2019

Is the Use of a Fresh-frozen Allograft More Effective than a Hamstring Autograft in Preserving Functional Knee Ability Post-surgery in ACL Reconstruction?

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Is the use of a fresh-frozen allograft more effective than a hamstring autograft in preserving functional knee ability post-surgery in ACL reconstruction?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 14, 2018

ABSTRACT

OBJECTIVE: The objective of the selective EBM review is to determine whether or not, "Is the use of fresh-frozen allograft more effective than a hamstring autograft in preserving functional knee ability post-surgery in ACL reconstruction?"

STUDY DESIGN: Review of two randomized control trials (RCTs) and one prospective randomized study published between 2011 and 2016, all in English language. The articles compared allograft tendon versus autograft tendon when undergoing ACL reconstructive surgery.

DATA SOURCES: Two randomized control trials (RCTs) and one prospective randomized study were found using PubMed, NCBI, and Cochrane databases. All articles were published in reviewed journals and selected based on correlation to topic choice, date of publication, and evaluation of POEMs.

OUTCOMES MEASURED: Subjective IKDC (International Knee Documentation Committee) Functional Knee Evaluation scoring system was used. It is a subjective scale questionnaire that produces an overall function score by assessing 3 categories: symptoms, sports activity, and knee function.

RESULTS: All three studies found no statistically significant difference in post-ACLR functioning and activity level when considering the Subjective IKDC scores for allograft versus autograft tendons. The study by Sun et al. showed no significant differences between the irradiated, fresh-frozen hamstring allograft and hamstring autograft groups ($p=0.208$) according to the subjective IKDC scores. Tian et al. concluded that patients receiving the fresh-frozen hamstring allograft showed no significant difference in subjective IKDC scores compared to the hamstring tendon autograft group ($p=0.633$). Lawhorn et al. also found no statistical differences between the mean IKDC subjective scores of the fresh-frozen anterior tibialis allograft group and the hamstring autograft group ($p>0.05$).

CONCLUSION: All three studies found no statistically significant differences in the subjective measures of knee stability and function when using an allograft versus an autograft tendon; however, further research is warranted as the studies noted limitations of their methods, and some acknowledged functional differences between the graft types when considering non-POEM results.

KEY WORDS: autograft, allograft, ACL reconstruction

INTRODUCTION

The anterior cruciate ligament (ACL) is a ligament in the knee that connects the posterior aspect of the lateral femoral condyle to the anterior aspect of the tibia. It keeps the tibia from shifting anteriorly during movement and provides rotational stability.[1] It is one of the most frequently injured ligaments with more than 120,000 cases occurring each year.[2] In the US, ACL reconstruction (ACLR) is considered one of the most common arthroscopic procedures with an estimated 200,000 surgeries each year.[3] Knee injuries, specifically ACL tears, are some of the most expensive sports injuries, as the patient often requires surgical reconstruction and post-operative rehabilitation to return to previous levels of functioning. One conservative cost estimate puts the cost of a single ACLR plus rehab between $17,000-$25,000, and the annual health care cost of ACL injuries exceeds $1.7 billion.[2]

Although surgical repair of ACLs is effective, it is continuing to undergo revision. Currently, surgical reconstruction is the most effective method at treating a torn ACL. The most commonly used options are allografts and hamstring, anterior tibialis, and patellar tendon autografts. Current non-operative treatment options include physical therapy focusing on hamstring strengthening and core stability, aquatic therapy, and bracing. These methods are typically reserved for the elderly and more sedentary population. All methods of treatment are proposed due to their success in regaining knee function.

The future of ACL reconstruction involves use of the quadriceps tendon autograft, stem cells, and tissue engineering. Most of the current research is focused on ACL prevention, as the mechanism of injury is multi-faceted. It is not yet well-understood how to completely and most effectively prevent ACL tears, especially in the populations at greatest risk for ACL injury which includes females and competitive athletes.[4] Injury prevention and reconstruction are so important

because ACL injuries can affect a person or athlete's career, performance, and life. Not only does an ACL injury increase a patient's risk of re-injury, but it also increases a patient's risk of developing osteoarthritis or chronic joint pain 10 to 20 years after the injury. Osteoarthritis occurs in about 50% of patients with ACL or meniscal damage.[5]

All of the options discussed in this paper, operative and non-operative, have a place in the rehabilitation of a patient and have good outcomes; however, as with all medicine, it is important to discern which treatment is the most effective for the populations being served. In the case of this paper, are allografts or autografts more effective when considering ACL surgical reconstruction? This paper evaluates two randomized control trials (RCTs) and one prospective randomized study that compare the efficacy of using different allograft tendons with hamstring autografts.

OBJECTIVE

The objective of this EBM review is to determine whether or not "Is the use of a fresh-frozen allograft more effective than a hamstring autograft in preserving functional knee ability post-surgery in ACL reconstruction?"

METHODS

The two RCTs and one prospective randomized study evaluated in this paper were published in peer-reviewed articles, written in English, and found on the PubMed, NCBI, and Cochrane databases. The keywords used in the searches were "autograft versus allograft" and "ACL reconstruction." The articles were selected based on whether the outcome was a patient oriented outcome (POEM) and satisfied the objective. The inclusion criteria required randomized, controlled studies published in the last ten years. Exclusion criteria included studies

that did not focus on ACLR involving allograft or hamstring tendon autograft reconstruction and only considered disease oriented evidence. Reported statistics include the p-value for each study.

The population includes males and females between the ages of 16 and 56 that injured their ACL and chose to undergo ACLR. The experimental intervention was non-irradiated, fresh-frozen or irradiated, fresh-frozen allograft. Studies varied in which tendon was used as the allograft. Sun et al. utilized an irradiated, fresh-frozen hamstring tendon allograft, while Lawhorn et al. utilized a fresh-frozen anterior tibialis tendon allograft and Tian et al. utilized a fresh-frozen hamstring allograft.[6,7,8] The control group in all three studies utilized hamstring tendon autografts.[6,7,8] The outcome evaluated in all three studies was functional knee ability demonstrated by the Subjective IKDC Functional Knee Evaluation score.

Table 1. Demographics and characteristics of included studies.

Study	Type	# Pts	Age (yrs)	Inclusion criteria	Exclusion criteria	W/D	Interventions
Lawhorn[6] (2012)	RCT	102	16.4-53.4 yo	Unilateral isolated ACL tear with a contralateral normal knee extension and flexion within 5° of the opposite knee before surgery and within 12 months of surgery; agree to be randomized	Unable to complete follow-up at 4 months, 1 and 2 years; Previous reconstruction of either knee; other injury in injured knee; DJD; Known metabolic bone, neoplastic, or collagen disease, or fracture	45	Arthroscopic ACLR surgery (hamstring tendon autograft versus fresh-frozen anterior tibialis allograft) and standardized aggressive postoperative rehabilitation protocol for both groups.
Sun[7] (2011)	Prospective randomized comparative study	67	18-54 yo	None specified; only primary unilateral reconstructions of ACL were included	Previous injury or surgery on affected knee; Multiple ligamentous injuries; Unable to complete protocol; ACLR or injury of other knee	11	ACLR (hamstring tendon autograft versus irradiated hamstring allograft) performed by the same surgeon. Pre/postoperative rehab was the same for both groups.

Tian[8] (2016)	RCT	121	18-56 yo	No previous injury, arthritic changes, or surgery on the affected knee; No multiple ligamentous injuries; No malalignment; Not a revision reconstruction; Not lacking ability to complete the study protocol	Patients with associated injuries of the posteriolateral corner; Deficiencies or a reconstruction of the ACL in the opposite knee; Tibial footprint site less than 14 mm; Notch width less than 12 mm	36	Arthroscopic ACLR surgery (hamstring tendon autograft versus fresh-frozen, non-irradiated hamstring allograft) performed by the same surgeon. Pre- and postoperative rehab was the same for both groups.

OUTCOMES MEASURED

The primary outcome measured in all three studies was the Subjective IKDC (International Knee Documentation Committee) score, a part of the IKDC Functional Knee Evaluation scoring system. Each patient answers a subjective scale questionnaire that produces an overall function score by assessing 3 categories: symptoms, sports activity, and knee function. The scores are added together and transformed into a scaled number from 0 to 100. Higher scores correlate with higher levels of function. The articles reported the score in terms of mean total subjective score for the control and experimental group. Tian et al. and Sun et al. reported their scores as mean +/- SD (range) while Lawhorn et al. only reported the mean score for the groups.[7,8,9] Other outcomes measured in the studies were intraoperative and radiographic findings, graft failure rate, rotational stability, anterior stability and laxity measured by pivot-shift and Lachman tests, and preoperative and postoperative stability according to the KT-2000 Arthrometer. These are important aspects to consider when determining superior graft type; however, they are not all POEMs and therefore are not considered in this paper when forming a conclusion.

RESULTS

The study by Lawhorn et al. selected patients 16.4 to 53.4 years old who had a unilateral isolated ACL tear within the past 12 months and agreed to participate in the trial concerning fresh-frozen anterior tibialis allograft and hamstring tendon autograft.[6] Of the original 147 participants, 45 people withdrew from the study because they failed to follow-up leaving only 102 to be evaluated (54 autograft, 48 allograft).[6] The study was not fully blinded; the patients underwent arthroscopic standardized ACL reconstruction surgery and did not know their graft type until after surgery, while the 5 surgeons were made aware of the graft type for each patient.[6] All patients were randomly allocated to groups which allowed the groups to be the same in all respects except graft type. All patients underwent a standardized, aggressive, post-operative rehabilitation protocol involving full weight bearing without a brace, early extension, and open and closed chain exercises. The surgeons evaluated the patients at 4 months, 1 year, and 2 years post-operation with a minimum of 2 years follow-up.[6] The mean subjective IKDC score was 91.0 for the autograft group and 90.9 for the allograft group ($p>0.05$), yielding clinically insignificant differences in knee stability and return to function per the patients' subjective scores on the questionnaire.[6]

Sun et al.'s prospective randomized clinical study followed 67 patients (36 autograft, 31 allograft) ranging from 18 to 54 years old who had a unilateral ACL injury, with no prior injury to that knee, requiring reconstruction.[7] The study compared irradiated, fresh-frozen hamstring allografts and hamstring tendon autografts. Of the original 78 patients, 11 people were lost due to problems on day of surgery (ie. undiagnosed PCL injury) and lack of follow-up. They compared irradiated (2.5 Mrads) hamstring tendon allograft to hamstring tendon autograft. This was not a fully blinded study as the senior surgeon informed the patients after surgical reconstruction of the type of surgery they had and their graft type.[7] All patients underwent the same operative

procedure by the same surgeon using the same technique, pre- and post-surgical rehabilitation with the same protocol, and follow-up was conducted at the 1st, 3rd, 6th, 9th, and 12th months, and yearly after.[7] There was no statistically significant difference between the 2 groups or in post-operative activity levels and functioning, as seen in Table 2 ($p>0.05$).

Table 2. Subjective Evaluation and Activity Level Scores at Final Follow-up.

	Auto	Allo	P- value
Lawhorn et al.	91	90.9	>0.05
Sun et al.	87±10 (66-100)	83±10 (58-100)	0.208
Tian et al.	90±11 (65-100)	89±12 (60-100)	0.633

*Some data given as mean +/- SD range. There were no statistically significant differences between the groups.

Tian et al.'s RCT evaluated patients 18 to 56 years old who had not sustained a prior injury to the same knee and were volunteering to receive unilateral ACLR. They compared non-irradiated, fresh-frozen hamstring tendon allograft and hamstring tendon autograft.[8] The study originally involved 157 patients, but 36 were lost due to exclusion at time of surgery due to anatomical differences in tibial insertion site and loss at follow-up. The study included 121 patients (62 autograft, 59 allograft) and surgery took place in China at Qingdao University.[8] From January 2010 to December 2011, patients underwent ACLR by the same senior arthroscopic surgeon and with the same surgical approach. The senior surgeon disclosed the type of surgery the patient had and their graft type to each patient after the ALCR procedure, failing to make this a blinded study.[8] All patients underwent rehabilitation with the same protocol, including pre- and post-surgical rehabilitation. Pre-surgical rehabilitation was focused on reducing swelling by gaining full range of motion (ROM) and normal gait. Post-surgical rehabilitation was focused on achieving full extension/ROM, strengthening the surrounding musculature, and stability.[8] Follow-up was conducted after surgery during the 2nd week, 1st, 3rd,

6th, 9th, and 12th month, and yearly after. Subjective evaluation included the scores from the IKDC subjective knee form. There was no statistically significant difference between the 2 groups in the IKDC score or subjectively reported post-operative activity levels, as seen in Table 2 ($p>0.05$).

All three studies agree that scores recorded through the Subjective IKDC evaluation show no significant difference between the two graft types in terms of patient perception of swelling, activity level, and knee function. The three studies all involved continuous data that was not able to be converted to dichotomous data. This made it impossible to determine treatment effects in terms of numbers needed to treat (NNT). Unfortunately, all three studies only provided the subjective evaluations at the final follow-up, so determining a mean change from baseline was impossible without a pre-procedure subjective evaluation score.[6,7,8] The significance of results can only be reported through the mean Subjective IKDC scores for each group and their associated p-value, seen in Table 2. Although we can still draw conclusions from this information, it would be more beneficial in future studies to include other values that could be used to determine treatment effects as well. The results of this review show that although no significant difference was found between the different grafts, that information itself has useful meaning and clarifies that patients will have a good chance at regaining functional knee capacity regardless of the graft type they choose.

DISCUSSION

All three studies showed no significant differences in use of allograft compared to autograft when considering Subjective IKDC Knee Evaluation scores as seen Table 2.[6,7,8] Although all studies concluded that subjective evaluation of patient stability, swelling, stiffness, pain, sports activity performance, and knee function were comparable between the two groups in

these three studies, there is still some debate in the academic world concerning which is the better graft type. This debate is largely due to objective outcomes that may differ between the two graft types. Sun et al. was the only study to state there is a difference in functional ability when comparing the two grafts due to differences in laxity measurements. The data used to make the conclusion that allografts were inferior to autografts was made when also considering objective outcomes and measurements (non-POEMs) and thus can't be considered in this review.

Sun et al. found no significant difference when comparing the grafts in terms of subjective assessment, but did note significant differences in the two groups regarding knee laxity (a non-POEM), which was worse in the irradiated allograft group.[7]Although this information is considered irrelevant in this review as it is a non-patient oriented outcome, it is important to note that any difference in terms of individual subjective scores among participants could potentially also be due to the use of irradiation. Irradiation at 2.5 mrads was used to sterilize the allografts used in this study as opposed to the fresh-frozen, non-irradiated allografts used in Lawhorn et al. and Tian et al.[6,7,8] It has been shown that irradiation and chemical treatments can have negative effects on the tissue, thus causing lesser clinical outcomes than autografts, so this should also be considered when comparing the studies and developing a conclusion regardless of considering subjective or objective results.[9]

The results of Sun et al. are different from Lawhorn et al. and Tian et al. Both concluded that subjective, as well as functional and stability outcomes, were high in both groups with no statistically significant difference and concluded that the fresh-frozen allograft and hamstring autograft had similar stability and functional outcomes at the 2 year follow-up.[6,8] Lawhorn et al. also noted some shortcomings in their methods: considerable non-participation rate, some

incomplete data with lack of radiographs at latest follow-up, and unequal matching in groups due to less females in the allograft group.[6]

Each study acknowledges limitations that could have affected the generalizability, significance, and legitimacy of their results. Sun et al. proposes that the differences in their results could be due to loss of patients during the follow-up period contributing to a small sample size.[7] Tian et al. also recognized a similar limitation in small group size even though there were no differences in results.[8] Another limitation both studies mentioned is observer bias because the information was collected by only one surgeon at one institution and was not collected in a blinded fashion.[7,8]

Another limitation is the lack of ability to maintain perfect consistency or quality in post-surgery rehabilitation in all three studies. This could have affected how the patients performed, or in the case of subjective reporting, perceived their rehabilitation and knee function. Even though the rehabilitation protocol was standardized and prescribed for both groups, a slight difference in the patient's effort during exercises or lack of perfect consistency due to treatment at different facilities could produce significant changes. It is very difficult to achieve perfect equality in terms of rehabilitation technique which can affect both subjective and measured outcomes. Although this is representative of real life, it does affect the ability to determine if the graft itself is superior or inferior or if it is due to the motivation and adherence of the participant. Also of note, hamstring tendons were the only autograft graft choice utilized in all three studies.[6,7,8] Patellar tendon autografts are also largely utilized and may have provided different results if examined.

Although it is important for studies to have heterogeneous groups to increase the generalizability of their results and appeal to the medical idea of utilitarianism, results may not

be accurate when considering females or more athletic populations. In the case of ACLR, the medical community would benefit from more precise studies including only female or younger athlete populations, as these are the groups most commonly affected by this injury. A recently published review article by Brown and Carter looks at the ongoing debate concerning autografts and allografts and notes that a definitive consensus has yet to be reached in the academic community.[9] Their review of literature did note that although the two graft types appeared equal in age-matched populations, the results showed that allografts were less desirable in younger populations (less than 25 years old) due to higher failure rates; however, other evidence shows that this can be negated if grafts are processed properly and rehabilitation is slower and less aggressive. This would be a good area to investigate in much needed future research.[9]

CONCLUSION

Based on the two RCTs and one prospective randomized study reviewed, all three studies agree that there is no statistically significant difference between the allograft and autograft tendons considered for ACLR when considering results of the Subjective IKDC score, making them both equally suitable choices for ACLR in terms of knee function.

Future studies are needed to determine a stronger conclusion on which graft is more effective for both subjective and objective functional outcomes. Although allograft and autograft subjective outcomes seem overwhelmingly equal, the functional outcome results are more debatable. This is largely due to small group size and lack of separating groups based on sex, age, and activity level. Females and competitive athletes are the most commonly affected populations, and their perception of return to normal functioning is very different than more sedentary people undergoing ACLR to resume minor daily activities. Future studies should separate these groups more exclusively, as Brown and Carter started to explain.[9] Although this

would decrease the generalizability of the results, it would more precisely provide relief to the populations that are continuing to injure and re-injure themselves with current protocol. This may allow for more appropriate results that can then be applied to the field of ACL prevention and reconstruction, which has thus far been less successful than hoped.

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