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| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

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| In college-aged female soccer player with an anterior cruciate ligament tear, does ACL reconstruction surgery utilizing an allograft effectively prevent re-injury after return to sport versus ACL reconstruction surgery utilizing an autograft. |

**AUTHOR**

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| **Prepared by** | Laura Rapp, SPTUNC-Chapel Hill DPT Student  | **Date** | November 2014 |
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**CLINICAL SCENARIO**

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| During my clinical rotation in outpatient orthopaedics, I encountered many young female athletes – mostly soccer players – who suffered from ACL tears and subsequent reconstruction surgeries. Out of curiosity, I often asked them whether they had used their own tendon for the graft repair or a cadaver graft. Although it appeared to me that there was a fairly even distribution of both allograft and autograft patients, one of the patients I worked with extensively had received an allograft and subsequently re-tore her ACL in return to sport only a year later. Following re-rupture of her ACL, a screw was surgically placed in her knee in order prevent another graft failure, and she was told that not only was her soccer career was over, but she should avoid any and all sports or activities that involve lateral cutting, “board sports,” and jumping/landing activities. I was shocked to hear that she was given such stringent limitations, and I was curious as to whether re-rupture and subsequent banning of activities was a common occurrence for individuals who received allografts in their original ACL reconstruction. Therefore, I decided to investigate whether there is any evidence for utilizing an autograft versus an allograft in preventing re-rupture of the ACL. Although I would assume an allograft reconstruction may allow for quicker return to sport considering there is only one surgical incision being made, there may be a decreased chance of re-injury in return to sport using an autograft since it is the patient’s own healthy tissue being utilized, and it has not undergone any sort of processing or sterilization. The implications of this sort of information plays an important role in informing patients of all their options prior to ACL surgery, particularly since one type of graft may be less invasive or seem as though it would allow for quicker return to sport, though it may not be the best long-term outcome. |

**SUMMARY OF SEARCH**

[Best evidence appraised and key findings]

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| * There are no statistically significant differences in clinical outcomes, measures of ACL laxity, rate of re-rupture, or reoperations in patients undergoing ACL reconstruction with hamstring autograft versus soft-tissue allograft.
* Functional outcomes and graft rupture may be less likely in autograft when compared to irradiated and chemically processed grafts, however, non-irradiated allografts demonstrated no significant differences from autografts in any of the measurable outcomes.
* Irradiation for the purpose of graft sterilization diminishes the biomechanical properties – reduces the stiffness and strength - of soft-tissue allografts, and with time, the functional and activity levels of the individuals with irradiated allografts may continue to significantly due to ACL laxity.
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**CLINICAL BOTTOM LINE**

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| Evidence suggests that following an anterior cruciate ligament tear, ACL reconstruction surgery utilizing an allograft just as effectively prevents re-injury after return to sport as utilizing an autograft in college-aged female soccer player. However, irradiated allografts are not as effective in preventing re-injury as autografts as a result of increased laxity. Further evidence on long-term outcomes postoperatively is required to determine on-going efficacy of allografts versus autografts in a young, athletic population. |

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| ***This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor*** |

*The above information should fit onto the first page of your CAT*

**SEARCH STRATEGY**

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| **Terms used to guide the search strategy** |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| female\* wom\* athlete\* soccer\*kneeanteriorcruciateligament\*tear\*rupture\* | knee ACLtear\* reconstruct\* allograft\* cadaver graft\* | kneeACLsurgery\*autograft\*hamstring\* graft\*patella\* tendon\* | prevent\* re-injury\* protect\* prior level of function\* PLF long-term\*recovery\* |

**Final search strategy:**



Although I was able to get fairly good results by modifying my search strategy in PubMED, EMBASE, and Cochrane, it was the Cochrane search that allowed me to really limit my findings to articles that were applicable to my topic. Rather than the 22,000 or so articles that were initially found, limiting my search and implementing specific filters allowed me to locate 7 articles that were within my parameters and applied well to my topic. However, my search was not turning up any topics related to my PICO question until I made some modifications to my search strategy. I had to widen the search to not only females but males and females combined. In addition, I had to look not just at college athletes or soccer players because there simply are not enough studies that study only those athletes. I also removed the “college” or “college age” search terms and then later sift through by age. The final search strategy utilized in Cochrane was:

(female\* OR wom\* OR athlete\* OR soccer\*) AND

(knee OR anterior OR cruciate OR ligament OR ACL) AND

(tear\* OR rupture\*) AND (allograft\* OR cadaver graft\*) AND

(autograft\* OR hamstring\* OR graft\* OR patella\* OR tendon\*) AND

(prevent\* OR re-injury\* OR protect\* OR prior level of function\* OR PLF OR long-term\* OR recovery\*)

Limitations/filters used were:

Studies between 1994-2014, English only

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| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| **EMBASE****PubMED****Cochrane** | **210****18****28** | **Female, include only reviews/controlled clinical trials/RCTs, humans only, English only, 1994-2014****Revised # results: 28****English only, 1994-2014, RCT****Revised # results: 3****English only, 1994-2014****Revised # results: 7** |

## INCLUSION and EXCLUSION CRITERIA

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| **Inclusion Criteria** |
| * Randomized controlled trials, controlled trials, uncontrolled trials
* Published between 1994 and September 2014
* Studied females between the ages of 17 and 23.
* Protocol included ACL reconstruction surgery
* Patients received physical therapy s/p surgery
* Follow-up on re-injury at least 1 year later or more
* Published in English
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| **Exclusion Criteria** |
| * Studies on only patients </= 16 years old
* Studies on non-surgical interventions for ACL tears
* Case studies
* Abstracts, letters to the editors, dissertations, conference proceedings, or narratives
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**RESULTS OF SEARCH**

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| A total of  | \_15\_ | relevant studies were located and categorised as shown in the following table (based on Levels of Evidence, Centre for Evidence Based Medicine, 2011) and PEDro (or AMSTAR) quality assessment rating scale. |

**Summary of articles retrieved that met inclusion and exclusion criteria**

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| **Author (Year)** | **Study quality score** | **Level of Evidence** | **Study design** |
| **Barber FA, Cowden CH, Sanders EJ. (2014)** | **5** | **3b** | **Retrospective Comparative Study (Case-Control)** |
| **\*\*Cvetanovich GL et al. (2014)** | **10** | **1a** | **Meta-analysis of RCTs** |
| **Edgar CM, Zimmer S, Kakar S, Jones H, Schepsis AA. (2008)** | **7** | **2b** | **Prospective Cohort Study** |
| **Kleipool AEB, Zijl JAC, Willems WJ. (1998)** | **5** | **2b** | **Prospective Cohort Study** |
| **\*\*Krych AJ, Jackson JD, Hoskin TL, Dahm DL. (2008)** | **9** | **2a** | **Meta-analysis of prospective non-randomized cohort studies** |
| **Lawhorn KW et al. (2012)** | **6** | **2b** | **Prospective Cohort Study** |
| **Mascarenhas R, Tranovich M, Karpie JC, Irrgang JJ, Fu FH, Harner CD. (2010)** | **7** | **3b** | **Matched-pairs Case Control** |
| **Noh JH, Yi SR, Song SJ, Kim SW, Kim W. (2011)** | **7** | **1b** | **Randomized Controlled Trial** |
| **Pallis M, Svoboda SJ, Cameron KL, Owens BD. (2012)** | **6** | **2b** | **Prospective Cohort Study** |
| **Poehling GG et al. (2005)** | **4** | **2b** | **Prospective Cohort Study** |
| **Prodromos C, Joyce B, Shi K. (2007)** | **5** | **3a** | **Meta-analysis of clinical series** |
| **Shelton WR, Papendick L, Dukes AD. (1997)** | **5** | **2b** | **Prospective Cohort Study** |
| **Sun K et al. (2011)** | **8** | **1b** | **Randomized Controlled Trial** |
| **Sun K, Tian S, Zhang J, Xia C, Zhang C, Yu T. (2008)** | **7** | **1b** | **Randomized Controlled Trial** |
| **Sun K, Zhang J, Wang Y, Xia C, Zhang C, Yu T, Tian S. (2011)** | **8** | **1b** | **Randomized Controlled Trial** |

\*\*AMSTAR Checklist was used for study quality scores in systematic reviews and meta-analyses. Both AMSTAR and PEDro quality assessment rating scales are out of 11.

**BEST EVIDENCE**

The following 3 studies were identified as the ‘best’ evidence and selected for critical appraisal. Reasons for selecting these studies were:

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| * **Cvetanovich GL et al. (2014)**

My choice of the meta-analysis by Cvetanovich GL et al. (2014) as one of my best quality studies was fairly straightforward. It is a meta-analysis that was conducted on RCTs, and its quality rating was 10 out of 11 on the AMSTAR. In addition, it was published just this year, leading me to believe that it likely took into account newer studies and clinical trials that an older meta-analysis might have missed. Furthermore, the review itself takes into account a large number of outcome variables of the grafts (which is good for my study on potential re-injury) and indicates where there may be limitations in the current research data along with possibilities for future study.* **Sun K, Zhang J, Wang Y, Xia C, Zhang C, Yu T, Tian S. (2011)**

My decision to choose the Sun K et al. (2011) study – the final study by Sun K et al. that is listed in my summary of articles – was for a number of reasons. First, during my search, I found that the authors of this paper have completed more than 5 different randomized controlled trials on different forms of allografts and autografts in ACL reconstruction. It seems the authors have a question in terms of the outcomes, conduct a well-controlled study to investigate it, and publish an article on their findings. But then they consistently go back and do another slightly different study in order to answer questions that they encountered during their first study. I chose to use this study because not only is it a high level of evidence, but it’s also a high quality study (scoring 8/11 on the PEDro scale) and it was one of only a handful of studies that found significant difference in outcomes between allografts and autografts in ACL reconstruction surgery.* **Krych AJ, Jackson JD, Hoskin TL, Dahm DL. (2008)**

The decision to select the article by Krych et al. (2008) as one of the best quality studies for my clinical question was quite clear to me. First of all, it is a meta-analysis that investigates the results of well-controlled prospective cohort studies comparing allografts to autografts in terms of long-term success. In general, meta-analyses are often some of the highest levels of evidence in terms of published studies. And though some may consider the fact that it investigates prospective cohort studies rather than randomized controlled trials to be a drawback, it is actually quite appropriate for my clinical question. I found in my search that there are *far more* prospective cohort studies on the topic of allografts versus autografts for ACL reconstruction because, in general, patients want to be able to choose their surgery rather than being randomized into a particular group. This means that a meta-analysis of prospective cohort studies may miss a few good randomized controlled trials, but it will have the freedom to use more specific inclusion and exclusion criteria given that there are great deal more well-conducted prospective cohort studies out there. Furthermore, the meta-analysis was conducted to investigate long-term success of allografts versus autografts, which is about as close an outcome as I could find to what my clinical question is asking. And furthermore, this meta-analysis is of high quality, scoring 9 out of 11 on the AMSTAR Checklist. |

**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of** “Arthroscopic anterior cruciate ligament reconstruction with at least 2.5 years' follow-up comparing hamstring tendon autograft and irradiated allograft” **by** Sun K, Zhang J, Wang Y, Xia C, Zhang C, Yu T, Tian S. (2011)

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| **Aim/Objective of the Study/Systematic Review:** |
| The objective of this study was to analyse and compare the clinical outcomes - in terms of laxity/stability and functional evaluation - of arthroscopic anterior cruciate ligament reconstruction utilizing a hamstring tendon autograft versus an irradiated hamstring allograft at least 2.5 years following the reconstruction. |
| **Study Design** |
| * The study was a randomized controlled trial of 78 patients with anterior cruciate ligament ruptures who underwent ACL reconstruction surgery
* Participants were randomized to either hamstring tendon autograft group (Auto group, n=39) or irradiated hamstring tendon allograft group (Ir-Allo group, n=39) on the day of their surgery by a computer but were informed of their group allocation postoperatively.
* Objective and subjective data was collected 1, 3, 4, 9, and 12 months and then yearly by an independent orthopaedic surgeon who was blinded to group allocation prior to examination
* Outcome measures were obtained using a variety of musculoskeletal special tests, the KT-2000 arthrometer; knee ligament evaluation from of the International Knee Documentation Committee (IKDC), and a variety of functional activity tests
* Subjective outcome measures included the Cincinnati knee score, IKDC Subjective Knee Form, Tegner activity score, and Lysholm knee scoring scale.
* All study participants underwent the same rehabilitation protocol both before surgery and after.
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| **Setting** |
| Participants in the study attended therapy at a clinic (unspecified location) before and after their ACL reconstruction surgery, which was performed by the same senior surgeon (K.S.) at The Affiliated Hospital of Qingdao University Medical College in Qingdao, Shandong, China. |
| **Participants** |
| * A convenience sample of 78 participants with ACL ruptures (recruited by unspecified means) who were to undergo ACL reconstruction initially met the selection criteria, gave consent to participate, and were allocated to the two groups: Auto or Ir-Allo.
* Patients were excluded if they had previous same-knee injury/surgery, multiple ligamentous, injuries, mal-alignment, associated injuries of PCL, previous ACL injury/reconstruction of the same or contralateral knee.
* Patients were included only if they were receiving a primary unilateral ACL reconstruction.
* 3 participants were excluded post group allocation during arthroscopic examination due to PCL injury or other surgical procedure overlooked by MRI and clinical examination. An additional 8 patients were lost to follow-up due to migration, personal reasons, drop-out, or un-related death, leaving a total of 67 patients for study group evaluation and follow-up.
* The final groups’ demographics were Auto: n=36, 8 female/28 male, age= 30.9 +/- 8.7 years, mean time from injury to surgery 1.6 months; and Ir-Allo: n=31, 7 female/24 male, age= 30.3 +/- 7.9 years, mean time from injury to surgery 1.8 months
* Most common cause of ACL rupture in the study participants was injury due to sports activities
* The mean follow-up after ACL reconstruction was 42.2 months
* There was no statistically significant difference between the two groups at baseline.
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| **Intervention Investigated** |
| *Control – Autologous Hamstring Tendon Graft (Auto)* |
| The bone-patellar tendon-bone (BPTB) autograft has been considered the gold standard for ACL reconstruction, but it is increasingly being replaced by hamstring tendon autografts given the improvements in surgical technique and comparable clinical results. Therefore, the hamstring autograft acts as a control in this study to investigate the clinical comparability of an irradiated hamstring allograft.* Autogenous gracilis and semitendinosus hamstring tendons were harvested from over the participants’ pes anserinus at the start of their ACL reconstructions. Tendons were cleaned, sutured together to form a 4-strand graft, and pre-tensioned under twenty pounds for 20 minutes.
* ACL reconstruction were all completed using the anteromedial portal technique by the same senior arthroscopic surgeon, and the graft was placed using the remnants of the native ACL as landmark guides. EndoButton were used to fix the femoral side of the graft. Preconditioning following femoral placement involved flexing and extending the knee from 0 to 120 degrees approximately 25 times prior to tibial-side screw placement. A final arthroscopic inspection confirmed positioning and tension of the grafts. Pre-existing tears in menisci were repaired, though no patient had severe OA or required any additional ligament surgeries at that time, and there were no statistically significant differences between the groups in terms of meniscal lesions or intraoperative findings. Following surgery, the knee was placed in a postoperative brace locked in extension.

Rehabilitation began prior to surgery and continued afterward for all patients in both groups. Patients participated in physical therapy in order to improve ROM, gait, and decrease knee swelling prior to surgery. Following, all patients followed the exact same postoperative protocol for accelerated rehabilitation to emphasize early full extension and strengthening using closed-chain exercises and non-weight bearing straight-leg raises with hamstring stretches. Rehab also included 2-hour twice daily PROM with progression of weight-bearing with crutches or cane as tolerated, depending on pain and swelling. (Exact number of hours and location of postoperative treatment was not included in the article.) Proprioceptive balance activities and aquatics were incorporated at 8 weeks postoperatively and extended through 4-6 months. Walking, jogging, and running were allowed at 3 months and contact sports were permitted at 6 months at the earliest, depending on the patient, though functional bracing was recommended during sports for first 1 to 2 years following reconstruction. |
| *Experimental – Irradiated Hamstring Tendon Graft (Ir-Allo)* |
| The use of allogeneic hamstring tissue as an alternative graft source is a rarely investigated intervention for ACL reconstruction. Gamma irradiation is important in sterilization of the allograft but may alter biomechanical properties of the graft and possibly affect clinical outcomes. Therefore, irradiated hamstring tendon allograft is the experimental intervention being compared to the hamstring autograft control.* Hamstring tendon allogeneic constructs of gracilis and semitendinosus tendons were fresh-frozen and supplied by a certified tissue bank in accordance with the American Association of Tissue Banks and the FDA. Before distribution, the allografts received a dose of 2.5 Mrad irradiation, and they were thawed at room temperature in sterile physiologic fluid on the day of the operation. They were prepared in an identical fashion to the autografts after harvest and pre-tensioned under twenty pounds for 20 minutes.
* The exact same technique for and during ACL reconstruction was applied to the Ir-Allo group as to the Auto group (see second bullet point in control group info above).
* Similarly, rehabilitation was the exact same protocol for both the hamstring allograft as for the hamstring autograft in order to reduce confounding variables (see final bullet point in control group info above).
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| **Outcome Measures** (Primary and Secondary) |
| All measures were completed preoperatively and again at the 1, 3, 6, 9, 12 months postoperatively, with a yearly follow-up after the first year. Not mention was made of whether outcomes were considered primary or secondary for this RCT.Objective:* Axillary temperature of the patient taken by nurses each day postoperatively in the hospital, with lab work conducted if above 37.2 degrees Celsius.
* Examination of knee laxity, conducted by independent orthopaedic surgeon blinded to group allocation, including:
* Lachman test – measures anterior translation of proximal tibia on the femur at 25 degrees of flexion, can be measured in mm, usually positive or negative result
* Anterior drawer test – measures anterior translation of proximal tibia on the femur at 80 degrees of flexion, can be measured in mm, usually positive or negative result
* Pivot-shift test - valgus and internal rotation force is applied to extended knee, which is flexed past 30 degrees, positive or negative result
* Varus/valgus stress test - one-plane lateral/medial instability assessment, positive or negative result
* Instrumented anteroposterior laxity using “KT-2000 arthrometer by the manual maximum test with knee positioned at 15 degrees of flexion” (Sun K et al., 2011, p.1198). Conducted by independent orthopaedic surgeon blinded to group allocation – measures displacement of tibia on femur anteriorly and side-to side, measured in mm
* Functional tests, conducted by independent orthopaedic surgeon:
* ROM – active and passive to flexion and extension, range 0 to 180 degrees
* Harner vertical jump test using Vertec unit with 3 trials on each leg, mean calculated to determine vertical jump index as (involved / uninvolved) x 100% for limb symmetry
* Daniel 1-leg hop test with 3 trials on each leg, measured by tape measure, and mean calculated in order to determine hop index as (involved / uninvolved) x 100% for limb symmetry
* Standard knee ligament evaluation of International Knee Documentation Committee (IKDC) – a combined score of laxity tests that can be conducted manually, by instrument (KT-2000), or x-ray using 134 N force (30 lbs). Graded with group grades as A (normal), B (nearly normal), C (abnormal), or D (severely abnormal) to provide an idea of standardized ligament laxity.

Subjective:* Cincinnati knee score – questionnaire rating of pain, swelling, instability, and functional activity. Higher scores relate to greater function and fewer symptoms. Maximum score is 100, minimum score 6. Scores of <30 are poor, 30-54 are fair, 55-79 are good, and >80 are excellent.
* IKDC Subjective Knee Form – questionnaire for patient rating of symptoms of pain, swelling, and instability. Higher scores reflect better knee function and fewer symptoms. The form is scored by adding the grades for the individual items, dividing by the maximum possible score of 87, and multiplying by 100. A score of 100 is interpreted to mean no limitation with activities of daily living or sports activities and complete absence of symptoms.
* Tegner activity score – subjective comparison of activity levels ranging from Level 0 (Sick leave or disability because of knee problems) to Level 10 (competitive sports – national elite) with Level 10 being greatest function and Level 0 being lowest.
* Modified Lysholm knee scoring scale – subjective report of pain and knee function with daily activities. Range is 0 to 100 with higher scores indicating greater function and fewer symptoms. <65 is poor, 65-83 is fair, 84-90 is good, and >90 is excellent.
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| **Main Findings** |
| * Analysis was conducted only on the 67 participants who were available to follow-up for the duration of the study, which was 85.9% of the initial pool.
* Complications following surgery between the two groups were comparable, and intraoperative findings showed no statistical significance between the groups (p>/=0.834).
* The χ2 test showed no significant difference between the Auto group and the Ir-Allo group in overall IKDC rating (p>0.05), however, a trend was noted in that the Ir-Allo group tended to have lower scores in each of the components of the IKDC outcome measure.
* In comparing number of knees with side-to-side displacement of <3mm at final follow-up as well as anterior tibial displacement in millimetres measured by the KT-2000, it was found that the Ir-Allo group had significantly higher displacement than the Auto group for both (p=0.00008 and p=0.00021 respectively).
* Significant differences were found between the Auto group and Ir-Allo group in terms of laxity based upon the pivot-shift, anterior drawer test, and Lachman’s test as well, with p=0.008, p=0.00016, and p=0.00011 respectively.
* No significant differences were found between groups concerning ROM, vertical jump, and 1-leg hop (p>/=0.490).
* All subjective clinical results (mean subjective IKDC, Cincinnati, Lysholm, and Tegner scores) demonstrated no significant differences between Auto and Ir-Allo groups (p=0.208, p=0.212, p=0.353, and p=0.071 respectively).
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| **Original Authors’ Conclusions** |
| * The authors concluded that though ACL reconstruction with irradiated hamstring tendon allograft is satisfactory when compared to hamstring tendon autograft in terms of subjective and functional clinical outcomes, there were significant differences between the two groups for instrumented laxity.
* They state that based on their findings as well as recent evidence from other studies, irradiation for the purpose of graft sterilization seems to diminish the biomechanical properties - reduce stiffness and strength - of both hamstring tendon and bone-patellar tendon-bone grafts in doses as low as 2 Mrad.
* “When comparing the clinical outcomes of ACL reconstruction with irradiated hamstring tendon allograft versus autograft, we found an increase in anterior laxity or rate of graft rupture in patients who underwent reconstruction with irradiated hamstring tendon allograft according to the ADT, Lachman test, and manual maximum KT-2000 test. The rate of rotational instability also increased according to the pivot-shift test. The difference was statistically significant… With so high a laxity rate, we do not advocate use of the irradiated hamstring tendon allograft.” (Sun K et al., 2011, p. 1201).
* “We believe that, with time, the functional and activity levels of the patients in the irradiated group will decrease significantly, because the operated knee will have shown serious laxity.” (Sun K et al., 2011, p.1201).
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| **Critical Appraisal** |
| **Validity** |
| In terms of the methodology of the study, the group of patients ended up being fairly small for a randomized controlled trial, although the authors did not indicate a number needed to treat. Nevertheless, the small sample size may be due to the fact that convincing people to consent to randomization for a fairly important surgery likely was not an easy task either. The article does not go into detail in terms of how participants were recruited, but rather states that these were patients who were to undergo ACL reconstruction. This suggests that the participants were a convenience sample from the researchers’ clinic and may not be representative of the general population. This introduces selection bias and may limit the generalizability of the study. In addition, although a follow-up time of two and a half years is one of the longer follow-ups in studies for autografts versus allografts, it’s still not very long. It does not address some of the laxity issues that could become more evident five, ten, or fifteen years later. Also, although the orthopaedic surgeon taking the outcomes assessments was independent and blinded prior to examination, the patients could have informed the assessor of their group allocation (they were not blinded) or the assessor may have seen the donor incision sites if it was an autograft. This could lead to bias in interpreting results and assessing the participants in both subjective and objective measures. Lastly, the generalizability may be compromised for the study because one surgeon performed all the surgeries. So while they may be more comparable to one another, they may not have high external validity. A χ2 test for statistical significance was a valid choice for the categorical variables of the outcome measures, but the fact that there were so many outcomes limits the reproducibility of the study and makes it difficult to sift through. Nevertheless, a randomized controlled trial has a fairly high level of evidence (1b), and this study in particular received a PEDro quality assessment rating of 8 out of 11.PEDro Score: 8/11: Yes; Random Allocation: Yes; Concealed Allocation: No; Baseline Comparison: Yes; Blind Subjects: No; Blind Therapist: No; Blind Assessors: Initially but not necessarily throughout; Adequate Follow-up: Fair; Intention-to-treat analysis: Yes; Between Group Comparison: Yes; Point Estimates and Variability: No. |
| **Interpretation of Results** |
| The outcomes most relevant to the clinical question are the mean rotational and angular stability (i.e. the pivot-shift test, the ADT, and the Lachman) and the knee stability according to the instrumented KT-2000 for both groups at final follow-up. Therefore, the effect size for knee stability using the KT-2000 was calculated to be r=-0.597 for anterior tibial displacement of the Auto group versus the Ir-Allo group and r=-0.568 for side-to-side displacement. In using Pearson’s correlation for effect size in which r=0.50 is considered a large effect size, both of the above values can be considered a large effect size.Overall, investigating the main outcome of ACL laxity dependent upon autograft versus allograft, this study provided fairly favourable results. The two groups in the study were comparable (there were no statistically significant differences prior to surgery, during surgery, or in surgical complications) in terms of the entire protocol except the graft choice, and statistically significant results were reported. However, those results are not yet clinically significant in that they do not appear to correspond to functional outcomes – at least not with only 2.5 years of follow-up. It is possible that there may be differences found functionally in patients with autografts versus irradiated allografts if follow-up period were longer. Further studies to investigate more long-term effects would be beneficial in order to determine whether or not there is clinical significance between autografts and irradiated allografts for anterior cruciate ligament reconstruction. However, the authors demonstrate that there is some evidence that irradiated allografts have an increase in anterior laxity or rate of graft rupture (p. 1201). The proposed advantage of using irradiated allograft is a decrease in the risk for disease transmission, but research indicates that irradiation affects the biomechanical properties of the allograft in a dose-dependent manner.Furthermore, this study provided useful information on the functional satisfaction hamstring tendon autografts for ACL reconstruction (p. 1201) being similar to those for bone-patellar tendon-bone autografts.Neither ACL reconstruction graft was superior to the other in terms of functional outcomes or subjective report based on this study, although longer-terms studies may be required to provide information 3+ years postoperatively. Further studies investigating alternative methods of sterilization for allografts other than irradiation along with their subsequent mechanical properties would also be beneficial in furthering understanding of the best possible long-term graft option for ACL reconstruction. |

**(2) Description and appraisal of “**Hamstring autograft versus soft-tissue allograft in anterior cruciate ligament reconstruction: a systematic review and meta-analysis of randomized controlled trials” **by** Cvetanovich GL, Mascarenhas R, Saccomanno MF, Verma NN, Cole BJ, Bush-Joseph CA, Bach BR. (2014).

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| **Aim/Objective of the Study/Systematic Review:** |
| The objective of this systematic review was to compare outcomes of ACL reconstruction with a hamstring autograft versus ACL reconstruction with a soft-tissue allograft.  |
| **Study Design** |
| The study design was a systematic review of randomized controlled trials comparing hamstring autograft with soft-tissue allograft in ACL reconstruction with a minimum of 6 months’ follow-up. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist. Search Strategy: * Search was conducted by two reviewers who independently searched PubMed, Cochrane Central Register of Controlled Trials, and Embase databases.
* ((((((anterior cruciate ligament [Title/Abstract]) AND hamstring [Title/Abstract]) AND allograft [Title/Ab- stract]) AND autograft [Title/Abstract]) AND random- ized [Title/Abstract]) AND (English[lang])
* Selection Criteria applied (see below)
* References within included studies were cross-referenced for inclusion if they were not already found in the initial search

Selection Criteria: * Inclusion Criteria
* Randomized controlled trials
* Hamstring autograft compared to soft-tissue allograft
* Follow-up minimum 6 months s/p ACL reconstruction
* English language only
* Exclusion Criteria
* Studies using bone-tendon-bone grafts
* Medical conference abstracts
* Case reports, retrospective studies, review articles, letters to the editor, basic science studies, biomechanical studies, imaging studies, surgical technique reports, classification studies

Methods: * Two reviewers extracted data using data abstraction forms that were otherwise unspecified.
* Duplicates were removed, with the version that contained more information (if applicable) included.
* Study, subject, and surgery parameters and demographics collected and analysed, including year of publication, years of subject enrolment, presence of study financial conflict of interest, number of subjects and knees, gender, age, diagnoses treated, operative time, graft type used, number of patients and knees available for follow-up, and surgical procedures performed.
* Clinical outcomes investigated:
* ROM
* Loss of terminal extension
* Lysholm score
* Anterior drawer test
* Lachman test
* Pivot-shift test
* KT arthrometer examination
* Reoperation rate

Statistical Analysis:* Descriptive statistics calculated and reported as mean +/- standard deviation.
* Significance set at *P*< .05
* Data pooled and meta-analysis performed using RevMan software when possible.
* Dichotomous data reported as risk ratio, continuous data reported as standardized mean differences and 95% confidence intervals
* Heterogeneity assessed using I2, of which anything less than 60% indicated enough homogeneity of the data in order to justify pooling
 |
| **Setting** |
| Study settings were unspecified |
| **Participants** |
| * 5 studies were included in the systematic review/meta-analysis for a total pooled sample size of 504 participants.
* Included studies all randomly allocated participants to hamstring autograft or allograft group and were either Level I (n=1) or Level II (n=4) RCT study designs
* Sample sizes ranged from 65 to 102 participants
* 251 patients had a hamstring autograft reconstruction (control group) and 253 patients had an allograft reconstruction (experimental group) of the 504 pooled sample
* Demographics were 374 male, 130 female with a mean age of 29.9 +/- 2.2 years
* Soft-tissue allografts of studies included fresh-frozen hamstring, irradiated hamstring, mixture of fresh-frozen and cryopreserved hamstring, fresh-frozen tibialis anterior, and fresh-frozen Achilles tendon graft sans bone blocks.
* Studies used varying methods of fixation meaning that meta-analysis of this variable was not possible. However, each study utilized the same fixation between autograft and allograft groups to decrease confounding factors.
* Mean follow-up period of studies was 47.4 +/- 26.9 months with a range of 24 months to 93 months
* Mean follow-up rate of studies was 83.3% +/- 8.6% with a range of 69.4% to 89.4%
 |
| **Intervention Investigated** |
| *Control – Autologous Hamstring Tendon Graft* |
| Surgical reconstruction with a bone-patellar tendon-bone (BPTB) autograft has been considered the gold standard for ACL reconstruction, but it is increasingly being replaced by hamstring tendon autografts given the improvements in surgical technique and comparable outcomes in the literature. Therefore, the hamstring autograft is considered the control in this systematic review in order to investigate the clinical comparability of any type of soft-tissue allograft. |
| *Experimental – Soft-tissue Allograft* |
| The use of allogeneic soft-tissue as an alternative graft source is an increasingly appealing option for ACL reconstruction in order to avoid donor-site morbidity and to reduce operative time. However, there are possible disadvantages to using soft-tissue allografts, including disease transmission, delayed graft incorporation, and long-term graft laxity and failure. Therefore, surgical reconstruction of the ACL using soft-tissue allografts is the experimental intervention in this systematic review being compared to the hamstring autograft control.Types of soft-tissue allografts include:* Fresh-frozen hamstring
* Irradiated hamstring
* Mixture of fresh-frozen and cryopreserved hamstring
* Fresh-frozen tibialis anterior
* Fresh-frozen Achilles tendon graft sans bone blocks
 |
| **Outcome Measures** (Primary and Secondary) |
| Objective* Examination of knee laxity using:
* Lachman test – measures anterior translation of proximal tibia on the femur at 25 degrees of flexion, can be measured in mm, usually positive or negative result
* Utilized in 3 studies: Noh et al., 2011; Sun et al., 2011; & Sun et al. 2011
* Anterior drawer test – measures anterior translation of proximal tibia on the femur at 80 degrees of flexion, can be measured in mm, usually positive or negative result
* Utilized in 2 studies: Sun et al., 2011 & Sun et al., 2011
* Pivot-shift test - valgus and internal rotation force is applied to extended knee, which is flexed past 30 degrees, positive or negative result
* Utilized in 4 studies: Lawhorn et al., 2012; Noh et al., 2011; Sun et al., 2011; & Sun et al., 2011
* Instrumented anteroposterior laxity using “KT-2000 arthrometer” – measures displacement of tibia on femur anteriorly and side-to side, measured in mm
* Utilized by all 5 studies included
* International Knee Documentation Committee (IKDC) – standard knee ligament evaluation using a combined score of laxity tests that can be conducted manually, by instrument (KT-2000), or x-ray using 134 N force (30 lbs). Graded with group grades as A (normal), B (nearly normal), C (abnormal), or D (severely abnormal) to provide an idea of standardized ligament laxity.
* Utilized by all 5 studies included, although authors did not indicate whether this objective component of the IKDC was used alone or in conjunction with the subjective

Subjective* Tegner activity score – subjective comparison of activity levels ranging from Level 0 (Sick leave or disability because of knee problems) to Level 10 (competitive sports – national elite) with Level 10 being greatest function and Level 0 being lowest.
* Utilized in 4 studies: Edgar et al., 2008; Noh et al., 2011; Sun et al., 2011; & Sun et al., 2011
* Modified Lysholm knee scoring scale – subjective report of pain and knee function with daily activities. Range is 0 to 100 with higher scores indicating greater function and fewer symptoms. <65 is poor, 65-83 is fair, 84-90 is good, and >90 is excellent.
* Utilized in 4 studies: Edgar et al., 2008; Noh et al., 2011; Sun et al., 2011; & Sun et al., 2011
* IKDC Subjective Knee Form – questionnaire for patient rating of symptoms of pain, swelling, and instability. Higher scores reflect better knee function and fewer symptoms. The form is scored by adding the grades for the individual items, dividing by the maximum possible score of 87, and multiplying by 100. A score of 100 is interpreted to mean no limitation with activities of daily living or sports activities and complete absence of symptoms.
* Utilized by all 5 studies included, although authors did not indicate whether this subjective component of the IKDC was used alone or in conjunction with the objective

No distinction was made between primary and secondary outcomes for the objective or subjective measures. |
| **Main Findings** |
| * In the meta-analysis of clinical outcomes, 2 of 5 studies found significantly longer operative time for surgery with an autograft versus surgery with an allograft. The mean times were 77.1 +/- 2.0 minutes for autograft and 59.9+/- 0.9 minutes for allograft, with a *P* = 0.008 indicating significant difference.
* There were no significant differences between the two grafts for any of the outcome measures that were part of the meta-analysis, including modified Lysholm score (RR, -0.07; 95% CI 0.28 to 0.15; *P* = .40), Tegner score (RR, 0.11; 95% CI, -0.15 to 0.36; *P* = .40), and IKDC grade (RR, 1.01; 95% CI, 0.96 to 1.05; *P* = .81).
* Reoperations were required in 7 autografts and 6 allografts due to graft failure (3 auto, 2 allo), arthrofibrosis (2 auto, 1 allo), symptomatic hardware removal (1 auto, 2 allo), and meniscectomy (1 in each group). However, there was no significant difference in reoperation rate between groups (RR, 1.14; 95% CI, 0.40 to 3.25; *P* = .81).
* There were no significant differences between the hamstring autograft and soft-tissue allograft in any of the examinations of laxity outcomes, including the Lachman test (RR, 1.37; 95% CI, 0.88 to 2.14; *P* = .16), the pivot-shift test (RR, 1.05; 95% CI, 0.92 to 1.20; *P* = .46), and KT arthrometer testing (RR, 1.11; 95% CI, 0.89 to 1.39; *P* = .36).
* However, meta-analysis of the laxity outcomes indicated high heterogeneity (I2=86%, I2=83%, I2=63%), leading the authors to assess the heterogeneity and find that the study by Sun et al., 2011 was the cause given that it was the only study to use irradiated allograft and therefore demonstrated increased laxity of the soft-tissue allograft on all measures. Removal of that study from laxity outcomes meta-analysis resulted in reduced heterogeneity below an I2 of 60% for reasonable pooling of data but did not affect the result of no significant difference (*P* > .05).
 |
| **Original Authors’ Conclusions** |
| * “This review and meta-analysis showed no statistically significant differences in clinical outcome measures, measures of ACL laxity, and reoperations in patients undergoing ACL reconstruction with hamstring auto- graft versus soft-tissue allograft.” (Cvetanovich et al., 2014, p.6)
* Two of five studies showed a statistically significant increased operative time for autograft ACL reconstruction versus allograft reconstruction, which authors concluded could lead to a “decreased rate of perioperative complications after ACL reconstruction, but this was not observed in these studies. Therefore, the clinical significance of this finding is unclear and must be weighed along with the other advantages and disadvantages of allografts and autografts” (Cvetanovich et al., 2014, p. 7).
* Authors advised that surgeons work with patients to determine the best graft selection for the individual based on age, activity level, goals, etc. They summarized that soft-tissue allografts have the advantages of no donor-site morbidity (such as knee flexion weakness and saphenous nerve damage) that may accompany hamstring autograft ACL reconstruction as well as reduced operative time. However, allografts also carry the “risk of disease transmission, higher rates of graft laxity and failure, and delay in graft incorporation.” (Cvetanovich et al., 2014, p.6)
* Despite the lack of statistically significant differences in clinical outcomes, laxity, and reoperations between hamstring autografts and soft-tissue allografts in their research (which was what was hypothesized), the authors argue that the currently available high-quality studies target too small of a population. They state that because the mean age for the participants in their review was 29.9 +/- 2.2 years, “the low rates of complications and graft failure in our meta-analysis may result from the fact that randomized studies to date have not evaluated younger patient population at the highest risk of graft failure.” (Cvetanovich et al., 2014, p. 6).
 |
| **Critical Appraisal** |
| **Validity** |
| * Methodologic quality of studies analysed using the 15-question Modified Coleman Methodology Score (MCMS) and 3-question Jadad scale. MCMS evaluates study methodology with scores ranging on a scale of 0-100 and “excellent” studies 85-100, “good” studies 70-84, “fair” studies 55-69, and “poor” studies under 55. Jadad evaluates study randomization, blinding, and withdrawals/dropouts with scores ranging on a scale of 0-5 and scores below 3 indicating poor quality.
* Although the authors did not use the methodologic quality of reviewed studies as inclusion/exclusion criteria, they found that based on both the MCMS and Jadad evaluations that the methodologic quality of the 5 studies was poor (mean MCMS 54.4 =/- 6.9, mean Jadad 1.6 +/- 1.5).
* The study design and selection criteria of the systematic review led to relatively few studies and participants for meta-analysis. This small sample size and subsequent lack of significance in outcome measures could indicate a type β error. Larger studies would help to reduce this error, although the lack of such studies points to the limitations in the current available literature.
* Furthermore, one out of the 5 studies was a multicentre study, which introduces selection bias given that single-centre studies have a smaller population to draw a sample from to begin with.
* In addition, patients were not blinded in any of the studies, and outcome observers were only blinded in one of the studies. This could lead to bias in subjective reports from patients/observers, interpreting results, and assessing the participants in outcome measures.
* The lack of distinction between types of allografts used in each study also limits the ability of this meta-analysis to detect differences between hamstring autograft and allograft if it was dependent on the type of allograft utilized.
* Average age of participants in the study being nearly 30 leads to a lack of extrapolation of results to a younger, more active patient population who are at a higher risk of graft failure.
* The average follow-up time of 47.4 months was likely not long enough to get a good picture of long-term rates of graft failure and repeat surgery and further high-level studies are needed to look at long-term outcomes.
* Additional differences between studies that could affect or obscure the reported differences between hamstring autografts and soft-tissue allografts include: difference in participant inclusion/exclusion criteria (particularly in terms of coexistent surgeries/injuries), gender of participants, and duration of final follow-up.

AMSTAR score: 10/11: ‘A priori’ design: Yes; Duplicate study selection/data extraction: Yes; Comprehensive literature search: Yes; Status of publication as criteria: Yes; List of studies provided: Yes; Characteristics of included studies provided: Yes; Scientific quality of studies assessed: Yes; Scientific quality considered in conclusions: Yes; Methods for Pooled Results: Yes; Likelihood of Publication Bias assessed: No; Conflict of Interest Stated: Yes. |
| **Interpretation of Results** |
| Overall, given that the aim of this systematic review was to investigate the generalized “outcomes” of ACL reconstruction dependent upon autograft versus allograft, this study provided fairly limited results. Although the five studies in the review were a high level of evidence (Level I or Level II), the methodological quality of the studies was collectively poor, and the demographics of the participants were not representative of the overall population who may receive ACL reconstructions. The meta-analysis found no statistically significant difference between the hamstring autograft and the soft-tissue allograft in terms of clinical outcomes, graft laxity, or reoperation rate. In addition, the results are not yet clinically significant in that they do not appear to correspond to functional outcomes. It is possible that there may be differences found functionally in patients with hamstring autografts versus soft-tissue allografts if the follow-up period were longer and if a larger and more representative (i.e. younger, more active) population were sampled. Further studies to investigate more long-term effects would be beneficial in order to determine whether or not there is clinical significance between autografts and allografts for anterior cruciate ligament reconstruction. However, the authors demonstrate that there is some evidence that irradiated as a means of sterilization and reduction of disease transmission risk for allografts also leads to an increase in laxity and graft failure (p.7). Nevertheless, this study provided useful information given its stated purpose of investigating general outcomes following ACL reconstruction using hamstring autograft versus soft-tissue allograft. Therefore, the authors took into account the various limitations that may be affecting their results and analysed how future studies may investigate, focusing on a younger, more active population as well as studies that have a longer follow-up time. Ideally, further high-level studies conducted over long-term on large samples of late teens and young adults would be able to provide more sensitive and clinically relevant information on the outcomes of ACL reconstruction with autografts versus allografts postoperatively.  |

**(3) Description and appraisal of** “Meta-analysis of Patellar Tendon Autograft Versus Patellar Tendon Allograft in Anterior Cruciate Ligament Reconstruction” **by** Krych AJ, Jackson JD, Hoskin TL, Dahm DL. (2008).

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| **Aim/Objective of the Study/Systematic Review:** |
| The objective of the study was to evaluate the efficacy of bone-patellar tendon-bone (BPTB) autograft compared to BPTB allograft in ACL reconstruction. |
| **Study Design** |
| The study design was a meta-analysis of prospective non-randomized cohort studies comparing BPTB autograft with BPTB allograft in ACL reconstruction with a minimum of 2 years follow-up. Search Strategy: * Conducted by two reviewers who searched published literature on MEDLINE, EMBASE, Scopus, and Web of Science.
* Subject headings and key words utilized were reported as: anterior cruciate ligament, surgery, reconstruction, allograft, or autograft.
* 548 relevant abstracts retrieved and reviewed
* Selection Criteria applied (see below)
* References within included studies were manually searched for inclusion if they were not already found in the initial search

Selection Criteria: * Inclusion Criteria
* Comparative studies of BPTB autograft with prospective data
* Minimum 2-year follow-up
* Identical rehabilitation protocols for autograft/allograft groups
* Subjective assessment of outcomes
* Objective assessment of outcomes
* Exclusion Criteria
* Studies using allografts other than BPTB

Methods: * Two reviewers extracted data using data abstraction forms that were otherwise unspecified.
* Minor inconsistencies were re-examined and resolved
* Clinical outcomes that were investigated in the meta-analysis (other outcomes from included studies were not evaluable due to inconsistency or not amenable to meta-analysis):
* Graft failure including re-rupture
* Re-operation
* Lachman test
* Pivot-shift scores
* Patellofemoral crepitus
* Return to sport
* Hop test greater than 90% of non-operative side
* IKDC scores for normal or nearly normal knee

Statistical Analysis:* Odds ratio (OR) for given outcome calculated for individual studies and then combined for an overall summary odds ratio, presented with 95% confidence intervals and *P* values.
* ORs calculated for the odds of a bad outcome for allograft versus autograft. Value >1 indicates outcome favouring autograft and value <1 indicates outcome favouring allograft.
* Statistical significance was considered *P* <.05
* The calculations for the meta-analysis were performed using DerSimonian and Laird random-effects method to calculate summary odds ratios, which also evaluates heterogeneity between studies
* Subsequent statistical tests for significant heterogeneity were performed using the Mantel-Haenszel Q-statistic
* Data analysis was performed using R statistical software version 2.2.1 and the package rmeta.
 |
| **Setting** |
| Study settings not specificed |
| **Participants** |
| * Of the 548 studies identified in the initial search, 6 studies were included in the systematic review/meta-analysis for a total pooled sample size of 534 participants.
* For studies that had than 1 follow-up time (3 of the 6 studies), the longest follow-up alone was specifically included in order to assess long-term issues grafts
* Sample sizes ranged from 60 to 268 participants
* 256 patients had ACL reconstruction with a BPTB autograft (control group) and 278 patients had ACL reconstruction with a BPTB allograft (experimental group) of the 534 pooled sample
* Although demographic data on age and gender were not available for all studies, there were no significant differences in age or gender of patients between allograft and autograft groups for any of the included studies. Average ages for each study and group (Allo/Auto) were 47.13/44.52 years, 25/28 years, 23.9/23.9 years, 28/28 years, 28/28 years.
* Surgical technique for fixation varied in that 5 studies used a single-incision and one used two-incision arthroscopic-assisted technique. All studies used an interface screw, absorbable interface screw, or EndoButton for fixation.
* Postoperative treatment amongst the studies varied but was consistent between autograft and allograft groups within the studies and generally involved early weightbearing and ROM exercises. Return to full activity was between 6 and 12 months for all studies.
* Follow-up period of studies was in a range of 24 months to 71 months with no mean follow-up for pooled studies reported.
 |
| **Intervention Investigated** |
| *Control – Autologous Bone-Patellar Tendon-Bone Graft* |
| ACL reconstruction utilizing a bone-patellar tendon-bone (BPTB) autograft has long been considered the gold standard for ACL reconstruction due to its strong initial fixation, tendinous biomechanical properties, durability, and long-term success (p.292). Therefore, the BPTB autograft is considered the control in this systematic review in order to investigate the clinical comparability of BPTB allograft. |
| *Experimental – Bone-Patellar Tendon-Bone Allograft* |
| The use of BPTB allograft as an alternative graft source is an increasingly appealing option for ACL reconstruction given its advantages of fewer harvest-related patellofemoral symptoms, shorter operative time, superior cosmesis, variable graft size options, and lack of donor-site morbidity that may occur with an autograft. However, there are possible disadvantages to using BPTB allografts, including disease transmission, delayed graft incorporation, possible immune reactions, and altered mechanical properties from sterilization (p.292). Therefore, surgical reconstruction of the ACL using BPTB allografts is the experimental intervention in this systematic review being compared to the BPTB autograft control. |
| **Outcome Measures** (Primary and Secondary) |
| Objective* Graft Failure/Re-rupture – whether or not participant had suffered graft failure or re-rupture at follow-up time
* Utilized in all included studies except Harner et al., 1996.
* Rate of re-operation – distinct from graft rupture. Rationale for re-operation included hardware removal, meniscectomy, notchplasty for cyclops lesion.
* Utilized in 3 studies: Kleipool et al., 1998; Barrett et al., 2005; & Peterson et al., 2001.
* Examination of knee laxity using:
* Lachman test – measures anterior translation of proximal tibia on the femur at 25 degrees of flexion, can be measured in mm, usually positive or negative result. For this meta-analysis, outcomes of Lachman grade 0 were reported versus outcomes of Lachman grade greater than 0, with 0 being normal laxity and greater than 0 (1, 2, or 3) being increased laxity.
* Utilized in 4 studies: Kleipool et al., 1998; Gorschewsky et al., 2005; Barrett et al., 2005; & Peterson et al., 2001.
* Pivot-shift test - valgus and internal rotation force is applied to extended knee, which is flexed past 30 degrees, positive or negative result
* Utilized in 3 studies: Kleipool et al., 1998; Barrett et al., 2005; & Peterson et al., 2001.
* International Knee Documentation Committee (IKDC) – standard knee ligament evaluation using a combined score of laxity tests that can be conducted manually, by instrument (KT-2000), or x-ray using 134 N force (30 lbs). Graded with group grades as A (normal), B (nearly normal), C (abnormal), or D (severely abnormal) to provide an idea of standardized ligament laxity.
* Utilized in 3 studies, although authors did not indicate whether this objective component of the IKDC was used alone or in conjunction with the subjective: Kleipool et al., 1998; Gorschewsky et al., 2005; & Harner et al., 1996
* Hop test – generally completed with 3 trials on each leg, measured by tape measure, and mean calculated in order to determine hop index as (involved / uninvolved) x 100% for limb symmetry. Hop test is considered normal if greater than 90% of non-operative side.
* Utilized in 3 studies: Kleipool et al., 1998; Gorschewsky et al., 2005; & Harner et al., 1996.

Subjective* Patellofemoral crepitus – authors stated that evaluations of this outcome varied, so it is being listed as subjective report
* Utilized in 3 studies: Gorschewsky et al., 2005; Barrett et al., 2005; & Peterson et al., 2001.
* Return to Pre-injury Activity Level – return to original sport, unspecified in how it was reported by various studies
* Utilized in 3 studies: Gorschewsky et al., 2005; Harner et al., 1996; & Victor et al., 1997.
* IKDC Subjective Knee Form – questionnaire for patient rating of symptoms of pain, swelling, and instability. Higher scores reflect better knee function and fewer symptoms. The form is scored by adding the grades for the individual items, dividing by the maximum possible score of 87, and multiplying by 100. A score of 100 is interpreted to mean no limitation with activities of daily living or sports activities and complete absence of symptoms.
* Utilized in 3 studies included, although authors did not indicate whether this subjective component of the IKDC was used alone or in conjunction with the objective: Kleipool et al., 1998; Gorschewsky et al., 2005; & Harner et al., 1996

No distinction was made between primary and secondary outcomes for the objective or subjective measures. |
| **Main Findings** |
| * Meta-analysis of graft failure or rupture was found to have an odds ratio of 5.03, which indicates that there were significantly more graft ruptures in the allograft group as compared to the autograft group (95% CI, 1.38-18.33; *P* = .01; Q-statistic = 4.14; *P* = .25).
* A total of 13 allograft patients and 8 autograft patients out of the pooled sample of 534 had to have reoperation for hardware removal, meniscectomy, or notchplasty for cyclops lesion. This was not significant, with an OR of 1.20 (95% CI, 0.44-3.27; *P =* .72; Q-statistic = 0.11; *P* = .95).
* In investigating ACL laxity using the Lachman test, outcomes were reported as grade of 0 (normal laxity) versus greater than 0 (increased laxity). The odds ratio was not statistically significant between the two groups (OR = 2.75, 95% CI, 0.70-10.81; *P* = .15; Q-statistic = 17.4: *P* < .01).
* The pooled quantitative data from the pivot-shift test – in which a pivot-shift of greater than 0 was abnormal – indicated no significant differences between the two groups in any of the studies (OR = 1.23, 95% CI, 0.51- 2.98; *P* =.65; Q-statistic = 1.9; *P* = .39).
* Patellofemoral crepitus was a dichotomous outcome measure as presence versus absence. The odds ratio of having patellofemoral crepitus in the allograft group versus the autograft group was 2.34, which was not statistically significant (95% CI, 0.76-7.27; *P* = .14; Q-statistic = 5.14; *P*= .08).
* Meta-analysis for not returning to original sport demonstrated no significanct differences between the two groups of any included studies (OR = 1.2, (95% CI, 0.72-2.0; *P* = .48; Q-statistic = 0.22; *P* = .90)
* The hop test data from the meta-analysis had an odds ratio of 5.66, significantly in favour of a BPTB autograft over a BPTB allograft for ACL reconstruction in terms of regaining hop distance to greater than 90% of the non-operative side (95% CI, 3.09- 10.36; *P* < .01; Q-statistic = 1.6; *P* = .45).
* In the meta-analysis of IKDC scores, calculation of ORs was normal (or nearly normal) versus outcomes worse than that. The OR for an IKDC score of a normal or nearly normal knee was 1.49 for autograft compared with allograft, which was not significantly different ((95% CI, 0.21-10.38; *P* = .69; Q-statistic = 26.7; *P* < .01).
* While completing the meta-analysis, the authors found that the Gorschewsky et al., (2005) study had a number of outcome results that were variable from the other studies. The Q-statistic test for heterogeneity was significant for the outcomes of abnormal IKDC (*P* <.0001) and abnormal Lachman (*P* = .0006) along with a trend for crepitus (*P* = .08) with this study included. The authors found that the Gorschewsky et al. (2005) study used irradiated BPTB allografts that had been dried in acetone, and when the data from this study were excluded, there was no longer significant heterogeneity. Following this change, the meta-analysis shows that BPTB autografts were not significantly favored over BPTB allografts in terms of the two previously statistically significant outcomes: graft rupture (*P* = .37) and hop test greater than 90% of non-operative side (*P* = .34). Furthermore, all of the other outcomes became more similar between groups, with no statistically significant differences.
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| **Original Authors’ Conclusions** |
| * “In an effort to clarify the clinical results in primary ACL reconstruction, we performed a meta-analysis of prospective trials comparing BPTB autograft with BPTB allograft and found that hop test and graft rupture were significantly better with BPTB autograft. However, when irradiated and chemically processed grafts were excluded, no significant differences were found in any of the measurable outcomes.” (Krych et al., 2008, p. 296).
* The authors posit that graft rupture is higher among BPTB allografts when compared with BPTB autografts but that it is likely due to the irradiation and chemical processing that some allografts undergo for sterilization purposes.
* In addition, the authors state that with respect to laxity and joint stability following allograft, they found no significant differences (as measured via Lachman and pivot-shift testing) with rehabilitation protocols that entailed return to full activity in 6 to 12 months. They therefore suggested that “if patients adhere to established rehabilitation protocols similar to those in this meta-analysis, there is likely no difference in graft stability between allograft and autograft reconstructions.” (Krych et al., 2008, p. 296).
* Because similar numbers from allograft and autograft groups were able to return to sport and those in the autograft group actually performed better on the hop test, the authors contested the idea that a patellar tendon autograft may significantly affect functional outcomes. However, they state that having not tested quadriceps strength or direct donor-site morbidity, conclusions about functional outcomes cannot be firmly made.
* “In contrast to fresh-frozen allografts, the Gorschewsky study allografts were sterilized with a combination of radiation (1.5Mrad and 15 kGy) and acetone solvent drying. It is certainly possible that this sterilization process negatively affected the outcome of the allograft group…” (Krych et al., 2008, p. 297).
 |
| **Critical Appraisal** |
| **Validity** |
| * Given that meta-analyses are effective in incorporating results of several primary trials while utilizing methods to control for error and bias, the meta-analysis is only as good as the studies examined. In this study, the authors aimed to determine if there were clinically meaningful differences between BPTB autograft and allograft. However, the authors did not use any sort of methodologic quality control in selecting their studies reviewed, nor did they grade the studies once chosen, making it hard to analyse the quality of the studies. And since none of the studies included had patients randomized to group, there is also significant risk of selection bias. However, no significant differences in patient demographics were found within individual studies, decreasing some risk of confounding.
* The study design of this meta-analysis resulted in relatively few studies to be analysed. This small sample size and subsequent lack of significance in outcome measures could indicate a type β error.
* Patients were not blinded in any of the studies, and independent examiners were used in only 3 of the 6 studies. This could lead to bias in subjective reports from patients/observers, interpreting results, and assessing the participants in outcome measures.
* However, each point identified by the the Oxman and Guyatt scoring system, which used to measure scientific quality of review articles, was addressed in the meta-analysis in order to try to control and combat any errors or methodologic flaws.
* In addition, using the DerSimonian and Laird method of meta-analysis allowed for evaluation of heterogeneity between included studies and thereby the exclusion of irradiated graft data from the Gorschewsky et al. (2005) study. Although this reduced the power to detect significant differences between groups (p.297), it also provided insight into some of the trends that were drawing a distinction between autografts and allografts for ACL reconstruction.

AMSTAR score: 9/11: ‘A priori’ design: Yes; Duplicate study selection/data extraction: Yes; Comprehensive literature search: Yes; Status of publication as criteria: Yes; List of studies provided: Yes; Characteristics of included studies provided: Yes; Scientific quality of studies assessed: No; Scientific quality considered in conclusions: Yes; Methods for Pooled Results: Yes; Likelihood of Publication Bias assessed: No; Conflict of Interest Stated: Yes. |
| **Interpretation of Results**[Favourable or unfavourable, specific outcomes of interest, size of treatment effect, statistical and clinical significance, minimal clinically important difference. You may calculate effect size or confidence intervals yourself from the data provided in the article.] Describe in your own words what the results mean. |
| The main purpose of this meta-analysis was to investigate how well the BPTB allograft compared to the gold standard of the BPTB autograft for ACL reconstruction. To that end, this study had fairly favourable results. The researchers found that, based on the literature reviewed, BPTB autografts are favoured over BPTB allografts in terms of graft rupture and functional outcomes indicated by a single-leg hop test. However, the statistically significant difference between these grafts was not present when irradiated allografts were excluded from the study, leaving only the fresh-frozen allografts. The results of this study thereby provide two interesting points: first, that there is a difference between BPTB allografts and BPTB autograft in terms of graft failure and functional outcomes when investigated generally. And secondly not all BPTB allografts are equal. Specifically, irradiated allografts have altered mechanical properties that ultimately lead to the difference between allografts and autografts investigated. However, the methodological quality of the studies was not addressed in this meta-analysis, which requires that readers understand any possible limitations of validity. Nevertheless, the results –although not yet clinically significant – lend set the stage for further research with larger studies that exclude irradiated allografts. By more specifically comparing BPTB autografts and BPTB allografts that have NOT been irradiated, researchers may be able to get a better idea of how the two grafts compare in terms of longevity and functional outcomes.  |

**IMPLICATIONS FOR PRACTICE and FUTURE RESEARCH**

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| For the clinical question: “In college-aged female soccer player with an anterior cruciate ligament tear, does ACL reconstruction surgery utilizing an allograft effectively prevent re-injury after return to sport versus ACL reconstruction surgery utilizing an autograft?” these studies are helpful but ultimately don’t quite provide *enough* information to answer this question fully. For one thing, in the randomized control trial and based on the demographic information we are provided in the systematic reviews/meta-analyses, there were a great deal more males involved in ACL reconstruction research than females. Furthermore, the age range of the vast majority of participants in the studies – both men and women – was late twenties through mid-forties. Middle-aged adult males don’t exactly represent the “college-aged female” population well, and results may not be as generalizable as one would hope. However, we can also see based on the demographics that the majority of the participants involved in the research initially sustained an ACL injury by participating in athletics, and long-term return-to-sport may provide a fairly good picture of the outcomes of their ACL reconstructions. Although the populations that are addressed in the research are not *perfect* for addressing the clinical question, they demonstrate the closest sample of that population in the currently available literature, and the outcomes and results from these studies provide guidance for future study. The studies investigated above also are beneficial in that they investigate outcomes using various types of autografts and allografts. Hamstring tendon autografts versus irradiated hamstring tendon allografts, hamstring tendon autografts versus any sort of soft-tissue allograft, and BPTB autografts versus BPTB allografts are all compared and analysed in order to present as comprehensive a picture as possible. Although the BPTB autograft has shown satisfactory long-term results (O’Neill, 2001), the fact that it may lead to significant donor-site morbidity, compromised quadriceps strength, and reduced functional capacity remains an issue (Seon et al., 2006) (Pigozzi et al., 2004). Therefore, a hamstring tendon autograft is an alternative and similarly effective graft choice that may cause less donor-site morbidity and faster quadriceps recover than the BPTB autograft (Li et al., 2011). However, being an autograft, there is still the problem of significant donor-site morbidity, including saphenous nerve damage and postoperative knee flexion weakness with a hamstring tendon autograft (Sanders et al., 2007). The use of allografts addresses these concerns, leading to their increased use in ACL reconstruction in recent years (Chechik et al., 2013). However, allografts come with their own possible risks and disadvantages, such as disease transmission, delayed graft incorporation, graft laxity, and even rupture (Barbour & King, 2003). This begs the question of what really is the most optimal for long-term outcomes. By addressing the various options, the studies above have demonstrated that, in most regards, the various types of graft are fairly equivalent in terms of outcomes – unless an allograft is irradiated for sterilization. It was interesting to see that one consistency across an RCT and two different meta-analyses: the data show similar outcomes in terms of clinical outcome measures, ACL laxity, functional tests, and rupture rate *except* for irradiated allografts. The implications of poorer outcomes following ACL reconstruction with an *irradiated* allograft are numerous. First, this means that when patients are seen in the physical therapy setting prior to ACL surgery, discussion about the options for graft choice is imperative. Although there is no substantial evidence pointing to autograft over allograft in terms of long-term outcomes, patients should know the possible risk associated with irradiated allografts in terms of altered biomechanical properties. Similarly, they should be aware that non-irradiated allografts have an increased risk of disease transmission. By educating patients and advising them to speak to their surgeon or doctor about graft options, patients have the ability to make an informed choice that is right for them and their own personal goals. For a college-aged female soccer player who is likely otherwise completely healthy and wants the best possible functional outcomes and stability, the possibility of disease transmission may not be as risky as someone who is older or has compromised health, and so a non-irradiated allograft may be a good choice. However, if this female athlete has time in the off-season to train and regain any muscular strength she may have lost from surgery, autografts would also be a viable option. Therefore, it depends upon the person’s situation, but either allograft or autograft would likely be a suitable choice for a female college-age soccer player, with the one exception of an irradiated allograft.Although these studies provided fairly good idea of long-term outcomes following autograft and allograft ACL reconstruction, future research is still indicated. A prospective study over the course of 10 or more years that addresses re-injury and functional outcomes following an ACL reconstruction with an autograft versus an allograft within the female college-athlete population would be the *ideal* study for this clinical question. However, there are currently no studies available to me that address that particular question. Nevertheless, based on the evidence both uncovered in these study and investigated in the literature previously, it appears that the results are pointing towards either an autograft *or* a non-irradiated allograft as a “safer” bet against re-injury due to the lack of irradiation changing the mechanical properties of the tissue and the importance of anterior knee stability in athletes – specifically soccer players – in order to prevent re-injury.  |

**REFERENCES**

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| Barbour, S.A., King, W. (2003). The safe and effective use of allograft tissued: An update. *Am J Sports Med, 31*, 791-797.Chechik, O., Amar, E., Khashan, M., Lador, R., Eyal, G., Gold, A. (2013). An international survey on anterior cruciate ligament reconstruction practices. *Int Orthop, 37*, 201-206.Cvetanovich, G.L., Mascarenhas, R., Saccomanno, M.F., Verma, N.N., Cole, B.J., Bush-Joseph, C.A., Bach, B.R. (2014). Hamstring Autograft Versus Soft-Tissue Allograft in Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Arthroscopy: The Journal of Arthroscopic and Related Surgery*, 1-9.Krych, A.J., Jackson, J.D., Hoskin, T.L., Dahm, D.L. (2008). A Meta-analysis of Patellar Tendon Autograft Versus Patellar Tendon Allograft in Anterior Cruciate Ligament Reconstruction. *Arthroscopy: The Journal of Arthroscopic and Related Surgery*, *24*(3), 292-298. Li, S., Su, W., Zhao, J., et al. (2011). A meta-analysis of hamstring autografts versus bone-patellar tendon-bone autografts for reconstruction of the anterior cruciate ligament. *Knee, 18*, 287-293.O’Neill D.B. (2001). Arthroscopically assisted reconstruction of the anterior cruciate ligament. A follow-up report. *J Bone Joint Surg Am*, *9*, 1329-1332.Pigozzi, F., Di Salvo, V., Parisi, A., Giombini, A., Fagnani, F., Magini, W., et al. (2004). Isokinetic evaluation of anterior cruciate ligament reconstruction: Quadriceps tendon versus patellar tendon. *J Sports Med Phys Fitness*, *3*, 288-293.Sanders, B., Rolf, R., McClelland, W., Xerogeanes, J. (2007). Prevalence of saphenous nerve injury after autogenous hamstring harvest: An anatomic and clinical study of sartorial branch injury. *Arthroscopy, 23*, 956-963.Seon, J., Song, E., Park, S. (2006). Osteoarthritis after anterior cruciate ligament reconstruction using a patellar tendon autograft. *Int Orthop, 2*, 94-98.Sun K, Zhang J, Wang Y, Xia C, Zhang C, Yu T, Tian S. (2011). Arthroscopic Anterior Cruciate Ligament Reconstruction With at Least 2.5 Years’ Follow-up Comparing Hamstring Tendon Autograft and Irradiated Allograft. *Arthroscopy: The Journal of Arthroscopic and Related Surgery*, *27*(9), 1195-1202.  |