2016

Fifteen-year survival of endoscopic anterior cruciate ligament reconstruction in patients aged 18 years and younger

Morgan Matthew

Lucy Salmon

Alison Waller

Justin Roe

Leo Pinczewski
University of Notre Dame Australia, leo.pinczewski@nd.edu.au

This article was originally published as:
Matthew, M., Salmon, L., Waller, A., Roe, J., & Pinczewski, L. (2016). Fifteen-year survival of endoscopic anterior cruciate ligament reconstruction in patients aged 18 years and younger. *American Journal of Sports Medicine, 44* (2), 384.
http://doi.org/10.1177/0363546515623032

This is the author's post-print copy of the article published as:

Morgan, M., Salmon, L., Waller, A., Roe, J., & Pinczewski, L. (2016). Fifteen-year survival of endoscopic anterior cruciate ligament reconstruction in patients aged 18 years and younger. *American Journal of Sports Medicine, 44*(2), 384-392. doi: 10.1177/0363546515623032

15 Year Survival of Endoscopic Anterior Cruciate Ligament Reconstruction in Patients Aged 18 and Under

ABSTRACT

Background. Within the young population, the literature examining the short term survival and the variables contributing to ACL injury after primary ACL reconstruction is limited. The long term evidence for the same is non-existent.

Purpose: To determine the long term survival of the ACL graft and the CACL after primary reconstruction in those aged 18 years and under, and to identify the factors that increase the odds of subsequent ACL injury.

Study Design: Case series; Level of evidence, 4.

Methods: Patients having undergone primary ACL reconstruction at age 18 or less between 1993 and 1998, included in a prospective database by a single surgeon were considered. Single-incision endoscopic ACL reconstruction was performed with either autologous bone-patellar tendon-bone graft (BPTB) or hamstring tendon graft (HT). At a minimum of 15 years after ACL reconstruction patients completed a subjective questionnaire regarding current symptoms, further ACL injury, family history of ACL and level of activity.

Results: 288 juveniles, aged 13-18 years, met the inclusion criteria of which 242 (84%) were reviewed at a mean of 16.5 years after ACL reconstruction. 75 (31%) patients sustained a further ACL injury of which 27 (11.2%) suffered an ACL graft rupture, 33 suffered a CACL injury (13.6%) and 15 sustained BOTH an ACL graft and a CACL rupture (6.2%) over 15 years. Survival of the ACL graft was 95%, 92%, 88%, 85% and 83% at 1, 2, 5, 10 and 15 years, respectively. Survival of the CACL was 99%, 98%, 90%, 83% and 81%, respectively. Survival of the ACL graft was less favourable in those with a positive family history (69% versus 90%, HR 3.6, p = .001). Survival of the CACL was less favourable in males than in females (75% versus 88%, HR 2.1, p = .03) and those that returned to competitive team ball sports (78% versus 89%, HR 2.3, p=0.05).

Conclusion: After ACL reconstruction in those aged 18 years or less, further ACL injury occurred to 1 in 3 over 15 years. The 15 year survival of the ACL graft was 83% and 15 year survival of the CACL was 81%. Family history of ACL rupture significantly increased the hazard for ACL graft rupture and CACL injury was more

common in males and those who return to team ball sports. High subjective scores and continued participation in sports were maintained over the long term after ACL reconstruction in the juvenile population.

Keywords: ACL reconstruction; graft rupture; juvenile; contralateral ACL; survivorship; long-term.

What is known about the subject: It has been demonstrated that younger populations are more likely to have a second ACL injury after ACL reconstruction, compared to adults. However the data is limited and the incidence of reinjury over the longer term (>5years) has not been reported in the juvenile population

What this study adds to existing knowledge: This study documents the long term incidence of ACL graft and contralateral ACL injury after reconstruction in a large population of juveniles.

INTRODUCTION

The incidence of anterior cruciate ligament injury in children and adolescents is increasing, especially in those who practice competitive sports[4, 7, 9, 12], reportedly accounting for 0.5-3% of all ACL injuries.[15] The increase in the rate of ACL injuries in the younger population is likely multifactorial and is a reflection on the increased awareness of this injury within this population, the higher rates of participation in high demand sports at an earlier age and improved rates of diagnosis as a result of better imaging and diagnostic tools.

As with their adult counterparts, the absence of ligamentous stability within the child's knee predisposes them to the risk of further meniscal and chondral injuries, potentially leading to early degenerative changes. As such, the current literature identifies a present trend towards ACL reconstruction as the preferred treatment option for ACL injuries in the young, especially given the poor outcomes associated with non-operative treatment.[5, 8, 26, 30] This trend towards surgical management of ACL rupture in children is reflected in the Australian population with the number of ACL reconstructions in children younger than 15 years of age increasing by almost 4 times over the last 15 years.[19]

Even more devastating than a primary ACL injury is the increased risk of further injury to either the ACL graft or the native ACL in the contralateral knee. Further ACL injury after primary ACL reconstruction is a well recognised complication, especially in the young, with several studies reporting a higher incidence of further ACL injury in this population compared with their older equivalents.[1, 2, 14, 16, 17, 27, 29, 31, 33] In their Danish ACL registry study, Lind reported an 8.7% risk of revision ACL reconstruction over a 5 year period in patient's younger than 20 years of age.[14] Similarly, in a series of 119 patients in this same age group, Magnussen reported a revision rate of 14.3% at a minimum of 6 months post primary reconstruction.[16] Shelbourne identified a 17% increased risk of further ACL injury after reconstruction in children aged under 18 over 5 years[29] and more recently, in their series of 110 young people aged <20 years, Webster reported an incidence of subsequent ACL injury of 29% at a minimum of 3 years post primary ACL reconstruction.[33]

In the current body of evidence surrounding repeat ACL injury in the younger population, the long term incidence is inadequately described. Therefore, the aim of this study was to determine the long term incidence of ACL graft and CACL rupture and to identify the factors that affect ACL graft and CACL survival in a population aged 18 years or less at a minimum of 15 years post primary ACL reconstruction.

MATERIALS AND METHODS

Patient Selection

Subjects included in the study were identified from a prospective database of knee surgery and had undergone a primary ACL reconstruction performed by a single surgeon [redacted] in a single unit between the years of 1993 and 1998 and were aged ≤ 18 years at the time of surgery. The exclusion criteria were: (1) patients who had had a previous CACL rupture, (2) those not wishing to be involved in a research project, (3) those who died (of unrelated causes) during the study period.

Patient demographics were recorded in a prospective database and included information on the side of surgery, age, gender, graft type, graft size and meniscal or articular cartilage injury seen at the time of surgery.

Participants were sent an information sheet via post or email detailing the project and inviting them to participate. Subjective outcome data was obtained by contacting all subjects meeting the inclusion criteria via telephone or email at a minimum of 15 years following the surgery. Those willing to participate in the study completed a telephone interview or written questionnaire, which was returned to us via post or email. A research physiotherapist or an honours medical student, both of whom had not been involved in the original surgery, performed the telephone questionnaires.

Ethical approval was sought and granted, after submission of the study protocol, by a local independent human ethics committee ([redacted]).

Subjective Evaluation

The questionnaire completed by patients included the full International Knee Documentation Committee (IKDC) subjective knee evaluation form in addition to questions relating to family history of ACL rupture, subsequent injury and/or surgery to either knee, whether return to pre-injury level of sport was achieved and the current level of activity of the subject. Family history was considered to be positive if the patient had a first degree relative (parents or siblings) who had sustained an ACL rupture at any time. A return to IKDC level 5 sports was defined as regular participation in very strenuous activities involving cutting or pivoting type manoeuvers, as in basketball or soccer.

All patients who reported further injury to either knee that had not previously been documented were invited to attend for further review. Graft rupture or CACL rupture was considered to have occurred only if: (1) the patient had had confirmed further knee reconstructive surgery (graft rupture) or primary reconstruction (CACL) performed in our unit or by another orthopaedic surgeon; (2) had clinical examination and/or an MRI scan reviewed by our unit to confirm ACL deficiency or (3) if the patient had reported another injury characteristic of an ACL tear to either knee and they had not been reviewed by us. For this last group we assumed a graft rupture or CACL rupture for the purposes of the survival analysis as a worse case scenario.

Operative Technique

ACL reconstruction was performed by the senior author in all cases using a technique previously described.[3] This was a single-incision, endoscopic technique with anteromedial portal femoral tunnel drilling. Two-types of grafts were used during this time period: autologous four-strand hamstring tendon (HT) and autologous bone-patellar tendon-bone (BPTB). There was no randomization involved in graft type selection. From the beginning of 1993 BPTB autograft was routinely used. In October 1993, use of HT autograft was commenced, and after April 1994, HT graft was used exclusively. Operative techniques for both graft types were identical. Fixation in both graft-types was achieved using 7×25mm titanium interference screws (RCI; Smith & Nephew, Mansfield, MA) in both the femoral and tibial tunnels. Patients were allowed to fully weight-bear immediately and no brace was used. Early accelerated rehabilitation was then commenced. Patients were allowed to return to competitive sports involving pivoting and sidestepping activity at 6-9 months according to objective assessment of whether the rehabilitation goals had been met.

Statistical Analysis

Statistical analysis was performed using SPSS software. Statistical significance was set at $p<0.05$. The probability of failure was estimated as a function of time using the Kaplan-Meier (K-M) survival method. Survival tables at 1, 2, 5, 10 and 15 years were collated. Comparisons of survival curves were made with univariate Cox proportional hazards. Factors that were significant, or nearly significant ($p <0.10$) on univariate analysis were entered into a multivariate Cox regression analysis. Factors were then eliminated one at a time in a stepwise fashion, until only the independent significant factors remained.

RESULTS

Between January 1993 and December 1998, 2835 patients underwent primary ACL reconstruction. Of these, 351 were aged 18 or less at the time of surgery. The following patients were excluded: (1) those with a previous contralateral ACL injury (n=57); (2) those who refused to participate in a research database (n=4); (3) those who died (of unrelated causes during the study period) (n=2). This left 288 patients in the study group of which 242 (84%) completed the subjective questionnaire at a minimum of 15 years after surgery. The participant flow is shown in Figure 1.242 patients completed the questionnaire at a mean of 16 years and 6 months (range, 15 years, 0 months – 20 years, 6 months) from surgery. Of the 242 patients, 167 (69%) had no subsequent ACL injuries and 75 (31%) sustained a further ACL injury. Of the 75 with further ACL injuries, 27 (11.2%) sustained an ACL graft rupture, 33 sustained a contralateral ACL injury (13.6%) and 15 sustained BOTH an ACL graft and a contralateral ACL rupture (6.2%).

Demographics (n=242)

There were 104 (43%) females and 138 (57%) males. The mean age at surgery was 16 years (range, 13-18). There were 109 left-sided and 133 right-sided reconstructions. Surgery was performed in the acute phase (within 3 weeks of injury) in 7 patients (3%), in the sub-acute phase (3-12 weeks) in 166 patients (69%) and in the chronic phase (> 12 weeks) in 69 patients (28%). BPTB autograft was used in 48 cases (20%) and HT autograft in 194 cases (80%). The mean diameter of the HT graft was 7.1mm (range 6-9mm) and the mean diameter of the BTPB graft was 9.7mm(range 9-11mm) (p=.001, Mann-Whitney U Test).

152 patients (63%) had an ACL reconstruction only and no meniscal debridement. 26 patients (11%) required partial or total excision of the medial meniscus performed at the time of the reconstruction and 52 patients (21%) required partial or total excision of the lateral meniscus. Meniscal sutures were used in 10 patients in the medial meniscus and 10 patients in the lateral meniscus.

The primary ACL rupture was most commonly sustained in the sports of rugby and soccer, which accounted for 48% of injuries (see Figure 2).

Subjective Outcomes

Of the 242 patients who completed the questionnaire at 15 years, 168 (69%) reported returning to their preinjury level of activity. Of the 74 who did not return to the preinjury level of activity, 30 (12%) reported it was due to their operated knee and the remaining 44 patients (18%) cited other reasons.

The mean overall IKDC score for patients with intact ACL grafts (n = 200) at 15 years was 89 (range, 30-100). There was no significant difference between the mean subjective IKDC score between males and females (87 v 88, p=.415), or hamstring and patellar tendon grafts (88 v 87, p=.746). At 15 year review, 131 (66%) were participating regularly in IKDC Level 4-5 sports. There was no significant difference between the proportion of those participating in Level 4-5 sports between males and females (84% v 84%, p=.99), or hamstring and patellar tendon grafts (85 v 79, p=.377).

ACL Graft Rupture

ACL graft rupture occurred in 42 patients (17%) over 15 years, equating to an annualised graft injury rate of 1.1% per year. The ACL graft rupture was confirmed at the time of revision ACL surgery in 37 patients and by MRI and clinical examination in 5 patients. Patients who reported characteristics of rupture in the questionnaire and had not undergone further reconstructive surgery were examined in our unit. Kaplan-Meier survival analysis for graft rupture is illustrated in Figure 3. ACL graft survival was 95%, 92%, 88%, 85%, 83% at 1, 2, 5, 10 and 15 years after reconstruction. The results of univariate analysis are shown in Table 1. A positive family history of ACL injury increased the hazard ratio of further ACL graft injury by a factor of 3.6 (p=.001). Factors that are significant, or nearly significant (p <.10) on univariate analysis (family history, graft type and gender) were entered into a multivariate Cox regression analysis. Factors were then eliminated one at a time in a stepwise fashion, until only the independent significant factors remained. On stepwise multiple regression analysis, only a positive family history remained a significant hazard for poorer ACL graft survival with a hazard ratio of 3.6 (95% CI 2.0-6.7, p < .001). The Kaplan-Meier chart of ACL graft survival and family history of ACL injury is shown in Figure 4.

Contralateral ACL Injury

48 patients (20%) were known to have sustained a CACL rupture during the study period, which equates to an annualized rupture rate of 1.3% per year. The incidence of reconstructed ACL injury (17%) was not significantly different from the incidence of CACL injury (20%) after reconstruction (p=.72). CACL injury was confirmed at the time of CACL reconstruction in 45 patients, and clinical examination and MRI in our unit in 3 patients. CACL injury occurred at a mean of 71 months (range, 8-202) from ACL reconstruction. Kaplan-Meier survival analysis for CACL rupture is illustrated in Figure 5. CACL survival was 99%, 98%, 90%, 83%, 81% at 1, 2, 5, 10 and 15 years respectively, after reconstruction. The results of univariate analysis are shown in Table 2. Male gender increased the hazard ratio of CACL injury by a factor of 2.1 (p=.03). Factors that were significant, or nearly significant (p <.10) on univariate analysis (graft type, gender and return to Level 5 sport) were entered into a multivariate Cox regression analysis. Factors were then eliminated one at a time in a stepwise fashion, until only the independent significant factors remained. On stepwise multiple regression analysis, poorer CACL survival was associated with male gender with a hazard ratio of 2.1 (95% CI 1.1-3.9, p =.03), and return to Level 5 sport with a hazard ratio of 2.3 (95% CI 1.0-5.4, p =.05). Graft type did not remain a significant factor on multiple regression analysis. The Kaplan-Meier curves for these significant factors are shown in Figures 6 and 7.

In those who received the hamstring tendon graft there was a trend to a higher incidence of ACL graft rupture at 15 years, compared to those who received a patellar tendon graft (p=.06). However, those who received a patellar tendon graft displayed a trend to a higher incidence of contralateral ACL injury (p=.08) (Table 3).

DISCUSSION

After a minimum of 15 years post primary ACL reconstruction, 69% of adolescents returned to their pre-injury level of activity, however, this was at a significant cost. Approximately one third of this population suffered a further ACL injury during the study period, with an incidence of 20% in the contralateral knee and 17% in the reconstructed knee. Further ACL injury in the adolescent cohort is relatively common with several factors being implicated in contributing to this increased risk.

The ACL graft survival 15 years after a primary ACL reconstruction in the adolescent population is significantly reduced in the presence of a positive family history. Those with a first degree relative with a history of ACL injury are almost 4 times more likely to suffer an ACL graft rupture than their peers with no family history. In this study, an intact ACL graft was seen in 90% of ACL grafts belonging to a child with no family history, and only 69% of ACL grafts in those with a positive family history. This finding is consistent with other published series[2, 6, 33] and although it is likely multifactorial, the reason behind this finding remains unclear. A preponderance of collagen gene defects described in the literature has been associated with an increase in the risk of ACL rupture.[24, 25] Type I and type V collagen are the major structural constituents of ligaments, therefore, variants in their associated genes, COL1A1 and COL5A1 respectively, have been reported to render the ACL vulnerable to rupture.[24, 25] More recently, in their 2014 study, Mannion[18] identified certain polymorphisms of proteoglycan genes that may account for an increase in susceptibility of ACL injury. Higher posterior tibial slopes are known to significantly increase the risk of further ACL injury after reconstruction[32], and it has been reported that posterior tibial slope is increased in those with a positive family history of ACL injury, compared to controls.[10] In addition to genetics, environment may also play a role in the relationship between family history and increased ACL graft rupture. An individual who is part of a family with a 'sporting' or 'active' culture will inherently be at risk of further ACL injury due to a likely increased exposure to physical activity. It would be expected that these factors would also increase the risk of CACL injury in those with a family history of ACL rupture, however, in this series, this was not the case.

Males and those who return to their pre-injury level of sport were found to have an increased risk of CACL rupture by a factor of 2.1 (p=.03) and 2.3 (p=.05) respectively. It is obvious that a return to sport, especially those that involve cutting and pivoting type manoeuvres, poses a potential risk to both the ACL graft and the native CACL. In this study, a return to sport significantly increased the odds of a CACL rupture, but not an ACL graft rupture. This may simply be due to the fact that the CACL is more vulnerable on return to sport after an ACL reconstruction due to the patient subconsciously protecting the reconstructed knee thereby increasing the stress on the contralateral knee.

Gender as an independent risk factor for CACL injury after primary ligament reconstruction remains controversial in the literature. A number of authors report no significant difference between males and females[11, 13, 23, 28, 33] while others report an increase in the incidence of CACL rupture in females[17, 22, 29] after ACL reconstruction. This result could be explained by a greater proportion of males returned to sports that were considered higher risk in terms of ACL rupture than females. Figure 2 illustrates that over 80% of subjects originally ruptured their ACL playing team ball sports (e.g. rugby, soccer, netball, touch football and hockey). 91% of males and 69% of females (p=.001) suffered their primary ACL rupture while playing these sports. Therefore, despite no significant difference in the overall number of males and females returning to sport (84% vs 84% respectively) after ACL reconstruction, it is possible that more males returned to one of these higher risk activities rendering their CACL vulnerable.

A large proportion of ACL graft ruptures occurred within the first two years of ACL reconstruction, as illustrated by the slope of the survival curve in Figure 3. We found one third of the total number of ACL graft ruptures to occur within one year of primary reconstructive surgery, an incidence of 5%. At the time of initial ACL reconstruction, it was standard practice to recommended that patients refrain from returning to vigorous sport for 6-9 months post reconstruction. Since those days, reports have suggested that the maturation process of the ACL graft continues for at least 12 months after reconstruction with neuromuscular performance of the knee being hindered for this time also.[21, 28] In fact, in their 2000 paper, Wojtys[35] noted ongoing neuromuscular deficits up to 18 months post ACL reconstruction. With this information and the

knowledge that the addition of specific neuromuscular and plyometric training into current ACL rehabilitation programs reduces the risk of further ACL injury,[20, 34] we recommend delaying a return to vigorous sport until a minimum of 12 months post-reconstruction.

We examined a number of variables to assess their influence on further ACL injury in this young population. Age less than 14 years at the time of ACL reconstruction did not significantly effect 15 year survival (p=.21), but this may reflect the low sample size of the very young cohort (n=23). Very young age may have more of a negative influence in the first 2 years when the incidence of graft rupture was 17% in the <14 year population, versus 7% in the >14 year population. Use of the hamstring tendon graft displayed a trend towards higher rates of ACL graft injury (p=.06), but lower rates of contralateral injury (p=.08), compared to the patellar tendon graft. Overall, 67% of the patellar tendon patients and 70% of the hamstring tendon patients had not sustained any further ACL injuries at 15 years (p=.912). Graft selection may influence which knee sustains further injury, but the overall rate of injury appears to be equivalent with hamstring and patellar tendon grafts in the young population.

An intrinsic weakness of this study needs to be recognised. Due to the design of the study, there was an inherent risk that the incidence of ACL graft and CACL rupture was incorrectly reported. At some stage during the follow up period, patients may have sustained a subclinical ACL injury and not noticed instability due to a reduction in their activity level. In an attempt to minimise this issue, patients who reported further injury to either knee during the study period via the subjective assessment were invited to attend our clinic for further assessment regarding the presence or absence of a subsequent ACL injury. It is unlikely that the incidence of further ACL injury was over-reported given the fact that further ACL injury was either confirmed at the time of revision (ACL graft) or primary (CACL) surgery or confirmed via clinical and/or radiological means.

Anterior cruciate ligament reconstruction in young people is a successful procedure resulting in 69% of patients returning to their preinjury level of sport and 66% of patients continuing to participate in regular

physical activity after a minimum of 15 years post primary ACL reconstruction. Despite this success, the risk of further ACL injury in this patient cohort is common. One third of patients aged 18 years and under who undergo a primary ACL reconstruction are at risk of further ACL rupture to either knee with no statistical difference in the risk between ACL graft and CACL rupture. Patients with a positive family history are four times as likely to rupture their reconstructed ACL, an injury likely to occur within the first 2 years after primary ACL reconstruction. Young male patients and those who return to cutting or pivoting sports are twice as likely to rupture their contralateral ACL when compared to females and those who refrained from sport.

Orthopaedic surgeons need to ensure they appropriately counsel their younger patients and their parents on the markedly increased risk of further ACL injury, especially in males with a positive family history who wish to return to their desired sport of choice. Young patients and their families need to understand the risk of returning to sport prematurely and should be strongly advised to refrain from this for at least 12 months post ACL reconstruction.

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FIGURES

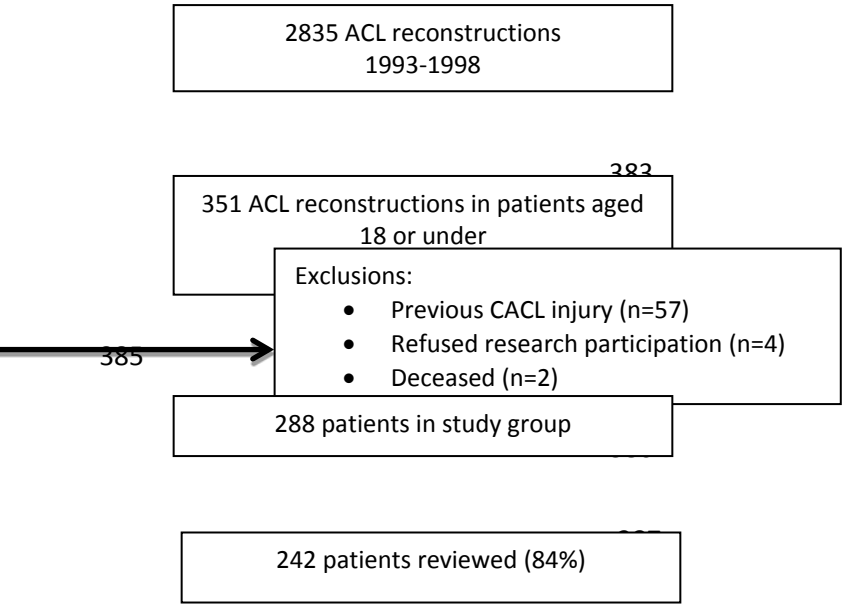


Figure 1: Participant Flow Chart

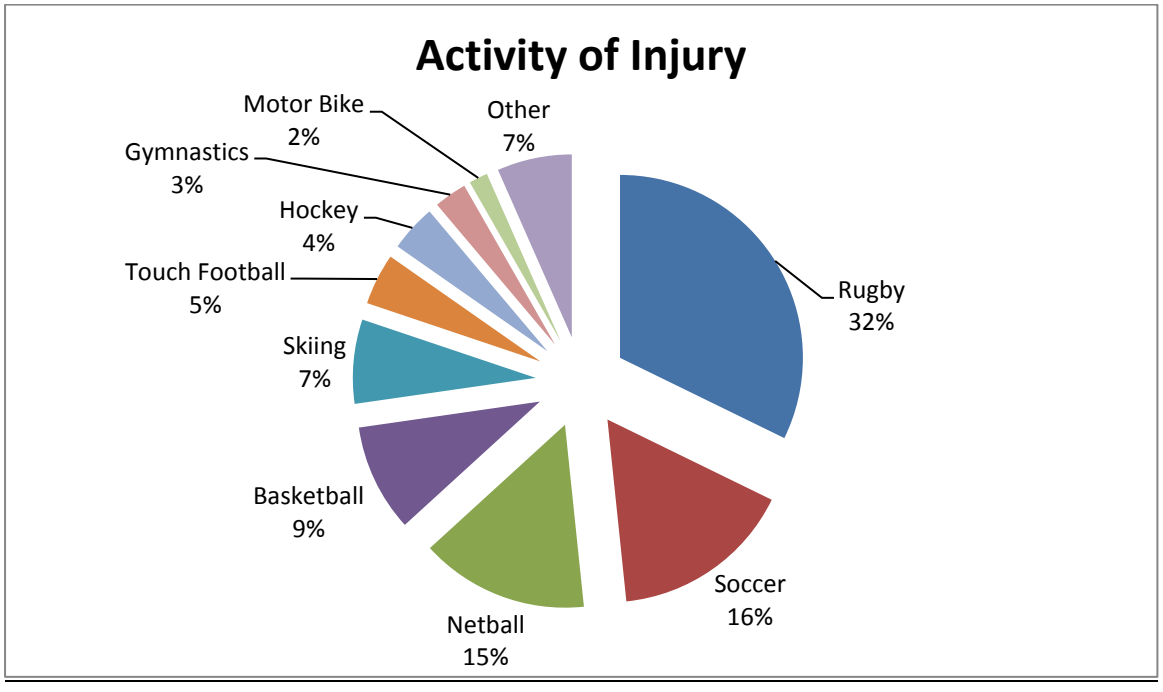
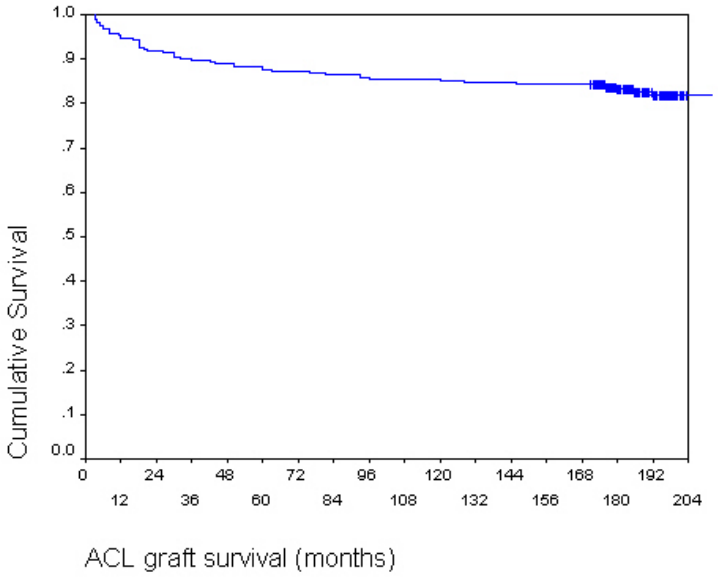


Figure 2: Activity responsible for the initial ACL injury.

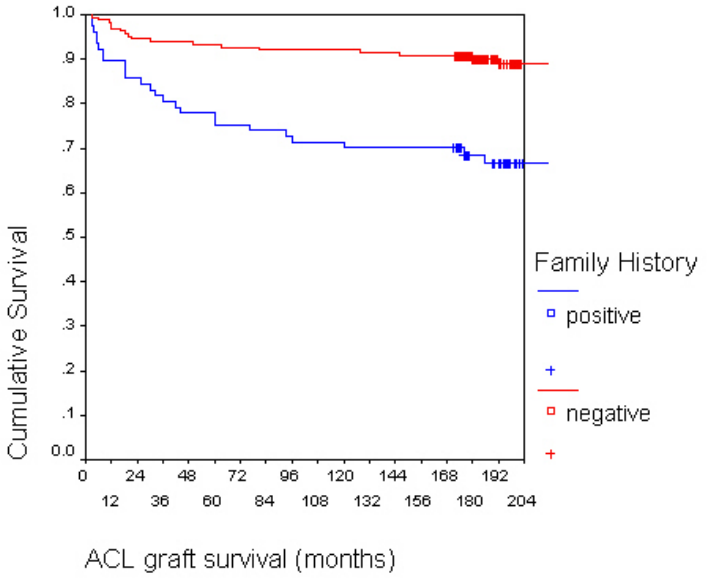


394

395 **Figure 3:** Kaplan-Meier curve for ACL graft survival.

396

397



398

399 **Figure 4:** Kaplan-Meier curve of ACL graft survival for those with and without a positive family history of ACL
400 injury (defined as first degree relative with known ACL injury).
401

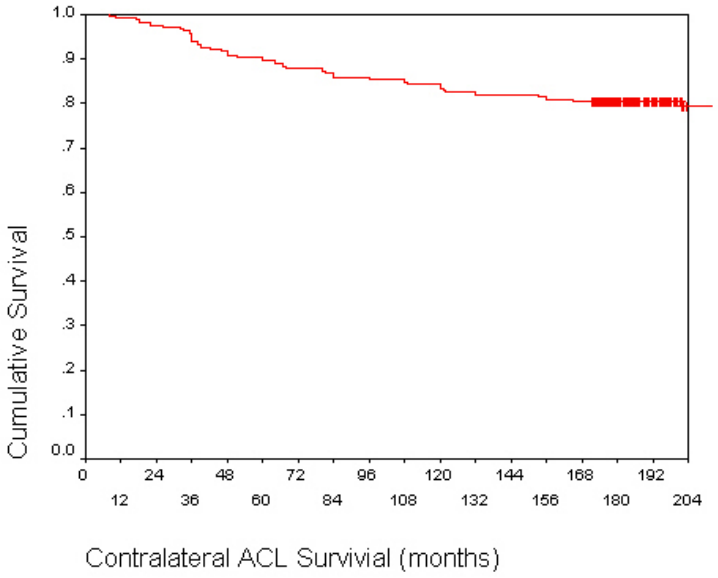


Figure 5: Kaplan-Meier curve of contralateral ACL survival

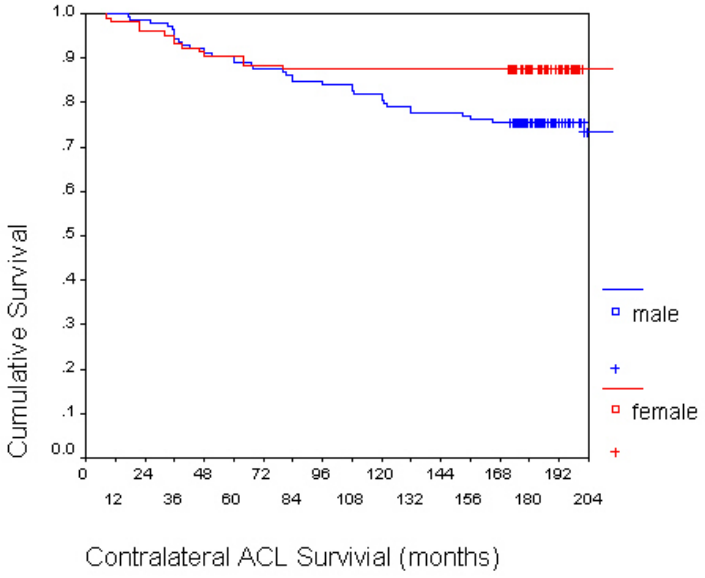
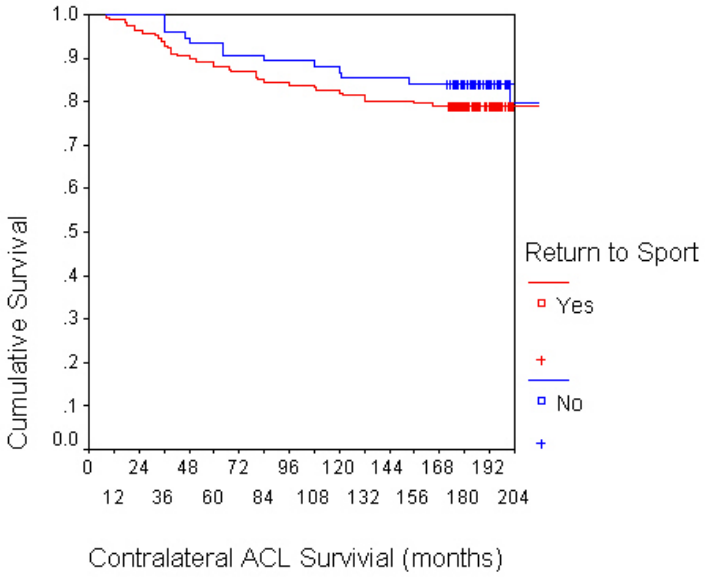


Figure 6: Kaplan-Meier curve of contralateral ACL survival for males and females.



409

410 **Figure 7:** Kaplan-Meier curve of contralateral ACL survival for those who return to IKDC Level 5 Sports and
411 those that did not.

TABLES

TABLE 1

Survival of the ACL graft with univariate hazard ratios for the examined variables

Factor and Category	No	1 year survival	2 year survival	5 year survival	10 year survival	15 year survival	Hazard Ratio	95% CI	p-value
ALL	**242**	**95**	**92**	**88**	**85**	**83**			
Age at surgery									
14 years or less	23	90	83	78	78	73	1.7	0.7-1.4	0.21
> 14 years	219	97	93	90	86	84			
Graft									
Hamstring	194	96	90	86	83	81	2.7	0.9-7.5	0.06
Patellar	48	98	98	96	94	92			
Gender									
Male	138	93	91	86	82	80	1.8	0.9-3.4	0.09
Female	104	96	94	89	89	88			
Return to Level 5 sport									
Yes	185	94	90	85	82	81	2.0	0.8-4.6	0.13
No	57	100	96	93	93	91			
Family History of ACL injury									
Yes	77	90	86	75	70	69	3.6	2.0-6.7	**0.001**
No	165	97	95	93	92	90			
Graft Diameter									
7mm or less	115	100	92	88	85	83	1.1	0.6-2.0	0.747
> 7mm	127	94	91	87	85	83			

TABLE 2

Survival of the contralateral ACL with univariate hazard ratios for the examined variables

Factor and Category	No	1 year survival	2 year survival	5 year survival	10 year survival	15 year survival	Hazard Ratio	95% CI	p-value
ALL	**242**	**99**	**98**	**90**	**83**	**81**			
Age at surgery									
14 years or less	23	100	100	91	87	78	1.1	0.4-2.8	0.83
> 14 years	219	99	97	90	83	81			
Graft									
Hamstring	194	99	98	92	87	83	1.8	0.9-3.3	0.08
Patellar	48	100	96	85	73	71			
Gender									
Male	138	100	99	91	80	75	2.1	1.1-3.9	**0.03**
Female	104	98	96	90	88	88			
Return to Level 5 sport									
Yes	185	99	97	88	81	78	2.3	1.0-5.5	**0.05**
No	57	100	100	95	93	89			
Family History of ACL injury									
Yes	77	100	99	88	84	81	1.0	0.5-1.9	0.94
No	165	99	97	90	83	81			

TABLE 3

Incidence of ACL graft and CACL injury with HT or BPTB grafts

	Patellar tendon graft (n=48)	Hamstring tendon graft (n=194)	p-value
No further ACL injury	32 (67%)	135 (70%)	P=.912
ACL graft rupture	2 (4%)	25 (13%)	P=.06
Contralateral ACL rupture	12 (25%)	21 (11%)	P=.08
ACL graft and contralateral ACL injury	2 (4%)	13 (7%)	