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Change in Anterior Cruciate Ligament Graft Choice and Outcomes Over Time

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Abstract

Purpose—To analyze failure rate in two-year increments to determine if graft choice changed over time and graft failure rate.

Methods—A prospective 2002–2008 database was used to identify risk factors for anterior cruciate ligament retear (ACLR). Subjects who had primary ACLR with no history of contralateral surgery and 2-year follow-up were included. Subjects who underwent a multi-ligament reconstruction were excluded. Graft type, age, sex, smoking status, body mass index, Marx activity level at index surgery, medial and lateral meniscus status at time of ACLR, sport played post-ACLR, and clinical site were evaluated. Analysis was repeated using 2002–2003 (early) and 2007–2008 (late) two-year databases. ANOVA with *post-hoc* analysis was performed to detect significant differences in age and Marx score by graft type over time.

Results—Two-year follow-up for graft failure was obtained on 2497/2692 (93%) subjects. There were 112/2497 (4.5%) ACLRs identified at two-year follow-up. The only predictor that changed between early/late periods was allograft use. Allograft odds ratio decreased from 13.1 to 9.5 ($p<.01$). Allografts were used in older patients (31–40 years) and with lower Marx scores (10–8) from early to late periods. Mean age of subjects receiving BTB autografts did not significantly change over time (22.8 to 23.5) Mean age of subjects receiving hamstring autografts fell (27.9 to 25.5). Mean age of subjects receiving allografts rose significantly (31.3 to 39.8, $p<.01$). Mean Marx score of subjects who received BTB and hamstring autografts did not significantly change over time. Mean Marx score of subjects receiving allografts decreased significantly ($p<.01$).

Conclusions—After early recognition allograft use in young active patients was a risk factor for retear, graft choice by surgeons changed in the late period to use of allografts in older and less-active patients, which correlated with significant decrease in retear risk.

Level of Evidence—Therapeutic-III, case control study

Introduction

Injuries to the anterior cruciate ligament (ACL) occur in the active general population, but are particularly common in athletes involved in cutting sports[1–3]. After an ACL injury, the knee has significant risk of functional instability, meniscal tears and subsequent osteoarthritis[4]. In order to restore knee stability and decrease risk of subsequent injury (e.g. meniscus tears), ACL reconstruction (ACLR) is often performed. Excellent results have been widely reported for ACLR in restoration of knee stability[4–6]. Despite the high reported success rates, ACLR is not to be taken lightly, as patients must invest a significant amount of time, discomfort, effort and money during the 6 – 12 month recovery period. ACL graft retear after undergoing surgery and rehabilitation is a devastating event for the patient as well as the family, coach, therapist and surgeon. After a tear of an ACL graft, patients often undergo a revision ACLR. In addition to the time, expense and risk of having a revision ACLR, it has been shown that revision ACLRs have inferior results to primary ACLRs[7, 8].

Risk factors for tear of the native ACL have been studied and several have been identified. Two of the most commonly reported risk factors are female sex and participation in cutting sports[3, 9–11]. Other risk factors to have been reported include: posterior tibial slope, notch

width, limb alignment and neuromuscular factors[2, 10, 12–15]. Major risk factors for ACLR graft retear have been identified, presented, and published within a multicenter prospective population[11, 16, 17]. These risk factors for graft retear were younger age, high activity, and allograft in younger patients. We also showed that the risk of graft retear in the patient with an allograft decreased as the age of the patient increased. Age and activity level were found to be highly collinear, so it can be extrapolated that this result would carry over to activity level as well[16]. The clinical relevance of being aware of these risk factors are: 1) to better educate patients and surgeons on the expected outcomes of an ACLR, especially graft failure; 2) to counsel patients on post-operative recommendations, and; 3) to facilitate efforts to decrease those risk factors which are modifiable, such as graft choice. The goal of this study was to analyze failure rate in two-year increments to determine if graft choice changed over time and the graft failure rate. We hypothesized that after clinicians were presented with risk factors for subsequent ACL graft failure, clinical decision-making would change and clinical outcomes would subsequently improve.

Methods

After Institutional Review Board approval was granted, data from the prospective database were used to identify the incidence and risk factors for ACLR graft retear. Subjects who had a primary ACL reconstruction at one of 7 sites and performed by one of 17 surgeons involved in the data collection with no history of contralateral knee surgery with 2-year follow-up data were included in the dataset. All patients followed a standardized post-operative rehabilitation protocol. A retear was defined as having to undergo a revision ACL reconstruction. Each time period's data were prospectively collected in identical fashion from the same set of surgeons with greater than 80% 2-year follow-up. Subjects who underwent a multi-ligament reconstruction (n= 107), had bilateral ACLR (n=23), had an ACL repair (12), or original entry into the database was an ACL revision (n=371) were excluded from the analysis. Graft type (autograft bone-patellar tendon-bone (BTB), autograft hamstring, allograft), age, sex, smoking status, body mass index (BMI), Marx activity rating score[18] at time of index surgery, medial and lateral meniscus status at the time of ACLR, sport played post ACLR, and clinical site were evaluated to determine their contribution to graft retear.

Using the statistical software STATA 9.0 (StataCorp LP, College Station, TX) multivariable logistic regression was used to determine if the chosen variables were associated with our primary outcome, ACL graft retear[19]. Odds ratios and 95% confidence intervals were reported for the variables associated with our outcome. Finally, the analyses were repeated for the two-year time periods at the beginning (enrollment years 2002–2003) and end (enrollment years 2007–2008) of the study timeframe. After analysis of the entire group and due to the smaller size of the "early" (2002–2003) and "late" (2007–2008) groups, the variables analyzed were limited to age, sex, Marx activity level score, and graft type. Chi square and t-tests were performed to test homogeneity between the "early" and "late" groups. Odds ratios and 95% confidence intervals were reported for the variables associated with our outcome. An ANOVA with *post-hoc* analysis was performed to detect significant differences in age and Marx score at time of index surgery by graft type over time.

Results

A total of 2692 subjects met all study inclusion/exclusion criteria; 2497/2692 (93%) had 2-year follow-up for graft failure obtained. There were 112/2497 (4.5%) ipsilateral graft retears and 90/2497 (3.6%) contralateral ACL tears identified in the entire group at two-year follow-up. Median time to follow up was 2/4 years (range 2.0 years–3.9 years). The number of subjects and percent graft retears are summarized for the variables tested in aggregate and for each time period in Table 1.

Risk factors for ACL graft retears in entire population

Significant risk factors for ipsilateral ACL graft retear were: use of an allograft (odds ratio: 5.91, p<.01, 95% CI 2.91 – 12.01); younger age (odds ratio: 0.90; p<.01; 95% CI 0.86 – 0.93); and higher Marx activity level score (odds ratio: 1.10; p<.01; 95% CI 1.03 – 1.18). Sex, sport, smoking status, medial or lateral meniscus status and clinical site were not predictors of a graft retear after primary ACLR (p>0.05). This is identical to our previously reported results of the entire group[11].

Predictors of ACL graft retears over time

The strength of the risk factors for ACL graft retear were compared between the early (2002–2003) and late (2007–2008) time periods. The early and late groups were statistically similar except for graft type (p<0.001) and sport played post ACLR (p=0.03) (Table 1). Younger age and allograft usage remained significant predictors of graft retear in both time periods (Table 2). The strength of age as a risk factor was not significantly different between the 02–03 and 07–08 time periods with odds ratios of 0.86 and 0.87 respectively. The strength of allograft as a risk factor did change over time. This is discussed below.

Post hoc analysis of change of age and Marx activity rating score by graft type over time

Average age and Marx activity rating score for each 2-year group are summarized in Table 3. The mean age (Figure 1) of subjects receiving BTB autografts did not significantly change over time, whereas the mean age of subjects receiving hamstring autografts fell while the mean age of subjects receiving allografts rose significantly over time (p< 0.01). The mean Marx activity rating score (Figure 2) of subjects who received BTB and hamstring autografts did not significantly change over time, whereas the mean Marx activity rating score of subjects receiving allografts decreased significantly over time (p< .01). Mean age of subjects receiving BTB autografts did not significantly change over time, whereas mean age of subjects receiving hamstring autografts fell, and mean age of subjects receiving allografts rose significantly.

Risk of retear by graft type over time

In 2002–2003, there were 36/750 (4.8%) retears compared to 33/879 (3.8%) in 2007–2008. The odds of retear for allograft subjects was 13.13 times higher compared to BTB autograft in the 2002–2003 group (p<.01) and decreased to 9.51 times higher in the 2007–2008 group (p<.01). The odds ratio between BTB autograft and hamstring autograft was not significantly different in the 2002–2003 (p=.06) or 2007–2008 groups (p=0.22). The only significant change in risk of retear by graft type between the two time periods was in

allografts, for which the odd ratio decreased by nearly 28% (13.13 to 9.51) and percentage of retears decreased 68% (11.7 to 3.7). Please see tables 1 and 2. The change in odds ratios over time by graft type are shown in Figure 3.

Sport

A qualitative review of the sport involved when the ACL retore revealed that in the entire population, 3.9% of those who did not play sports retore their ACL compared to 6.6%, 8.4%, and 4.1% for football, soccer, and basketball respectively. With respect to a change in risk between the early and late time periods, football and basketball did not change (7.1% to 8.3% and 4.0% to 4.4%, respectively), whereas the risk in soccer appeared to drop approximately 29% (9.1% to 6.5%).

Discussion

The current study supports our hypothesis that after clinicians were presented with risk factors for subsequent ACL graft failure, their clinical decisions would change and that the risk factors and clinical results would subsequently change over time. When orthopaedic surgeons were shown high quality prospective evidence that allograft use in younger patients was a major risk factor for subsequent graft failure, their practice patterns changed. They started using allografts in older and less active patients and the odds of graft retears in the allograft patients fell by 27%.

A retear of an otherwise successful ACLR is not only frustrating to all involved, but often necessitates a revision ACLR, which subjects the patient to additional expense, surgical risk, physical therapy and time away from their sport[20]. It has also been shown that revision ACLRs have inferior results to primary reconstructions[7, 8]. Understanding the risk of reinjury is important in order to appropriately counsel patients and surgeons on expected long-term results and avoid graft failure by modification of one or more risk factors[21–30]. Minimization of the risk of ACL graft failure should be a priority of clinicians caring for ACLR patients[31].

Allograft vs Autograft

It has been reported by us, others, and confirmed by a meta-analysis that allograft ACLRs have a high retear risk compared to autografts in younger and/or highly active athletes[11, 32–38]. In this group, the use of allograft tissue (as well as youth and high activity) was a predictor of graft retear in the early time frame. When this became apparent in 2005–6 during the analysis of the 2-year follow-up of the 2002/03 group, it was reported internally to all study surgeons. The analysis of risk of retear by graft type with increasing age, as shown in Figure 4, was presented to the group as well. No formal recommendation of change in practice patterns was done. However, in the population of patients who were given allografts the average age and activity level changed in the subsequent time period. Surgeons started to use allografts in older and less active patients and this correlated with a corresponding decrease in the risk of retear. Over time the standard allograft patient increased in age by 8.5 years and decreased in activity by 2.2 Marx points while his/her risk of retear fell by 27%. This is of interest as it demonstrates that motivated surgeons presented

with high quality prospective outcomes data with outstanding follow-up will change their practice patterns to produce better outcomes. Potentially another factor in modifying graft choice was that every surgeon knew his/her failure rate and outcomes in 2007–2008 would be prospectively tracked individually, and no surgeon desires a higher failure rate of ACLR than his/her peers.

Many of the allografts in this group had low dose irradiation to address superficial contamination of the graft. It has been shown in several studies that irradiated allograft with higher doses (>2.5mRad) fail at a high rate[16, 39–43]. Other studies have shown that allografts, particularly fresh frozen, non-irradiated allografts, have similar retear risk as autografts; however, these studies tended to also have a much older patient group in the allograft group[5, 44–51]. In the MARS data[52] when the extent of low dose versus no irradiation in allograft in revision ACLR was examined, the failure rates between the two were no different. This study has demonstrated that a change in a surgeon's use of allograft to older patients will significantly decrease their failure risk. Further research into the influence of donor characteristics, processing techniques, tissue type and recipient characteristics on allograft ACLR outcomes should be performed by allograft industry and surgeons who utilize allografts.

Age and Activity Level

Younger age and higher activity at index ACLR were significant predictors of graft retear as previously reported[11, 16]. In previous studies, authors found that the risk of retear decreased by 9% for each year increase in age and increased by 10% for each increase of a point on the Marx activity scale[11, 16]. We suspect that the level of returned to activity is the driver of both these findings. Though this current study did not directly measure the returned to level of activity, the activity level at the time of index ACLR has been shown to be a significant predictor of activity level at two years[11, 53]. We suggest that the returned to level of activity needs to be controlled for in any future analysis of predictors of graft retear.

Sport

The fact that 3.9% of those patients who did not play sports retore their ACL correlates well with the fact that patients with a high Marx activity level who played football and soccer retore at a higher percentage (6.6% and 8.4% respectively). Overall the sport of football, soccer, or basketball in previous multivariable analysis was not a risk factor[11]. With respect to a change in risk between the early and late time periods, it is interesting that the male dominated sport of football did not change, but the percentage of coed athletes who played soccer decreased by 28.6% between the time periods. This may be explained by a possible disproportionate higher use of allografts in the early time period in which the subsequent decrease in allograft use in the late time period benefited in their retear risk. Another explanation could be a more rigorous use of ACL injury prevention programs in the later time period by female athletes, thus the differential benefit to the coed sport versus football.

Sex

Though being a strong predictor of native ACL injury, in this study female gender was not a risk factor for retear of an ACL graft. This matches reported findings[11, 16] and other reports[11, 54–57].

Limitations

This study was a retrospective analysis of prospectively collected data, thus it has some of the weaknesses of any retrospective analysis. As far as applicability, this study looked at results from surgeons at seven academic centers and as such, may not be generalizable to a larger more diverse group of surgeons. In this study, retear was defined as having to undergo a revision ACL reconstruction and as such probably under reports graft failures, but the same definition was used in both time frames. In addition, other potential risk factors for graft retear such as tibial slope and graft size were not analyzed as they were not part of the prospective data set.

Conclusions

After early recognition that allograft use in young active patients was a risk factor for graft retear, graft choice by the surgeons changed in the late time period to use of allografts in older and less active patients which correlated with a significant decrease in graft retear risk.

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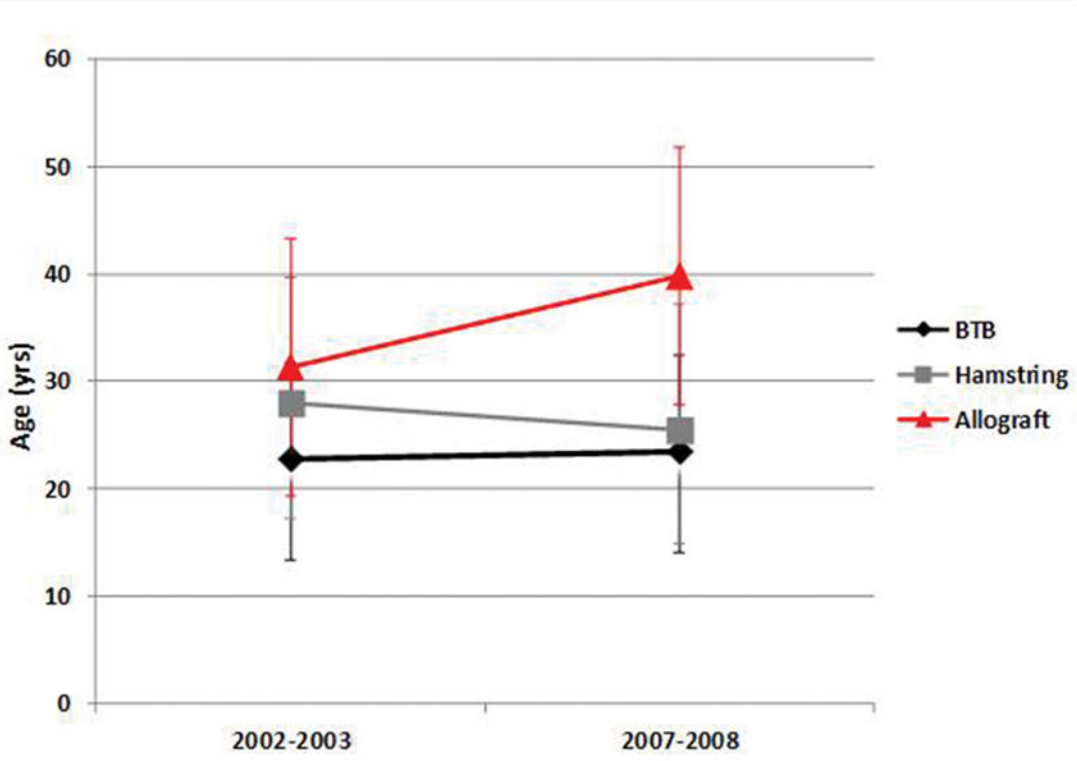

Figure 1.
Change in age by graft type over time.

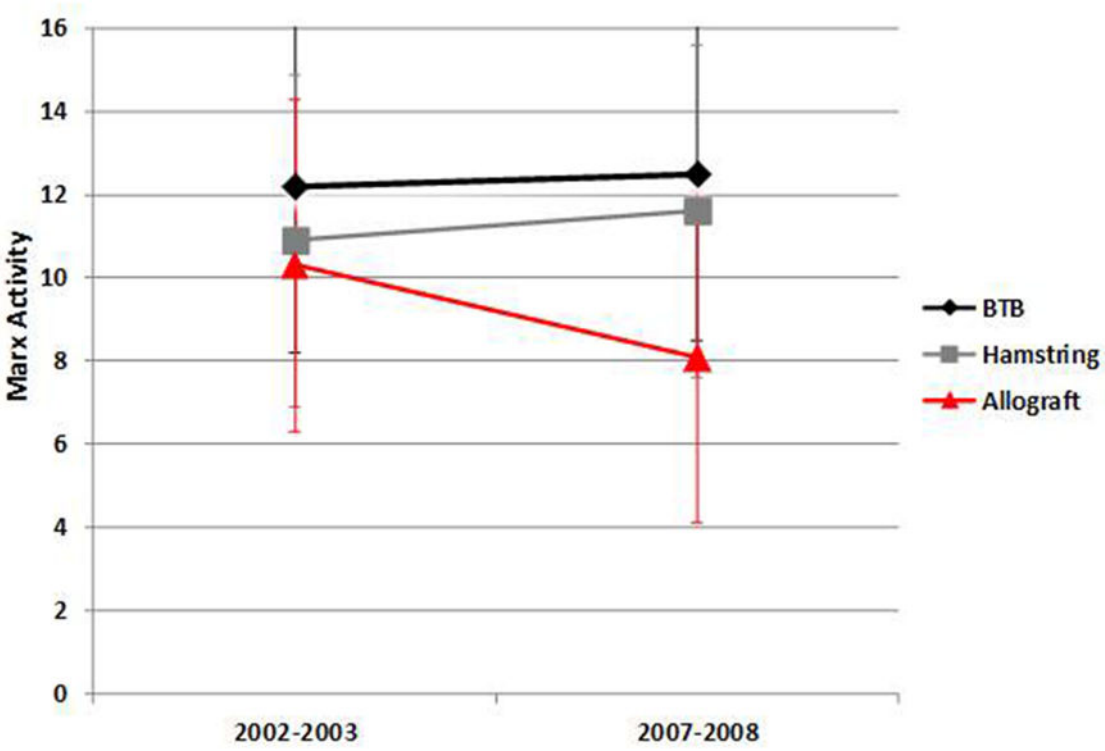

Figure 2.
Change in Marx score by graft type over time.

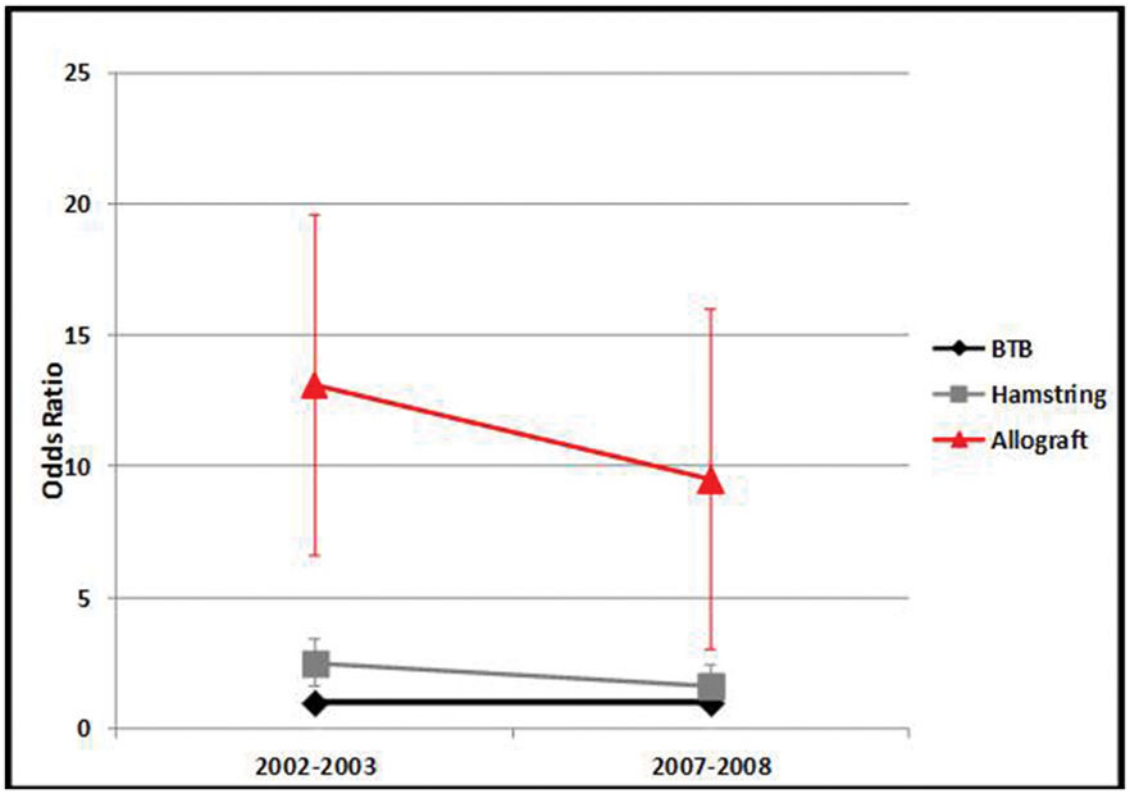

Figure 3.
Odds ratio by graft type over time.

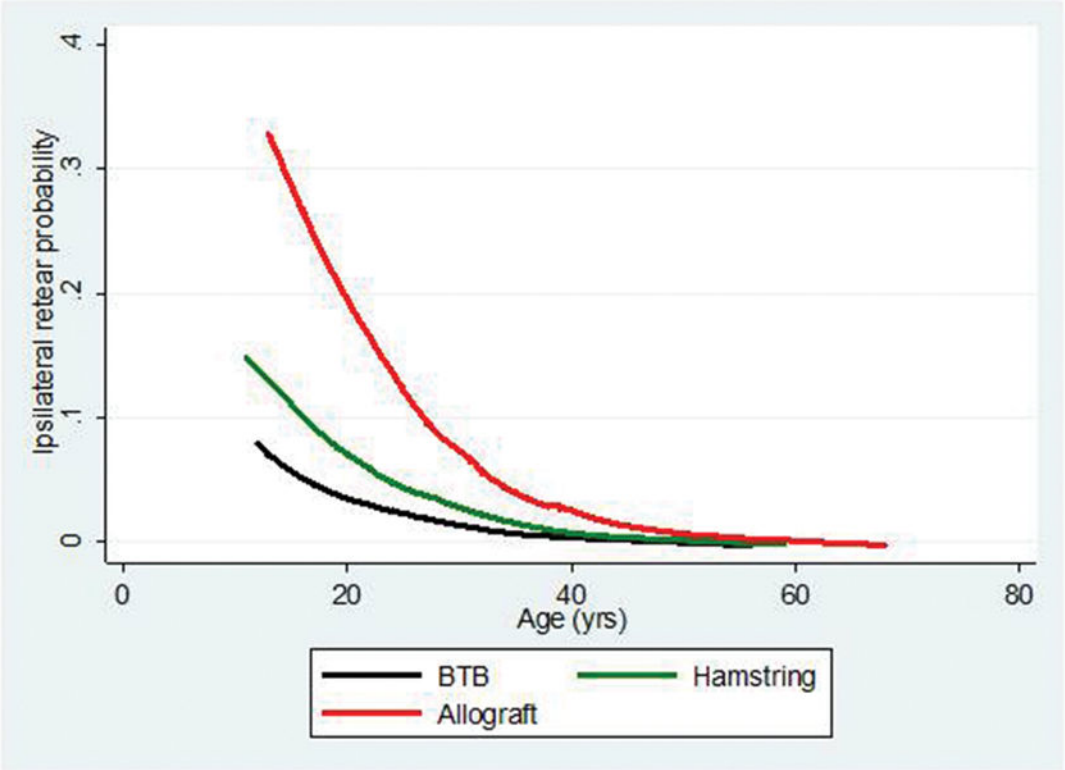

Figure 4.
Probability of graft retear as age increases.

Table 1

ACL Graft Retears

	2002–2003 (n=750)		2007–2008 (n=879)		*p*	Entire Population (n=2497)	
	N	**% Retear**	**N**	**% Retear**	**value**	**N**	**% Retear**
Graft type					**<.001**		
Autograft BTB	334	2.4	375	3.2		1132	3.2
Autograft Hamstring	269	4.1	385	4.4		891	4.8
Allograft	145	11.7	109	3.7		460	7.0
Sex					.43		
Male	407	5.4	494	3.8		1368	4.8
Female	343	4.1	385	3.6		1129	4.2
Smoking Status					.39		
No	602	5.5	708	4.2		1995	5.2
Quit	75	2.7	98	1.0		257	1.2
Current	69	1.4	66	3.0		214	2.3
Sport post ACLR					**.03**		
None	123	4.9	173	1.7		464	3.9
Football	84	7.1	96	8.3		272	6.6
Basketball	201	4.0	181	4.4		588	4.1
Soccer	77	9.1	107	6.5		275	8.4
Other	265	3.4	322	2.2		898	3.2
Medial Meniscus					.29		
No Tear	520	5.2	588	3.9		1733	4.9
Tear	230	3.9	291	3.4		764	3.5
Lateral Meniscus					.07		

	2002–2003 (n=750)		2007–2008 (n=879)		*p*	Entire Population (n=2497)	
	N	**% Retear**	**N**	**% Retear**	**value**	**N**	**% Retear**
No Tear	503	4.8	552	4.3		1617	4.6
Tear	247	4.9	327	2.8		880	4.3
	2002–2003		2007–2008			Entire Population	
	No Tear	Tear	No Tear	Tear		No Tear	Tear
	$\bar{x}$ (SD)		$\bar{x}$ (SD)			$\bar{x}$ (SD)	
Age	26.7 (11.1)	18.3 (5.4)	26.8 (11.5)	18.5 (3.7)	.64	26.9 (11.4)	19.1 (6.5)
BMI	25.5 (4.7)	24.3 (4.7)	25.5 (4.9)	24.0 (4.5)	.84	25.5 (4.8)	23.9 (4.4)
Marx Activity Level	11.2 (5.2)	14.3 (3.7)	11.4 (5.2)	14.4 (4.0)	.54	11.3 (5.2)	14.3 (3.8)

BTB, bone-patellar tendon-bone; ACLR, anterior cruciate ligament reconstruction; SD, standard deviation

Table 2

Strength of Risk Factors for Graft Tears

	2002–2003		2007–2008	
ACL Graft Retear	**Odds ratio**	**p-value**	**Odds ratio**	**p-value**
Age	**0.86**	**<.001**	**0.87**	**<.001**
Marx Activity Level (t0)	1.08	.20	1.09	.18
Autograft BTB	REF	REF	REF	REF
Autograft Hamstring	2.51	0.06	1.62	0.22
Allograft	**13.13**	**<.001**	**9.51**	**.002**
Male	REF	REF	REF	REF
Female	0.58	0.15	0.70	0.34

BTB, bone-patellar tendon-bone.

Table 3

Age and Activity Level of Subgroups

	2002–2003	2007–2008
Age	**Mean (SD)**	**Mean (SD)**
Autograft BTB	22.8 (8.9)	23.5 (9.4)
Autograft Hamstring	27.9 (11.7)†	25.5 (10.7)†
Allograft	31.3 (12.0)*	39.8 (10.9)*
ACL Graft Retear		
No retear	26.7 (11.1)	26.8 (11.5)
Retear	18.2 (5.4)	18.5 (3.7)
Marx Activity Level	**Mean (SD)**	**Mean (SD)**
Autograft BTB	12.2 (4.9)	12.5 (4.9)
Autograft Hamstring	10.9 (5.2)	11.6 (5.0)
Allograft	10.3 (5.3)#	8.1 (5.6)#
ACL Graft Retear		
No retear	11.2 (5.2)	11.4 (5.2)
Retear	14.3 (3.7)	14.4 (4.0)

SD = standard deviation; BTB = bone-patellar tendon-bone

† Age was significantly different between the 2002–03 and 2007–08 groups (p = 0.01)

* Age significantly increased over time (p < .001)

Marx significantly decreased over time (p = 0.001)