Patient Predictors of Contralateral

Anterior Cruciate Ligament Reconstruction

- A Cohort Study on 9061 patients from The Swedish National Knee Ligament Register, with 5-Year Follow-up

Master thesis in medicine

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TABLE OF CONTENTS

ABSTRACT 4

Background 4

Purpose 4

Study Design 4

Methods 4

Results 4

Conclusion 5

BACKGROUND 5

Anatomy and function of the Anterior Cruciate Ligament 5

Morbidity – ACL injury 6

Epidemiology 7

Mechanism of injury 7

Risk groups for index ACL surgery 7

Treatment 8

Surgical technique 9

Contralateral ACL Injury Rate and Risk Factors 10

Return to Play after Index and Contralateral ACL Reconstruction 11

The Swedish National Knee Ligament Register 11

AIM 12

MATERIALS AND METHODS 12

Patients and Investigated variables 12

Ethics 13

Data Extraction....13
Statistical analysis....14
RESULTS....16
Patient sex....18
Patient age at index ACL reconstruction....18
Activity at index ACL injury....18
Timing of index ACL reconstruction....19
Graft selection at index ACL reconstruction....19
Graft harvest at index ACL reconstruction....20
Meniscal and chondral injuries....20
DISCUSSION....22
Patient sex....22
Patient age at index ACL reconstruction....23
Activity at index ACL injury....23
Timing of index ACL reconstruction....24
Graft selection at index ACL reconstruction....25
Graft harvest at index ACL reconstruction....25
Meniscal and chondral injuries....25
CONCLUSION....26
ACKNOWLEDGEMENT....26
POPULÄRVETENSKAPLIG SAMMANFATTNING....27
REFERENCE LIST....29

ABSTRACT

Background

An injury to the contralateral anterior cruciate ligament (ACL) and a subsequent reconstructive surgery is one of the most serious complications after ipsilateral index ACL reconstruction. It may be career ending for an athlete. To be able to prevent a future injury it is important to identify predictors associated with contralateral ACL reconstruction.

Purpose

To investigate if seven patient variables were predictors of contralateral surgery after ACL reconstruction.

Study Design

Prospective cohort study; level of evidence, 2

Methods

This register study is based on data from the Swedish National Knee Ligament Register. Patients who underwent index ACL reconstruction during the period of January 1, 2005 through December 31, 2008 were included. The inclusion criteria were age between 13 and 59 years with hamstring tendon or patellar tendon autografts in their index reconstruction. Follow-up started on date of index ACL reconstruction. Patients were followed; for five years, until the end of 2013 or until contralateral ACL reconstruction, whichever event occurred first. Following variables were investigated: patient sex, age at index reconstruction, activity at index injury, timing of surgery, graft selection, graft harvest site, meniscal and chondral injury. Relative risks (RRs) and 95% confidence intervals were calculated and adjusted for confounders using multivariate statistics.

Results

A total of 9061 participants were included in the cohort. During the 5-year follow-up period of this study, a total of 270 contralateral ACL reconstructions were performed. The contralateral reconstruction rate was 3% (95% CI, 2.7-3.4). Regression analysis revealed two significant associations. There was a significant higher risk of a contralateral

ACL reconstruction for young patient (males, RR=2.4 [95% CI, 1.7-3.4] and females, RR=2.9 [95% CI, 1.9-4.5], p<0.001) and for females with contralateral graft harvest (RR=3.3 [95% CI, 1.4-7.8], p=0.006).

Conclusion

The most important findings were that age less than 20 years at the time of index ACL reconstruction predicted an almost 3 times higher risk of contralateral ACL reconstruction. Graft harvest from the contralateral knee at index ACL reconstruction predicted a more than 3 times higher risk for contralateral ACL reconstruction among female participants. There were no association between patient sex, activity at index injury, graft selection, meniscal and chondral injury and subsequent contralateral ACL reconstruction.

BACKGROUND

Anatomy and function of the Anterior Cruciate Ligament

The Anterior Cruciate Ligament (ACL) is one of the four major ligaments of the knee. It connects the femur with the tibia and originates from the posteriomedial aspect of the lateral femoral condyle and inserts distally on the anterior part of the medial tibia. The main function of the ACL is mechanical as a constraint of joint motion. Primarily, it is a restraint to anterior tibial translation, prevents the tibia from sliding forward relative to the femur. It also prevents internal tibial rotation and controls the valgus angulation. Additionally, the ACL has a proprioceptive function. Mechanoreceptors in the ligament provide the central nervous system with afferent information about the position of the joint via the tibial nerve.

The ACL is composed of at least two major fiber bundles; the anteriomedial (AM) bundle and the posteriolateral (PL) bundle, named after their different insertion sites on the tibial plateau. When the knee is extended, the PL bundle is tight and ensures rotation stability. As the knee is flexed, the femoral attachment becomes more horizontal, causing the AM bundle to tighten and providing antero-posterior stability.

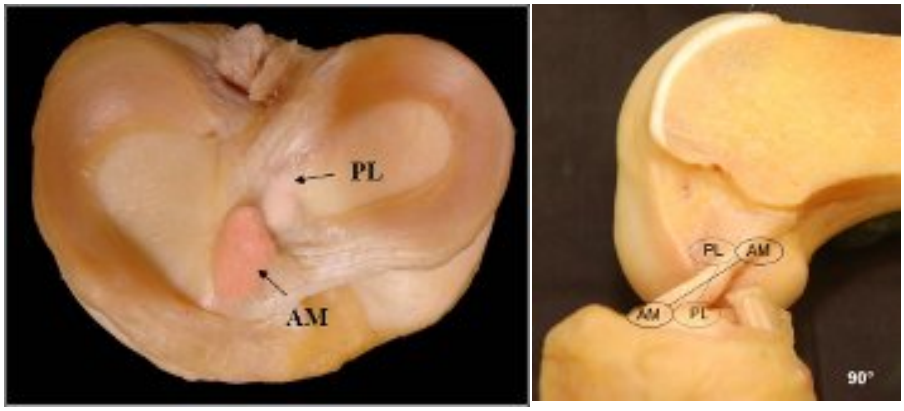

Figure 1, Left: insertion sites on the tibial plateau. Right: the two fiber bundles; an anteriomedial (AM part and a posteriolateral (PL) at the right knee. Reprinted with permission from University of Pittsburgh Medical Center, USA.

Morbidity – ACL injury

Rupture of the ACL leads to an unstable knee witch is functionally disabling both in activities of daily living and exercise. The ACL rupture will also cause a loss of proprioceptive information, which together with the increased instability may lead to episodes where the patient feels that the knee folds, "giving way". These episodes of giving way predispose the knee to further injuries, such as meniscus injury and damage to the joint cartilage [1]. Knee kinematics will also change during walking and exercise. This might promote an early onset of degenerative changes such as osteoarthritis (OA) in the knee. Development of post-traumatic OA is multifactorial and several risk factors such as intra-articular injuries, age, sex, genetics, obesity, joint deformity, sports participation, and muscle weakness have been suggested. However, the most important factor for the development of post-traumatic OA is a meniscus injury at the time of reconstruction. (Engelbretsen) Long-term data has shown that radiographic signs of osteoarthritis are much more prevalent ten to fifteen years after ACL reconstruction in those with combined ACL and meniscal injury and/or chondral lesion (21-48%) compared with isolated ACL injury (13%). [2]

Epidemiology

Injury to the ACL is very common among athletes and the annual incidence in Sweden is suggested to be 80 per 100,000 people per year. Close to 6000 individuals suffer ACL injuries every year in Sweden of which half choose ACL reconstruction. [3]

ACL injuries are more common among men, accounting for 60% of all injuries. Female patients are more likely to get injured at an earlier age. The mean age for diagnosis is 32 years and the average age of patients undergoing ACL surgery in Sweden is 27 years. [3, 4]

Mechanism of injury

Most of the ACL injuries occur in sports or exercise activities, primarily in activities with knee-pivoting movements such as soccer, floorball, team handball, basketball, and alpine skiing.

Previous studies based on video analysis of injury cases have shown that nearly three quarters of all ACL injuries occurred in noncontact situations. [5, 6] Studies have shown that most injuries occurred during sudden deceleration or landing maneuvers [7]. A relatively straight knee and knee valgus was seen frequently in the event of injury. The knee was also minimally rotated in either direction. Biomechanically the ACL is most vulnerable during anterior tibial translation, where the ACL is subjected to large shear forces. These forces occur during low flexion of the knee joint as well as large quadriceps muscle force.[8]. In such situations the damping capabilities of the knee are reduced.

Risk groups for index ACL surgery

Identifying risk factors for ACL injury and predisposing patients variables are the basis to introduce prevention. A variety of external and internal factors have been suggested to increase the risk for injury. [8] Type of sport activity is proposed to be an important external risk factor. ACL injuries are common in competitive sports. This makes the incidence rates much higher among athletes compared to the general population where the risk of suffering an injury to ACL is quite low. Environmental factors are primarily related to weather conditions, playing surface and shoe characteristics. Dry weather conditions as well as artificial turf, may increase the risk of ACL injuries compared to natural grass. [9]

The risk factor most commonly studied in sports is probably the influence of sex on the ACL injury risk. Female players have a two to three time higher ACL injury risk compared to their male counterparts. Females also tend to sustain their ACL injury at a younger age than males. [10] Other proposed internal risk factors for ACL injury include lower extremity alignment, femoral intercondylar notch size, ACL elevation angle, hormonal variation and neuromuscular control related biomechanical factors. [8]

The risk factors for an index ACL injury have been studied in Norwegian team handball. Top players were followed for two seasons and had an ACL injury rate on 1,8% among females and 1% among men. This indicates that top-level females injure their cruciate ligament twice as often as their male counterparts. Injuries occurred up to 75 % during games. Most injuries seemed to occur in situations where the friction between shoe and floor is of importance. [11]

Treatment

After an ACL injury, treatment can take the form of physiotherapy-controlled rehabilitation alone or ACL reconstruction and rehabilitation. In Sweden it is estimated that nearly half of all ACL injuries are treated non-surgically [4]. Approximately 40% of the patients who undergo ACL surgery are women. [4]

An ACL injury can be partial or complete. A complete rupture of the ligament is unable to heal due to biomechanical reasons; non-contact between the ACL remnants, a hostile environment towards chemotaxis, and a longer healing process due to the slow proliferation of ACL fibroblasts [12]. A partial tear might have the capacity to heal in case of an intact synovial lining. The difficulty in the treatment of an incomplete rupture is to know if the rupture has the capacity to heal or not. A return to a high activity level, mostly in pivoting sports, and high demands on function in daily life will necessitate an increase in the need for surgical treatment. The main indication for an ACL reconstruction is, lasting symptoms in the form of functional instability. ACL reconstruction leads to improved stability and by that, better function in sports and work.

Typically, patients who undergo an ACL reconstruction are young and have an ambition to return to pivoting sports. However, it has been shown that patients over 40 years have a

greater improvement in patient-reported variables after an ACL reconstruction than their younger counterparts. [13]

Surgical technique

Previously attempts have been made on ACL repair; however, due to very high risk of rerupture, only reconstruction is performed in modern health care. Great improvements have been done and todays ACL reconstruction is one of the most common frequent orthopaedic procedures. There are several options regarding choice of graft. The most common graft choice is an autograft, i.e. a tendon harvested from the patient. It is also possible to use an allograft, a tendon from a donor patient, however it is more expensive and studies have shown an increased risk of rerupture by using an allograft. [14] Patellar tendon (PT) graft has been the "gold standard" until a decade ago and is now secondary to hamstring tendon (HT) graft. In Sweden 2012, 98 % of surgeons used the HT graft as a transplant in ACL reconstruction. [4] Studies have shown that ACL reconstruction with PT graft yields more harvest site morbidity with anterior knee pain and pain when kneeling. [12].

The surgical technique in ACL reconstruction has undergone a major development in the last three decades. In 1980 the first arthroscopically assisted reconstruction was performed. Today, focus is to recreate the native anatomy, so-called anatomic ACL reconstruction. The concept is based on graft placement into the native insertion site. It also includes restoration of the functional bundles and to recreate the native tension pattern in the ligament. The aim of this anatomic ACL reconstruction is to achieve native ACL function and original knee kinematics. The rapid development of surgery technique and development of an anatomic ACL reconstruction leads to great demand on surgical precision, regarding tunnel and portal placement.

Figure 2, Upper: Patellar tendon autograft. Lower: Hamstring tendon autograft. Reprinted with permission from University of Pittsburgh Medical Center, USA

Contralateral ACL Injury Rate and Risk Factors

Injury to the contralateral ACL is a significant health issue and one of the most serious complications after index ACL reconstruction. [15-17] The evidence presented in the literature shows that the risk of sustaining a contralateral ACL injury is greater (11.8%) than the risk of sustaining a first time ACL injury (5.8%). [15-19] There are few studies reporting the long-term rate of contralateral ACL rupture. A case series study found that one quarter of patients with isolated index ACL rupture had had a contralateral ACL rupture at 15-year follow-up. [20]

The most prominent risk factors for sustaining a contralateral ACL injury is young age and return to a high level of activity. Among patients younger than 20 years, 1 in every 3.5 patient undergoing ACL reconstruction sustain a further ACL injury to either knee within a 5-year period.[21]

Several studies have not revealed any significant correlation between sexes and incidence of a contralateral injury, meaning that the risk for sustaining a contralateral ACL rupture is equal for men and women. [15, 18, 22-24]

Graft choice at the index ACL reconstruction may also influence the risk for a rupture at the contralateral ACL. Two long-term follow up studies, where PT and HT grafts were compared, reports contralateral ACL rupture to be significant in association with PT graft. [23, 25]

Crucial to the risk for a future contralateral injury may also be which side is affected. A study among soccer athletes showed that ACL reconstruction on the non-dominant limb leads to a

higher future rate of contralateral ACL reconstruction (16%) compared to ACL reconstruction on the dominant limb (3.5%). Reconstructive ACL surgery on the non-dominant limb potentially places the dominant limb at risk for future ACL injury. [26]

Return to Play after Index and Contralateral ACL Reconstruction

ACL rupture is a potentially serious injury and it may be career ending. Therefore many affected athletes wonder whether they will be able to return to their previous activity level. Statistically, the prognosis for this is bleak. Less than half of participants undergoing surgery return to competitive sport.

Several reasons for not returning to the same level of sports activity have been suggested in the literature, including low knee-related quality of life, knee instability, pain or increased age. [27] Reduced function of the knee and a sense of not trusting the knee are some additional reasons. [28] A recent study have, however, found that approximately 90% of participants achieved normal knee function regarding outcomes such as laxity and strength, suggesting other factors than reduced function to be the reasons why these participants do not return to competitive sport. [29]

Among soccer players, females and older are less likely to return to play than males or younger. Among soccer athletes men were more likely than women to attribute their ACL injury as the primary reason they were no longer playing soccer. [26]

The number of ACL ruptures per individual plays a role for the prognosis. Patients with bilateral ACL injuries reports poorer knee function and quality of life compared with those who undergo unilateral ACL reconstruction. It is less likely for those with bilateral injuries to return to their previous activity level compared to patients with unilateral ACL-reconstruction, 23% compared to 43%. [28]

The Swedish National Knee Ligament Register

The Swedish National Knee Ligament Register is a nationwide clinical database, established January 1, 2005 [30]. The purpose of the register is to ensure the quality and to develop cruciate ligament surgery. The initial goal was to report every ACL reconstruction performed in Sweden. Today the register covers 90% of all ACL reconstructions in Sweden [4]. Before

2010 it was only a surgical register and therefor patients who were treated non-surgically were not represented. Today, however, the aim is to include non-surgical individuals with ACL injuries as well.

The register data are reported through a web based protocol consisting of 2 parts; one for the surgeon-reported section and one patient-reported section. In the surgeon section, information about age and sex, activity at injury, time from injury to reconstruction, graft selection and fixation method, single- or double-bundle reconstruction is reported. Previous surgery and all concomitant injuries are also registered as well as information on smoking habits.

AIM

The purpose of this study was to identify patient characteristics that may be associated with an increased risk for contralateral ACL injury after an index ACL reconstruction. The hypothesis was that there are specific patients that have a higher risk of sustaining a contralateral injury after a index ACL reconstruction.

MATERIALS AND METHODS

In this study data was extracted from the Swedish National Knee Ligament Register, 2005-2013.

Patients and Investigated variables

All patients registered for index ACL reconstruction during the period of January 1st 2005 through December 31st 2008 and registered for contralateral surgery from January 1st 2005 to December 31st 2013 were eligible for inclusion. Patients were followed for 5 years (1826 days) after index surgery. Follow-up ended with either ACL reconstruction surgery in the contralateral knee or on December 31st 2013. A large proportion of contralateral ACL ruptures occur during the second and third years after reconstruction. [17] Therefore, it is reasonable to set a five years follow up period. Five years follow-up also enables data extraction from a larger sample.

Males and females were expected to differ significantly in baseline demographics and anthropometric data; therefore data was analysed separately.

Following seven patient variables were investigated: patient sex, age at index reconstruction, activity at index injury, timing of surgery, graft selection, graft harvest site, meniscal and chondral injury.

Ethics

Participation in the Swedish National Knee Ligament Register is voluntary for patients and for surgeons. No written consent is necessary for national databases in Sweden. All information about patients in the register is strictly confidential as it complies with the Swedish legislation relating to data security. Extracted data in research purposes is anonymous and investigators only had access to unidentifiable patient data. The Regional Ethical Review Board in Gothenburg, Sweden, approved the study. This cohort study was conducted according to the WMA Declaration of Helsinki. [31]

Data Extraction

31 000 surgeries were registered in the Swedish Knee Ligament Register from January 1, 2005 to December 31, 2013. Of these 20 852 were excluded because of either misclassification, ACL reconstruction was not the primary one, index ACL reconstruction after December 31, 2008 or duplicates. Remaining individuals, with index ACL reconstruction during January 1, 2005 to December 31, 2008, were eligible for inclusion.

Patients who appeared two or more times were manually reviewed in search of ACL reconstructive surgery at the contralateral knee. Among these the inclusion criteria were (1) ACL reconstruction with HT or PT graft, (2) age 13-59 years, (3) no concomitant fractures (of tibia, fibula, patella or femur or where it was unknown if fracture occurred), (4) no concomitant ligament injuries (LCL, MCL and PCL), (5) index ACL reconstruction after January 1, 2005 (Figure 1). After application of the abovementioned criteria, 9061 patients were included in the study.

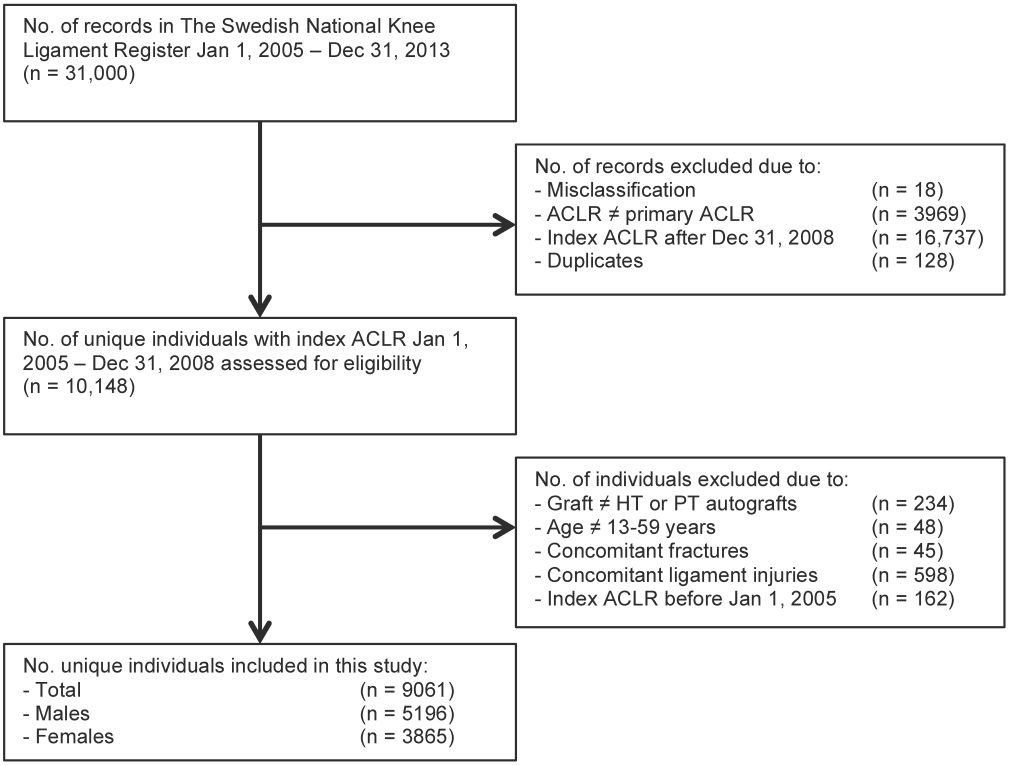

Figure 3, Flow diagram of inclusion and exclusion criteria. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; HT, hamstring tendon; PT, patellar tendon.

Statistical analysis

Tables and diagrams were generated using Microsoft® Excel® for Mac 2011, version 14.3.5 (Microsoft Corporation, Redmond, Washington, USA). SPSS® Statistics, version 20.0.0 (IBM, Armonk, New York, USA) was used for performing statistical analysis. The independent samples t-test was used to compare sets of independent and normally distributed continuous data. For comparison of non-parametic continuous data the Mann-Whitney U test was used. Two-tailed p-values for categorical data were calculated by use of Fisher's exact test and the two-tailed chi-square test with Yates' correction for continuity. Risk estimates with relative risks (RR) were calculated by use of a stratified relative risk regression model for binary dependent variables. A 95% confidence interval was used for presentation (95% CI). Confidence intervals for proportions were calculated with the Agresti-Coull method for interval estimation of binomial proportions. Possible confounding factors (patient age, smoking, activity, injury-to-surgery interval, graft selection, harvest site, graft fixation, single-bundle and double-bundle reconstruction, graft width, meniscal injury and

chondral injury) was adjusted for in multivariate analysis. Statistical significance was defined as a 95% CI for relative risks not including 1.0.

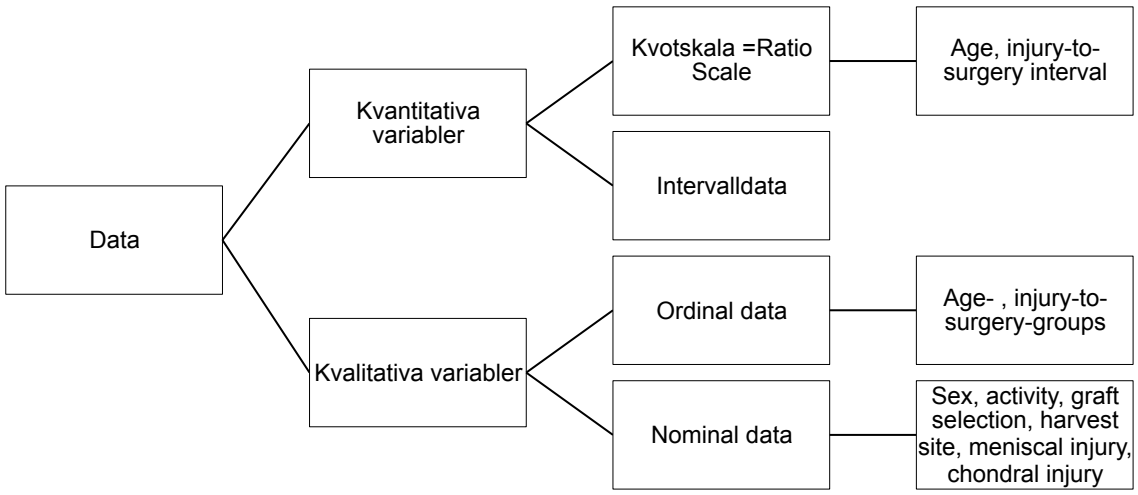

Figure 4, Data was characterized as nominal scale data and ratio scale data. Ratio scale data was stratified into ordinal scale data when comparing risk estimates in order to attain clinically

.

RESULTS

A total of 9061 participants were included in our cohort (males, n=5196; 57.3% and females, n=3865; 42.7%). (Figure 1) Median age at index ACL injury was 22 years and 25 years at index ACL reconstruction. Male participants were significantly older (p<0.001) and the proportion of adolescents (age 13-19 years) was doubled among female participants (42% vs. 20%; p<0.001) (Table 1). The most commonly used graft at the index ACL reconstruction was HT graft (n=8047; 88.8%); the majority of these (96.8%) were single-bundle reconstructions. The PT graft was used in 11.2% (n=1014). The proportion of contralateral graft harvest was similar among males and females (p=0.931). The proportion of smokers was 5.2%, with not significant difference between males and females (p=0.084). The most common activity at index injury was football, accounted for 43.7% of index injuries. Football was more common among male participants (49.5% vs. 35.9%; p<0.001).

During the 5 year of follow-up period, 3.0% (95% CI, 2.7-3.4) underwent contralateral ACL reconstruction (n=270; males, n=158; females, n=112). There was no significant difference in crude contralateral reconstruction rates between males and females (males, 3.0% [95% CI, 2.6-3.5] and females, 2.9% [95% CI, 2.4-3.5]; p=0.695).

Two factors were significantly associated with contralateral ACL reconstruction. Being young (< 20 years) and among female participants, graft harvest from the contralateral knee.

TABLE 1

Baseline demographics and anthropometric data

	Males n = 5196	Females n = 3865	p-value
Age at index ACL injury (n = 8107), y	25.8 ± 8.5; 24.0 (5-57)	23.4 ± 9.7; 19.0 (6-58)	< 0.001[1]
Age at index ACL reconstruction, y	27.8 ± 8.9; 26.0 (13-59)	25.4 ± 10.1; 22.0 (13-59)	< 0.001[1]
Adolescents (age 13-19 y), %	20.3 (19.2-21.4)	41.6 (40.0-43.1)	< 0.001[2]
Height (n = 2442), m	1.81 ± 0.06; 1.80 (1.58-2.02)	1.68 ± 0.06; 1.68 (1.50-1.89)	< 0.001[1]
Weight (n = 2476), kg	83.1 ± 11.6; 82.0 (57.0-184.0)	66.7 ± 11.0; 65.0 (34.0-175.0)	< 0.001[1]
Body Mass Index (n = 2437), kg/m^2	25.5 ± 3.4; 25.1 (18.0-62.9)	23.7 ± 3.6; 23.1 (12.1-56.8)	< 0.001[1]
Smokers (n = 2483), %	4.5 (3.5-5.7)	6.1 (4.8-7.6)	0.084[2]
HT autografts, %	86.8 (85.9-87.7)	91.5 (90.7-92.4)	< 0.001[2]
Contralateral graft harvest, %	1.5 (1.2-1.9)	1.6 (1.2-2.0)	0.931[2]
Single-bundle HT reconstructions, %	96.8 (96.2-97.3)	96.9 (96.4-97.5)	0.701[2]
Graft width (n = 1979), mm	8.3 ± 1.0; 8.0 (5.0-14.0)	7.9 ± 0.9; 8.0 (5.5-13.0)	< 0.001[1]
Surgery duration (n = 8394), min	75 ± 25; 70 (20-220)	74 ± 24; 70 (20-246)	0.057[1]
Outpatient ACL reconstruction, %	63.7 (62.4-65.0)	61.1 (59.5-62.6)	0.010[2]
Meniscal injury, %	42.0 (40.6-43.3)	37.3 (35.8-38.9)	< 0.001[2]
Cartilage injury, %	30.0 (28.8-31.3)	24.0 (22.7-25.4)	< 0.001[2]
Injury-to-surgery interval (n = 8067), days	588 ± 860; 295 (0-7227)	573 ± 871; 279 (0-7226)	0.034[3]
Football at index injury (n = 8983), %	49.5 (48.1-50.9)	35.9 (34.4-37.4)	< 0.001[2]

Data are presented as sample mean ± standard deviation; sample median (min-max values) or proportion (95% confidence interval). No. of participants with complete data are presented when missing data occurred. The injury-to-surgery interval displayed a marked positive, right-tailed skew with a sample mean of 581 ± 865 days. The median interval was 288 days (min-max, 0-7227). ACL = Anterior Cruciate Ligament; HT = Hamstring Tendon.

1. Independent samples t test; 2. Fisher's exact test; 3. Independent samples Mann-Whitney U test

Patient sex

There was no significant difference between females and males in risk of subsequent contralateral ACL reconstruction (males, RR=1.3 [95% CI, 0.8-2.0] and females, RR=0.8 [95% CI, 0.5-1.3], p=0.334).

Patient age at index ACL reconstruction

Regression analysis showed that age less than 20 years was associated with a significantly increased risk of contralateral ACL reconstruction compared with older patients (males, RR=2.4 [95% CI, 1.7-3.4] and females, RR=2.9 [95% CI, 1.9-4.5], p<0.001). Significantly reduced risk of contralateral ACL reconstruction was seen in the patient group aged 30 years or more (males, RR=0.4 [95% CI, 0.2-0.6] and females, RR=0.3 [95% CI, 0.1-0.5], p<0.001) (Table 2).

TABLE 2

Patient age at index ACL reconstruction and the 5-year risk of contralateral ACL reconstruction

	Males		Females	
Age interval, y	*Adjusted RR (95% CI)*	*p-value*	*Adjusted RR (95% CI)*	*p-value*
< 20	2.4 (1.7-3.4)	< 0.001	2.9 (1.9-4.5)	< 0.001
20-29	1.1 (0.7-1.5)	0.742	0.7 (0.5-1.2)	0.192
≥ 30	0.4 (0.2-0.6)	< 0.001	0.3 (0.1-0.5)	< 0.001

ACL = Anterior Cruciate Ligament; RR = Relative Risk; CI = Confidence Interval. The analysed age interval was compared with all other age intervals.

Activity at index ACL injury

Playing Football, basketball, floorball, handball, volleyball and racket sports, grouped as “cutting/pivoting” activities, at the index ACL injury was not a significant predictor for risk of contralateral ACL reconstruction (males, RR=1.1 [95% CI, 0.6-1.9], p=0.829 and females, RR=1.9 [95% CI, 0.8-4.8], p=0.168).

Timing of index ACL reconstruction

Association between injury-to-surgery and risks of contralateral ACL reconstruction was seen among females. Those who had index ACL reconstruction in the intervals of less than 3 and 6 months after injury underwent significantly more contralateral surgery, compared with all other intervals (< 3 months, RR=3.3 [95% CI, 1.4-7.9], p=0.006 and < 6 months, RR=2.4 [95% CI, 1.1-5.3], p=0.037 respectively). There was no such association among male participants (Table 3).

TABLE 3

Timing of index ACL reconstruction and the 5-year risk of contralateral ACL reconstruction

	Males		Females	
Injury-to-surgery interval, m	*Adjusted RR (95% CI)*	*p-value*	*Adjusted RR (95% CI)*	*p-value*
< 1 m	3.3 (0.9-12.7)	0.081	3.9 (0.6-26.0)	0.163
< 3 m	1.2 (0.5-2.7)	0.702	3.3 (1.4-7.9)	0.006
< 6 m	1.7 (1.0-2.9)	0.070	2.4 (1.1-5.3)	0.037
< 12 m	1.5 (0.9-2.7)	0.153	2.3 (0.9-5.8)	0.076
< 24 m	0.9 (0.5-1.8)	0.765	7.0 (1.0-51.8)	0.056

ACL = Anterior Cruciate Ligament; RR = Relative Risk; CI = Confidence Interval. The analysed injury-to-surgery interval was compared with all other time intervals.

Graft selection at index ACL reconstruction

There was no significant difference between the HT and PT graft groups in risk of subsequent contralateral ACL reconstruction.

TABLE 4

Graft selection at index ACL reconstruction and the 5-year risk of contralateral ACL reconstruction

	Males		Females	
Graft selection	*Adjusted RR (95% CI)*	*p-value*	*Adjusted RR (95% CI)*	*p-value*
HT autograft	0.8 (0.4-1.5)	0.460	1.3 (0.3-5.3)	0.747
PT autograft	1.3 (0.7-2.4)	0.460	0.8 (0.2-3.3)	0.747

ACL = Anterior Cruciate Ligament; RR = Relative Risk; CI = Confidence Interval; HT = Hamstring Tendon; PT = bone-Patellar Tendon-bone.

Graft harvest at index ACL reconstruction

There was a significant association between graft harvest from the contralateral knee at index ACL reconstruction and risk of contralateral ACL reconstruction among females (RR=3.3 [95% CI, 1.4-7.8], p=0.006). There was no similar association among male participants (RR=0.5 [95% CI, 0.1-3.3], p=0.448).

Meniscal and chondral injuries

Meniscal and chondral injury at index ACL reconstruction was reported in 40.0% (n=3624) and 27.5% (n=2488) respectively. Meniscal and chondral injuries were not associated with the risk of contralateral ACL reconstruction (Table 5).

TABLE 5

Injuries registered at index ACL reconstruction and the 5-year risk of contralateral ACL reconstruction

	Males		Females	
Type of injury	*Adjusted RR (95% CI)*	*p-value*	*Adjusted RR (95% CI)*	*p-value*
Meniscal injury	1.5 (1.0-2.3)	0.031	1.0 (0.6-1.6)	0.960
Chondral injury	0.9 (0.5-1.6)	0.675	0.6 (0.3-1.3)	0.194

ACL = Anterior Cruciate Ligament; RR = Relative Risk; CI = Confidence Interval.

DISCUSSION

The main findings were that age less than 20 years at the time of index ACL reconstruction predicted an almost 3 times higher risk of contralateral ACL reconstruction and among female participants, graft harvest from the contralateral knee at index ACL reconstruction predicted a more than 3 times higher risk contralateral ACL reconstruction. Patient sex, activity at index injury, graft selection, meniscal and chondral injury were not predictors of subsequent contralateral ACL reconstruction. To our knowledge, this is the first study based on nationwide register data to investigate predictors of contralateral ACL reconstruction.

Prospective cohort studies are known to be one of the best in observational studies linking exposure to outcome. However, it is not possible to distinguishing true causality between patient predictors and contralateral ACL reconstruction in the present study, only association. This study design also needs a follow-up time to be sufficient for outcomes to occur. A 5-year follow-up might not be sufficient to detect a significant change related to a specific exposure and variables may require a longer follow-up time.

The strengths of this study include the large cohort of patients. The Swedish National Knee Ligament Register has also a great coverage in the country and the diversity in the register makes our findings generalizable to a larger population.

Limitations of this study include the fact the study is based on a surgical register and our end-point was contralateral ACL reconstruction. This means that only those who had a index surgery and later on a contralateral ACL reconstruction were included. Patients receiving conservative treatment were not included. By using contralateral ACL ruptures as an endpoint the true ACL ruptures were probably underestimated. This could also be a source for selection bias because of study participants may not be representative, since treatment might differ in different patient categories. Another limitation in our study is that information about activity level and return to sports was not available in the register and therefore not included in our study.

Patient sex

This study found no differences regarding contralateral ACL reconstruction risk between men and women. Similar findings have been reported in other long-term studies, with

follow-up varying from 3 to 15 years. [17, 20, 21, 25, 32, 33] In an recent meta-analysis [24] three articles where analysed [18, 19, 22] and did not reveal any significant correlation between sexes and incidence of a contralateral ACL reconstruction. In contrast, some studies have found that female patients are more prone to suffer a contralateral ACL injury than male patients. [19, 34]

Awareness of different confounders is important when interpreting these results. First, studies have indicated that women more seldom return to cutting/pivoting activities than men. [27, 29] If so, women may be at a lower risk for sustaining a new ACL rupture. This study consists of follow-up data in outcome after index ACL reconstruction and it includes a lower number of women than men. It is therefore likely that more women suffer a contralateral rupture but never end up in our surgical registry.

Patient age at index ACL reconstruction

Subsequent contralateral ACL reconstruction was associated with young age at the index procedure. Being younger than 20 years at the first reconstruction predicted an almost 3 times higher 5-year risk of contralateral anterior cruciate ligament reconstruction. This is consistent with the findings of the recent case control study by Webster et al, who found that 1 in every 3.5 patients who underwent ACL reconstruction and were younger than 20 years sustained a further ACL injury to either knee within a 5-year period. Young age have previously in literature been reported as a risk factor for further ACL injury [19, 20, 23, 25, 32, 33]

Different explanations to the increased risk for young patients have been suggested. One explanation could be the fact that young people are more active and are more likely to return to cutting and pivoting sports than older patients. [19, 21, 26, 33] Another explanation may be an incomplete neuromuscular maturation and biomechanical factors in young patients. It has been reported that neuromuscular impairments are risk factors for a new ACL rupture. [34]

Activity at index ACL injury

There was no significant increased 5-year risk of contralateral ACL reconstruction for patients registered as cutting/pivoting athletes. Our finding is in contrast to the findings

based on a case study based on 612 patients by Salmon et al. who found that a return to high level sport (competitive side-stepping, pivoting, or jumping sports) increased the five-year risk for contralateral ACL injury by a factor of 10. Returning to activity at lower level showed a much lower incidence of injury. [17] Webster et al. also reported an increased risk for contralateral ACL rupture for patients returning to cutting/pivoting sports. [21]

Cutting and pivoting sports (Football, floorball, handball, basketball, racket sports and volleyball) involve movements that predispose knees to ACL rupture. It is possible that elite athletes are more likely to suffer a index ACL injury than amateur athletes. It is therefore reasonable to assume this difference even among contralateral ruptures. Our study is based on data from a register where no information about activity level is available.

Other explanation to our findings could be that many athletes never return to their reinjure level of sport participation and thereby reduce their risk of a new ACL rupture. Arden et al. found that less than half of patients undergoing surgery return to competitive, high-level sport. [29]

Neither information about activity level or return to previous sport are available in The Swedish National Knee Ligament Register and because of that it is not possible to adjust for these factors.

Timing of index ACL reconstruction

This study found a significant association between injury-to-surgery and risks of contralateral ACL reconstruction. There was a higher risk among females who had their index ACL reconstruction early, less than 3 and 6 month after injury. In our study no such difference was seen among men.

It is important to take into consideration possible bias; patients with early reconstruction probably have higher functional demands and thus a higher risk of exposing the knee to high-risk activities. Activity level could therefore be a confounding factor in this analysis. A second reason for bias results towards a more unfortunate outcome with early ACL reconstruction could be the fact that patients undergoing early index reconstruction are more likely to undergo subsequent contralateral ACL reconstruction at an early stage as well and then be detected within the five-year follow up time.

Graft selection at index ACL reconstruction

The most common graft in this cohort was HT graft, 89 %. There was no significant difference in outcome in the HT graft and PT graft groups in 5-year risk of subsequent contralateral ACL reconstruction.

Similar findings have been reported in a case study by Salmon et al. including 612 ACL patients, where no significant differences between the two graft types was found. [17] However, our finding is discordant with recent long-term follow-up studies that have found a significant higher 15-year risk of contralateral ACL ruptures for patients receiving a PT graft compared to those receiving a HT graft. [25, 32] Pinczewski et al. reported also significantly more contralateral ACL ruptures in the PT group at 10-year follow-up. [23]

Graft harvest at index ACL reconstruction

Among females we found a significant association between graft harvest from the contralateral knee at index ACL reconstruction and risk of contralateral ACL reconstruction. Graft harvest from the uninjured knee predicted a more than 3 times higher risk of contralateral ACL reconstruction.

To our knowledge there have been no previous study investigate contralateral graft harvest for association with risk of contralateral ACL reconstruction.

Literature indicates that tendon regeneration occur at the harvest site. Despite this, harvesting a tendon from the healthy knee would possibly lead to structural and functional alterations including abnormalities in biomechanical and neuromuscular control. [35] In a recent current concepts article, where Hewett et al. presented the latest evidence related to risk factors associated with contralateral injury, biomechanical and neuromuscular control deficits and imbalances found to be strongly associated with secondary ACL injury incidence.

Meniscal and chondral injuries

The incidence of meniscal injury in our cohort was 40 % and 27.5 % in chondral injury at index ACL reconstruction. We found that injuries to these structures were not associated with the risk of contralateral ACL reconstruction. Similar findings have been reported in literature [17, 32, 33]

CONCLUSION

Young patients at index ACL reconstruction show a significantly higher risk for contralateral ACL injury in five years. Among female patients, graft harvest from the contralateral knee was also a predictor of contralateral ACL injury.

More research has to be done. Information about anthropometric factors as predictors for ACL surgery would be important and lead us to focus preventive efforts on the right individual.

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POPULÄRVETENSKAPLIG SAMMANFATTNING

Främre korsbandsskador är vanligt förekommande bland idrottsaktiva. I Sverige drabbas ca 6000 individer varje år. Av dessa genomgår ungefär hälften rekonstruktiv kirurgi, vilken syftar till att funktionellt återskapa det främre korsbandet och därmed återfå stabilitet och funktion i knät. De patienter som inte opereras genomgår en konstruktiv behandling i form av enbart rehabilitering. En främre korsbandsskada är en allvarlig händelse för den drabbade individen och ofta så allvarlig att den kan innebära slutet på en idrottskarriär. Att ta sig tillbaka efter en sådan skada, med lång tid av rehabilitering, ställer stora krav på individen och på sjukvården. Att efter rehabilitering återigen drabbas av en korsbandsskada på det andra knät är en fruktad händelse. Mycket av dagens forskning går idag ut på att vi i framtiden ska kunna skräddarsy behandling, rehabilitering och preventiva insatser utefter varje individ. Forskning som syftar på att kartlägga faktorer och personer som löper stor risk att drabbas av en ny korsbandsskada är en del i denna individanpassning.

Syftet med uppsatsen är att identifiera prediktorer för en kontralateral korsbandsskada hos patienter som genomgått en primär rekonstruktion av främre korsbandet. I tidigare studier där man undersökt riskfaktorer har man sett att ålder och kön kan vara prognostiska faktorer för en högre risk för kontralateral främre korsbandsskada. Detta är dock inte en vedertagen sanning och ämnet måste studeras ytterligare. Så vitt vi vet är detta den första riksomfattande registerstudien i världen som går ut på att undersöka prediktorer för kontralaterala korsbandsskador.

Svenska Korsbandsregistret har funnits sedan 2005, och är en klinisk databas i vilken all information om främre korsbandskirurgi som genomförs i Sverige registreras. Denna studie baseras på data från Korsbandsregistret. Studien gick till så att patienter följdes i fem år efter sin primära korsbandsoperation för att undersöka risken att under den tiden drabbas av en ny korsbandsskada på det andra knät. Vi jämförde därefter olika subgrupper med avseende på hur stor andel i varje grupp som genomgått en ny operation på det andra knät. De faktorer som analyserades är kön, ålder, aktivitet, tid mellan skada och kirurgi, val av graft, vilken sida graften skördades samt samtidiga menisk- och broskskador.

Resultaten visar att unga individer (yngre än 20 år) har en 3 gånger högre risk att drabbas av en korsbandsskada på det andra knät. För kvinnliga patienter spelade det roll vilken sida

korsbands-graften skördades. De kvinnor, som blivit opererade med graft från det friska knät löpte en 3 gånger högre risk att drabbas av korsbandsskada på det kontralaterala knät. Vi fann ingen korrelation mellan kön, aktivitet, vilken typ av graft, menisk- och broskskador och risken att i framtiden drabbas av en ny korsbandsskada på det andra knät.

Studien har gett oss mer kunskap om vilka patienter som löper ökad risk för kontralaterala korsbandsskador.

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