarc, Inc, Denmark) that ensured alignment of the x-ray beam corresponding to the medial tibial plateau (10° caudal x-ray beam). The Synaflexer Frame standardized the placement of the knee in approximately 20° of flexion and 5° of external rotation for an anterior-posterior view of the TF joint.[25] For the PF joint, standing radiographs with skyline projections and medio-lateral projections were taken with the knee in approximately 40˚ of flexion in a specifically designed frame.[37] All radiographs at both follow-ups were read by one senior musculoskeletal radiologist and classified according to the Kellgren & Lawrence classification.[24] Our senior musculoskeletal radiologist has previously revealed a kappa of 0.77 for intra-rater reliability [36,37].

K&L≥2 has previously been used as the cut-off for the presence or absence of radiographic knee OA[50]. Originally K&L2 was defined as 'definite osteophytes and possible narrowing of joint space', but at least five different descriptions have since been published using K&L classification of knee OA[50]. Recently, Felson et al[11] suggested a clearer distinction of the K&L2 by dividing K&L2 into K&L2/ost, when *only* definite osteophyte is present and K&L2, defined as definite osteophyte *and possible joint space narrowing.* This definition has also recently been used by Beart et al.[4] to define those with "osteophyte and possible joint space narrowing'. Accordingly, we divided K&L2 into K&L2/ost (only definite osteophyte) and K&L2 (definite osteophyte and possible joint space narrowing), and used the K&L2 as cut-off for the presence of radiographic TF and PF OA.

Symptomatic OA has previously been defined as subjects with K&L≥2 and those who answered yes on the following question: "During the past 4 weeks, have you had knee pain in the involved knee?"[36,41,48] In the current study this pain question was related to the involved knee[36,36] and thus used to define symptomatic TF and PF OA (pain + K&L≥2).

Progression of radiographic knee OA

Felson et al.[11] defined incidence as new-onset K&L2 with definite osteophyte. Hence, we used changes in K&L score from K&L0 and K&L1 to ≥K&L2/ost from the 15 to 20-year follow-up as new-onset ('New OA'). To identify subjects during the five-year follow-up period who were radiologically stable, subjects were either labelled "Stable Early OA" with K&L2/ost at both follow-ups, or "Stable Established OA" with K&L2, K&L3, or K&L4 at both follow-ups[4]. Finally, in line with previous literature, progression was defined as an increase in one K&L grade or more[10,11]. Subjects who changed at least one K&L score (ie. from K&L2/ost *to* K&L2, or from K&L2 *to* K&L3, or from K&L3 *to* K&L4, or changed more than one K&L grade) from the 15 year to the 20-year follow-up were defined as "OA Progressors".

Clinical tests and patient reported outcome measure

The subjects' weight and height were measured at the follow-ups and presented as body mass index (BMI: kg/m^2). The knee arthrometer test (KT-1000 knee arthrometer)[17] were used to record the anterior displacement of the tibia relative to the femur at 30lb and the manual maximum test, but only data for the manual maximum test is presented.

The Knee injury and Osteoarthritis Outcome Score (KOOS) was included to evaluate patients perception of symptoms and function.[47] Furthermore, the Tegner Activity Scale[53], measuring type and level of leisure time/walk/sport activities. Isokinetic knee extension and flexion muscle strength tests (Cybec 6000; Cybex Lumex Inc, Ronkonkoma, New York) were performed to measure quadriceps and hamstring muscle strength during five repetitions of maximum effort at a test velocity of 60 degrees per second for knee extension and flexion, respectively. Muscle strength tests are presented as peak torque in Newton meter (Nm) and also as Nm/body weight (Nm/kg). Prior to the muscle strength testing, the subjects warmed-up using a stationary bicycle for 6-8 minutes. All tests were carried out by the same team of surgeons and physical therapists as for the 15-year follow-up[36].

Additional Injuries

If the involved knee had sustained no other injuries from the index ACL injury evaluated at the time of inclusion to the 20-year follow-up, it was classified as an isolated ACL injury. The involved knee was classified as 'combined injuries' if the subject had suffered an additional The involved knee was classified as 'combined injuries' if the subject had suffered an additional meniscus injury or a chondral lesion (ICRS classification grade III or IV[33]) or both at time of inclusion (evaluated intraoperatively) or during follow-up. To identify ACL ruptures (and re-ruptures), chondral lesions, meniscus injuries and other ligament injury data were recorded from the medical records or surgical files. All medical records or surgical files were collected and thoroughly read to extract all information from the index surgery to the 15-year follow-up. At the 20-year follow-up all subjects were asked if they had any new injuries, re-injuries, or if they had gone through any surgical procedures or other treatments for their knees during the previous five years. If they answered yes, medical records or surgical files for these subjects were collected and data extracted for the described additional injuries, re-injuries, and surgical treatment procedures.

Statistical Analysis

Mean and standard deviations (SD) or frequencies were calculated for subjects characteristics and outcome measures. Chi-square tests were used for group comparisons of two or more categorical variables (K&L grades), and McNemar tests were used for categorical data for group comparisons between the 15 and 20 year follow-up (K&L grades). Student paired t-tests were used for analyzing changes from the 15 to 20-year follow-up when normality was accepted (Skewness normality test), and Wilcoxen-Signed Rank tests were used when normality was rejected. Independent Student t-tests or Man-Whitney U tests were used for group comparisons (i.e. isolated and combined) as appropriate (based on normality). PASW Statistics (SPSS 18.0, SPSS Inc, Chicago, Illinois) was used for all statistical analyses.

RESULTS

Subject characteristics

One hundred and sixty-eight subjects of those who had attended the 15-year follow-up (80%) participated in the 20 year follow-up. The mean age and follow-up time post-ACLR were 45.2 (±9.1) years and 17.8 (±1.8) years, respectively, while 43% were female. A flow chart of included subjects appears in Figure 1, while subject characteristics are presented in Table 1. There were no statistically significant differences between those who participated at the 20 year follow-up (n=168) and those who did not (n=42) with regard to age, gender, BMI, KOOS, K&L grade, or combined injuries (at the 15 year follow-up). One subject was excluded from radiographic assessment due to current pregnancy, leaving 167 subjects with radiographic evaluation. Furthermore, one subject had undergone total knee arthroplasty since the 15 year follow-up and was not included in Table 3a and 3b as K&L=4 (see footnote Table 3a and 3b).

At 20-year follow-up, subjects had a median (range) Tegner activity level of 4 (0-9). There was no statistically significant change in Tegner activity level from the 15 (median 4) to the 20 year follow-up (p=0.076), but 32 (19%) decreased their Tegner activity level with a score of 2 or more from the 15 to 20-year follow-up.

There was a highly significant increase in BMI from the 15 to 20 year follow-up, but only with a mean change in BMI of 0.54 (±1.94), and a mean change in body weight of 1.1 (±5.7) kg (p<0.0001).

Additional injuries

For the involved knee at the 20 year follow-up, 106 (63%) subjects had combined injuries and 62 (37%) had isolated ACL injury (Table 2). At 20 year follow-up, 12 (7%) had injured their involved knee during the previous five years (12 subjects with 13 injuries). At 20-year follow-up, there was an 8% ACL graft re-rupture rate for the involved knee. At 20-year follow-up, 47 subjects (28%) had injured their contralateral knee. Of these 47 subjects, 29 had undergone ACLR (Table 2).

There were a total number of 26 new injuries in 22 subjects between the 15 and 20-year follow-up, 12 subjects with injuries to their involved knee and 10 subjects with injuries to their contralateral knee (Table 2). Fourteen injuries were meniscus injuries treated with partial meniscectomy, and an additional three meniscus injuries that were not surgically treated (combined with either ACL re-rupture: n=2; or a new ACL reconstruction: n=1). Additionally, five injuries were cartilage lesions, all of which underwent arthroscopic debridement, except one that underwent a microfracture procedure.

Tibiofemoral and patellofemoral OA

Involved knee

The prevalence of radiographic TF and PF OA for the involved (isolated and combined injuries) and for the contralateral knee (uninjured and injured) are given in Table 3a and 3b. Radiographic TF and PF OA were present in 70 (42%) and 35 (21%) subjects, respectively (Table 3a and 3b). Significantly more radiographic OA was present in the involved knee compared to the contralateral knee, both for the TF joint (p=0.001) and for the PF joint (p<0.001). Figure 2a and 2b were included to visualize the percentage of subjects within each K&L grade for the TF and PF joints based in the data presented in Table 3a and 3b. Combined TF and PF OA was present in 24 (14%) subjects, while 11 (7%) had isolated PF OA. At the 20-year follow-up

There was a significantly higher number of subjects with TF OA in those with combined injuries compared to those with isolated ACL injury (p<0.0001). Similar results were seen for the PF joint (p=0.011).

Forty-one subjects (25%) had symptomatic TF OA at the 20-year follow-up. In addition, a significantly higher number of those with symptomatic TF OA (n=41) had combined injuries (n=36, 88%) compared to those with isolated ACL injury (n=5, 12%) (p<0.0001). Similar results were seen for those with symptomatic PF OA; 21 (88%) subjects had combined injuries compared to three (12%) subjects with isolated ACL injury (p=0.014).

There was a 13% increase in the number of subjects with radiographic TF OA (p=0.001), and a 7% increase in the number of subjects with radiographic PF OA (p=0.015) from the 15 to 20 year follow-up. Furthermore, there was an 11% increase in the number of subjects with symptomatic TF OA (p=0.005) and a 7% increase in the number of subjects with symptomatic PF OA (p=0.011) from the 15 to 20 year follow-up. However, the largest proportion of subjects were classified as Stable OA for both for the TF joint (54%) and PF joint (57%) (Figure 3). For the TF joint, 34% were classified as Stable Early OA, 20% as Stable Established OA, and 13% as No OA. For the PF joint, 50% were classified as Stable Early OA, 7% as Stable established OA, and 14% as No OA.

There was a significantly higher number of subjects with combined injuries (22% and 20%) who progressed compared to those with isolated ACL injury (7% and 5%) from the 15 to 20 year follow-up, for the TF joint (p=0.016) and the PF joint (p=0.014), respectively.

Contralateral knee

The prevalence of OA in the contralateral knee was 21% for the TF joint and 5% for the PF joint at 20 year follow-up (Table 3a and 3b). There was a significantly higher number of subjects with TF OA in those with an injury to their contralateral knee compared to those who were uninjured (p<0.0001), but not for those with PF OA. From the 15 to 20 year follow-up, there was a 10% increase in the number of subjects with TF OA in the contralateral knee (p<0.0001), but only a 3% increase in those with PF OA (p=0.180). A higher proportion of subjects who were classified as OA Progressors for the contralateral knee had sustained an injury to their contralateral knee, both for the TF joint (13%) and PF joint (11%), compared to those with an uninjured contralateral knee (3%).

Knee Function

The KOOS subscale scores at 20-year follow-up ranged from the highest for KOOS-ADL (93±12) to the worst for KOOS sport/recreation (72±26) (Table 4). Those with combined injuries reported significantly worse outcome for all KOOS subscales (p<0.05), except for the KOOS QoL subscale (p=0.056), compared to those with isolated ACL injury (Table 4). However, there were no significant differences in quadriceps or hamstring muscle strength between those with isolated and combined injuries (Table 4). Knee symptoms and function deteriorated significantly over the 5 years for all variables except for KOOS QoL (p=0.14) (Table 4).

There was a significant deterioration in quadriceps and hamstring muscle strength (p<0.0001) for both the involved and contralateral side (Table 4). Percent deterioration in quadriceps was 9.7% for the involved side and 10.8% for the contralateral side from the 15 to 20-year follow-up. Similarly, hamstring muscle strength deteriorated with a mean of 7.1% for the involved side and 8.1% for the contralateral side.

DISCUSSION

In middle-aged subjects 20 years after ACLR, we reveal a prevalence of radiographic TF and PF OA of 42% and 21%, respectively. Importantly, the majority of subjects with combined injuries had TF OA (57%) whereas only 16 % of those with isolated ACL injury had TF OA. The same trend was evident for the PF joint with 25% had PF OA of those with combined injuries and only 19% of those with isolated injury. These rates are in line with previous data reported in our systematic review of TF OA more than 10 years post-ACLR[35]. While there is a lack of data on PF OA after ACLR, a recent narrative review reported a prevalence of mild radiographic PF OA of 10-47%, assessed with the K&L or OARSI classification systems, 6-12 years post-ACLR[8]. Very few cases of moderate PFOA were reported (1%). Barenius et al[5] reported prevalence data for PF OA 14 years after ACLR between 21-25%, similar to our data 20 years after ACLR (21%) (Table 3b).

The prevalence of symptomatic TF and PF OA was 25% and 14%, respectively, indicating that, of those with radiographic TF OA, only 41% reported knee pain in their involved knee (31% for those with radiographic PF OA). Estimates of prevalence of symptomatic knee OA in similar age groups have reported 3.6% in men and 4.3% in women[31]. Based on these National Health Interview Survey (NHIS) data[31], female, obese individuals with an age of 67 years would have a similar prevalence of symptomatic knee OA as found in our study (25%).

Degenerative changes in the knee after ACL rupture may be caused by several factors. Such factors include recurrent injury secondary to knee instability, subchondral bone, cartilage, or meniscal lesions sustained during the original injury or secondary to subsequent trauma. These injuries and subsequent lesions may alter knee joint loading patterns, as well as initiating factors activating inflammatory pathways during injury and surgery[44]. Our data extends previous reports showing a significant increase in the number of subjects with OA following a combined injury (concurrent meniscus and/or cartilage lesions) compared to those with isolated ACL injury. Concurrent and/or subsequent additional injuries, particularly meniscal injuries, seem to drive post-traumatic OA development and progression The meniscus should therefore be preserved whenever possible[32,49,51] and treatment strategies for patients with knee OA is exercises such as quadriceps muscle strengthening and aerobic exercises, as well as normalizing body weight for those who are overweight or obese[34,39].

While the prevalence of radiographic OA reported in the current study is in line with previous reviews[8,35], there is a large variation in the reported prevalence of TF and PF OA after ACLR (10-90%)[8,35]. This variation is likely to be explained by differing study designs, ACL populations, surgical procedures, and in particular differences in reported cut-off for radiographic OA, as well as different radiological classification systems.[1,21,24,35] Most studies have used the K&L2 as cut-off for defining radiographic knee OA, but there are at least 5 different descriptions of the K&L classification system (and in particular the K&L2 grade)[50] in addition to many other radiological classification systems in use. [1,21,24,35] Thus, comparing results from studies that have defined knee OA using different classification systems should be done cautiously[9]. Furthermore, we acknowledge that the original K&L system was described only for the TF joint, but we used it also for the PF joint in our study.

We found a 13% increase in radiographic TF OA in the involved knee from 15 to 20-year follow-up. However, the majority of the subjects were radiological stable (TF joint) over the 5 years, with 54% categorized as Stable OA and 13% categorized as No OA . Two-thirds of individuals with isolated ACL injury seem to have good long-term radiographic outcome, suggesting our focus should not only be on ACL injury prevention programs[52], but also secondary injury prevention programs after ACLR. Very few studies have prospectively evaluated aged-related changes in OA[12], but studies have shown significant decrease in joint space width (JSW) with older age [16]. In the uninjured contralateral knee in the current study, the rate of radiographic TF OA increased from 4% to 13% over the 5 years follow-up (Table 3a), indicating also a significant deterioration over time for the uninjured knee. Radiographic TFOA increased from 31% to 41% in the injured contralateral knee over the 5 years (11%), a similar increase as for the uninjured contralateral over 5 years (9%) for the TF joint. These data might suggest an age-related increase in TF OA of 9% for these middle-aged individuals. But we cannot rule out that these individuals' contralateral knee, although not injured, has been exposed to risk factors due to ACL injury in their involved knee. The literature lack data on normal age-related changes in knee OA in middle-aged individuals. For older individuals the prevalence of knee OA has shown to increase from 26% in the age group 55-65 years to 50% in the age group 75+years[22,28]

The deterioration in KOOS pain, symptoms, ADL and sport/recreation subscales for the whole ACLR group were below previously reported clinical meaningful changes of 8 points (mean changes in our study were between 2 and 7 points). This brings into question whether the deterioration in knee symptoms and function were clinically important. However, it is important to evaluate combined injuries and isolated ACL injuries separately, as they appear to be distinct entities differing in outcome as well as progression over-time. It is clear from our data that individuals with combined injuries have a higher rate of radiographic progression, as well as symptomatic and functional decline, compared to those with isolated ACL injuries, and age and sex matched normative data[40].

During the five year follow-up, there was a highly significant decline in quadriceps muscle strength in both involved leg (9.7%) and contralateral leg (10.8% decline) ($p<0.0001$), as well as for the hamstrings muscle strength (7.1% and 8.1%)($p<0.0001$). Previous studies have reported a 8-10 % age-related decline in muscle strength per decade starting from 40 years of age[27], indicating a 4-5% decline over five years. Other studies have found no age-related decline in muscle strength until 50 years of age, but thereafter a decline rate of 12-15% per decade[15,23,56]. The mean change in quadriceps muscle strength over the 5-years was 14.7Nm (Table 4), which does not exceed the minimal detectable change previously reported for peak torque isokinetic knee extension strength test (22.8Nm).[29] Hence, these changes over the 5-year period may be of questionable of clinical importance. However, as quadriceps muscle strength have reported to be a significant risk factor for development of knee OA as well as being significant for reducing symptoms in patients with symptomatic knee OA, this patient group should be encouraged to perform quadriceps muscle strengthening exercises as part of their daily life activities.

Our 20-year follow-up study after ACLR has some limitations. We could have included joint space width (JSW) measurements in addition to K&L grades. The OARSI Structural Change Working Group continues to support the use of conventional radiography as one option for assessing structural change, but they recommend JSW measurements in addition to OA classification systems, in particular when examining progression over time. [7] The use of MRI has developed considerably during recent years, and ideally would be included in addition to radiographs[7]. The K&L classification system has been extensively used in the literature[12,43], but the way progression has been defined varies[6,11]. Studies have shown that using JSN to define progression results in more knees being accurately described as having progressive disease compared to using the K&L score[7]. However, we have recently reported that JSW is significantly different for each qualitative JSN description for the K&L grades, with the exception of K&L0 and K&L2/ost which both described JSN as being absent[9]. Hence, defining OA progression using the K&L was considered appropriate for the current study. As there are very limited high quality, prospective, long-term studies after ACL injury, our next research questions based on data from this 20-year prospective study will address risk factors for long-term progression of radiographic and symptomatic TF and PF OA.

At the time of the surgical procedure 20 years ago, this tunnel placement was the conventional way of performing the surgery. We recognize that the location of the tunnel is not quite that of the femoral anatomic insertional site that has only recently been documented[13,42]. We do not advocate that this technique should be used presently and we have changed our technique. However, it should be mentioned in this context that the new techniques have yet to show consistently less long term OA. So far, no graft, although anatomical replaced has shown to reestablish normal kinematics of the knee.

CONCLUSION

The prevalence of radiographic OA is high for both TF (42%) and PF compartments (21%) 20 years after ACLR. However, only 25% had symptomatic TF OA and 14% had symptomatic PF OA. There was a significant increase in both TF and PF OA from 15 to 20 years after ACLR, but still the majority of the subjects were radiographically stable over the 5-year follow-up period (67%). Those with combined injuries progressed both radiographically and functionally more than those with isolated ACL injury. Individuals following ACLR should not be considered as a homogenous group, as they differ in OA prevalence and OA progression, as well as symptomatically and functionally.

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Figure legends
Table 1. Subject characteristics at the 20 year follow-up (n=168)

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Figure 3. Percent of subjects with No OA, New OA, Stable OA, and OA Progressors for both the tibiofemoral (TF) and the patellofemoral (PF) joints from the 15 to 20-year follow-up, for isolated ACL injury and combined injuries, involved knee (n=167)

Table X. Kellgren and Lawrence (K&L) classification[24] of radiographic tibiofemoral and patellofemoral knee osteoarthritis included recent suggested adjustments of the K&L grade 2[11]

K&L 0	**K&L 1**	**K&L 2/ost**[11]	**K&L 2**[24]	**K&L 3**	**K&L 4**
No changes	Doubtful narrowing of the joint space, possible osteophytic lipping	Definite osteophyte	Definite osteophyte and possible joint space narrowing	Moderate multiple osteophytes, definite narrowing of joint space, some sclerosis, possible deformity of bone ends	Large osteophytes, marked narrowing of joint space, severe sclerosis, definite deformity of bone ends

Table 1. Subject characteristics at the 20 year follow-up (n=168)

Variables [a]	Mean (SD)
Age, years	45.2 (9.1)
Females, number (%)	73 (43)
Body Mass Index, kg/m^2	26.7 (4.0)
Number of subjects graft type: BPTB [b] autograft, (%)	144 (86)
Time between injury and surgery, years	2.2 (4.3)
Time between surgery and 20 year follow-up, years	17.8 (1.8)
Tegner Activity Scale, median (minimum - maximum)	4 (0-9)
KT-1000 manual maximum test[c], mm	1.8 (3.1)
KT-1000 manual maximum test[c], unilateral ACL injury only (n=139), mm	1.5 (3.2)

[a] Values are given as mean (SD, standard deviation) ; [b] BPTB bone-patellar-tendon-bone autograft; [c] involved limb result minus uninvolved limb result

Table 2. Number of subjects (%) with injuries at the 20 year follow-up for involved and contralateral knee and number of subjects with new injuries (%) between the 15 and 20 years follow-up (n=168)

Type of injury	Number of subjects (%)
ACL unilateral	139 (83)
Injury involved knee	
Combined injuries[a] involved knee	106 (63)
Subjects with new injuries	12 (7)
Type of new injury [b]:	
• Cartilage	2
• Meniscus	10
• Re-rupture ACL	1
Injury contralateral knee	47 (28)
Subjects with new injuries	10 (6)
Type of new injury [c]	
• ACL reconstruction	2
• Cartilage	3
• Meniscus	7
• Re-rupture ACL	1

[a] Combined injuries: ACL injury with additional meniscus or cartilage injuries detected intraoperatively at baseline or during follow-up

[b] Number of injuries: one subject with more than one injury

[c] Number of injuries: three subjects with more than one injury

Table 3a. Number of subjects (%) with Kellgren & Lawrence grade (K&L) 0-4 for the tibiofemoral joint at the 15 and 20-year follow-up for the involved knee and contralateral knee

	15-year follow-up (n=210)							20-year follow-up (n=167)						
Radiograghic grading	K&L0	K&L1	K&L2/ost	K&L2	K&L3	K&L4	Total (100%)	K&L0	K&L1	K&L2/ost	K&L2	K&L3	K&L4	Total (100%)
Involved:	19 (9)	40 (19)	89 (42)	11 (5)	40 (19)	11 (5)	210	10 (6)	12 (7)	75 (45)	24 (14)	35 (21)	11 (7)*	167
- Isolated[1]	13 (16)	22 (27)	38 (46)	2 (2)	7 (9)	0 (0)	82	7 (11)	5 (8)	40 (65)	6 (10)	4 (6)	0 (0)	62
- Combined[2]	6 (5)	18 (14)	51 (40)	9 (7)	33 (26)	11 (8)	128	3 (3)	7 (7)	35 (33)	18 (17)	31 (30)	11 (10)*	105
Contralateral:	115 (55)	46 (22)	28 (13)	7 (3)	11 (5)	3 (1)	210	49 (29)	32 (19)	51 (31)	17 (10)	15 (9)	3 (2)	167
- Uninjured	107 (65)	37 (23)	13 (8)	4 (2)	3 (2)	0 (0)	164	43 (36)	25 (21)	37 (31)	9 (8)	6 (5)	0 (0)	120
- Injured	8 (17)	9 (20)	15 (33)	3 (7)	8 (17)	3 (7)	46	6 (13)	7 (15)	14 (30)	8 (17)	9 (19)	3 (6)	47

[1]Isolated: ACL injury without additional meniscus or cartilage injury at baseline or during follow-up.
[2]Combined injuries: ACL injury with additional meniscus or cartilage injuries detected intraoperatively at baseline or during follow-up
*One patient (n=1) had a total knee arthroplasty (0.6%) due to TF OA, here scored as K&L4.

Table 3b Number of subjects (%) with Kellgren & Lawrence grade (K&L) 0-4 for the patellofemoral joint at the 15 and 20-year follow-up for the involved knee and contralateral knee

	15-year follow-up (n=210)							20-year follow-up (n=167)						
Radiograghic grading	K&L0	K&L1	K&L2/ost	K&L2	K&L3	K&L4	Total (100%)	K&L0	K&L1	K&L2/ost	K&L2	K&L3	K&L4	Total (100%)
Involved:	37 (18)	26 (12)	120 (57)	21 (10)	6 (3)	0 (0)	210	13 (8)	20 (12)	99 (59)	24 (14)	10 (6)	1 (1)*	167
- Isolated[1]	22 (27)	15 (18)	39 (48)	5 (6)	1 (1)	0 (0)	82	7 (11)	10 (16)	39 (63)	4 (7)	2 (3)	0 (0)	62
- Combined[2]	15 (12)	11 (9)	81 (63)	16 (13)	5 (4)	0 (0)	128	6 (6)	10 (10)	60 (57)	20 (19)	8 (8)	1 (1)*	105
Contralateral:	74 (35)	46 (22)	86 (22)	3 (1)	1 (0)	0 (0)	210	46 (28)	27 (16)	85 (51)	4 (2)	5 (3)	0(0)	167
- Uninjured	69 (42)	38 (23)	55 (34)	1 (1)	1 (1)	0 (0)	164	39 (33)	20 (17)	57 (48)	2 (2)	2 (2)	0 (0)	120
- Injured	5 (11)	8 (17)	31 (67)	2 (4)	0 (0)	0 (0)	46	7 (15)	7 (15)	28 (60)	2 (4)	3 (6)	0 (0)	47

[1]Isolated: ACL injury without additional meniscus or cartilage injury at baseline or during follow-up.

[2]Combined injuries: ACL injury with additional meniscus or cartilage injuries detected intraoperatively at baseline or during follow-up.

*One patient (n=1) had a total knee arthroplasty (0.6%) due to TF OA, here scored as K&L4.

Table 4. Mean and standard deviation (SD) for patient reported outcomes, and muscle strength at the 20 year follow-up, mean change (SD) from the 15 to 20-year follow-up, and group differences between isolated and combined injuries at the 20 year follow-up (n=168)

Variables		**20 years (n=168) Mean (SD)**	**Mean change[a] (SD) 15 to 20 years**	**P-value (mean change)**	**P-value (group differences[b])**
KOOS[c] pain (0-100)	All	87 (16)	-2.7 (13.2)	0.008	
	Isolated	91 (12)			
	Combined	85 (17)			0.003
KOOS symptoms (0-100)	All	83 (17)	-3.3 (13.2)	0.001	
	Isolated	87 (13)			
	Combined	80 (19)			0.019
KOOS ADL[d] (0-100)	All	93 (12)	-2.0 (10.0)	0.011	
	Isolated	96 (10)			
	Combined	92 (14)			0.022
KOOS sport/recreation (0-100)	All	72 (26)	-5.9 (20.8)	0.000	
	Isolated	80 (23)			
	Combined	67 (27)			0.002
KOOS QoL[e] (0-100)	All	74 (23)	-1.9 (16.3)	0.140	
	Isolated	78 (22)			
	Combined	71 (23)			0.056
Quadriceps muscle strength PT (Nm)[f] (60°/sec):	All	137 (42)	-14.7 (32.1)	0.000	
- Involved knee	Isolated	137 (42)			
	Combined	136 (42)			0.906
- Contralateral knee	All	151 (43)	-18.4 (27.2)	0.000	
	Uninjured	153 (43)			
	Injured	146 (43)			0.388
Hamstrings muscle strength PT (Nm)[f] (60°/sec):	All	89 (28)	-6.9 (21.9)	0.000	
- Involved knee	Isolated	89 (28)			
	Combined	90 (28)			0.848
- Contralateral knee	All	94 (28)	-8.1 (16.1)	0.000	
	Uninjured	94 (28)			
	Injured	94 (29)			0.999

[a] Mean change from the 15 to 20-year follow-up (negative numbers indicate deterioration)
[b]Between group differences for isolated and combined injuries (or injured and uninjured contralateral knee) at the 20-year follow-up,
[c]KOOS: Knee Injury and Osteoarthritis Outcome Score
[d]ADL:, activites of daily living,
[e]QoL: quality of life;
[f] PT(Nm): peak torque in Newton meter.

Figure 1. Flow chart of the subjects included in the 20-year follow-up.

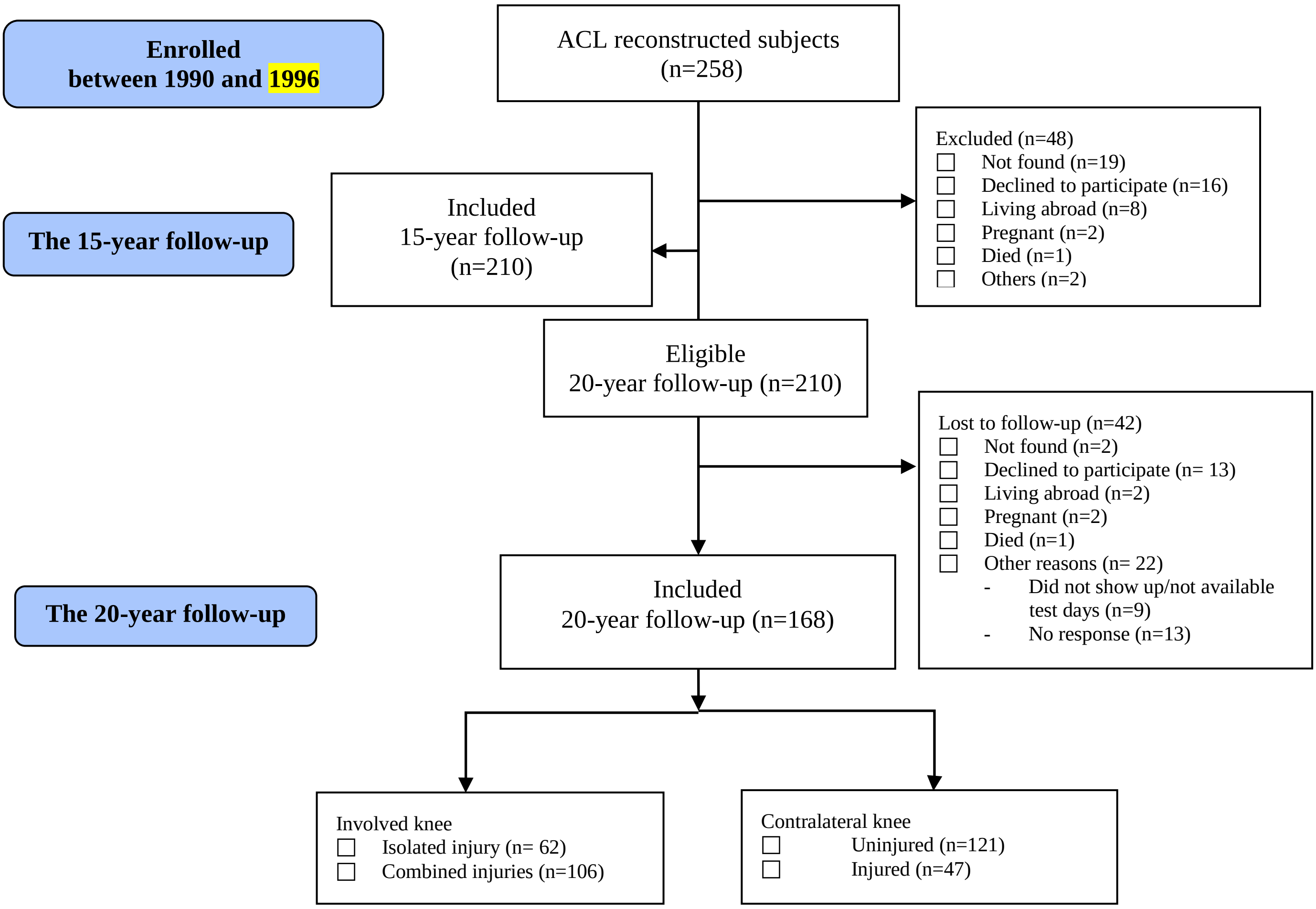

Figure 2a. Percentage of subjects within each Kellgren & Lawrence grade for the tibiofemoral joint at the 15 and 20-year follow-up after ACL reconstruction in isolated and combined injuries (involved knee)

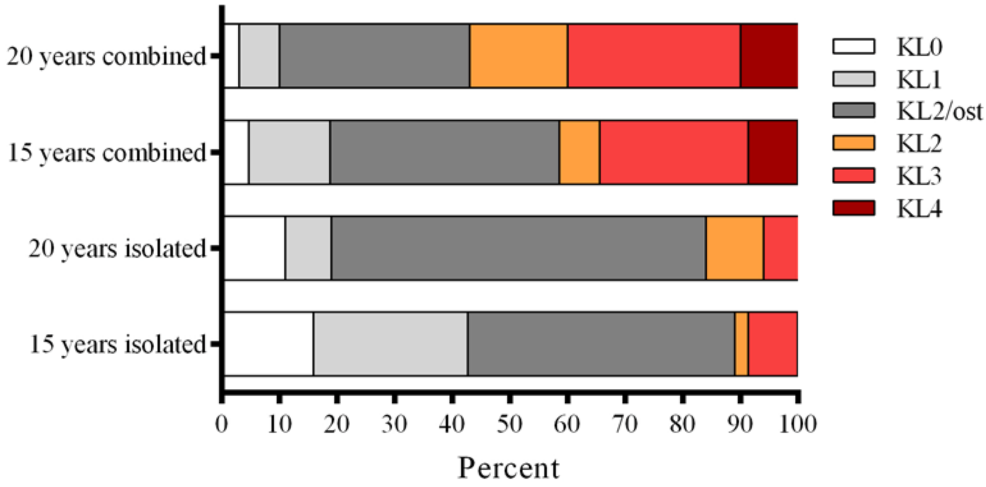

Figure 2b. Percentage of subjects within each Kellgren & Lawrence grade for the patellofemoral joint at the 15 and 20-year follow-up after ACL reconstruction for isolated and combined injuries (involved knee).

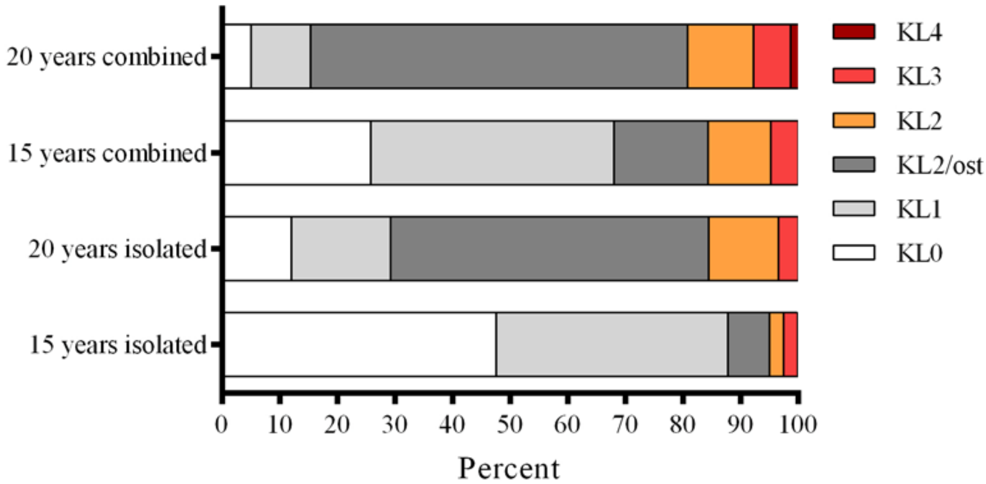

Figure 3. Percent of subjects with No OA, New OA, Stable OA, and OA Progressors for both the tibiofemoral (TF) and the patellofemoral (PF) joints from the 15 to 20-year follow-up, for isolated ACL injury and combined injuries, involved knee (n=167)