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Meta-Analysis

Current status of graft choice in adults for anterior cruciate ligament reconstruction: a systematic review and meta-analysis

Mahantesh Magadum[1]*, Joshua Smith[2], Karl J. New[3]

[1]Department of Orthopedics Surgery, Meenakshi Medical College Hospital and Research Institute, Kanchipuram, Tamil Nadu, India
[2]High Performance Manager, AmaZulu Football Club, South Africa
[3]Faculty of Life Science and Education, University of South Wales, CF371DL, United Kingdom

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***Correspondence:**
Dr. Mahantesh Magadum,
E-mail: mahanteshmagadum@yahoo.co.in

ABSTRACT

The anterior cruciate ligament (ACL) is a frequently performed surgical procedure in the field of sports medicine, and graft selection is an essential aspect of ACL reconstruction (ACLR) that has been shown to optimize post-operative rehabilitation, facilitate return to full sporting function and reduce the risk of complications. However, there needs to be more agreement regarding optimal graft choice. The present study aims to identify the optimal graft choice in the adult population undergoing ACLR. The current systematic review explores the electronic database of online libraries of academic institutions from 2011 to 30 September 2022 and compared the clinical outcomes of autograft and allograft for ACLR, which provides an evidence-based approach for graft selection. The findings of our present study delineate that ACLR in adult populations with autograft is the most promising choice for ligament tear over allograft based on lower failure rate, reduced complications, and high cost-effectiveness. However, there was no significant difference in overall IKDC, pivot shift, Lachman test, and Tegner activity. This critical analysis recommends that for an adult population, ACLR with autograft can provide better clinical results than an allograft, but further studies carried out about other parameters affecting the long-term stability, quick return, and physical therapy adopted outside the supervision of the respective surgeon would be required.

Keywords: ACLR, Autograft, Allograft, Randomized clinical trials, Adults

INTRODUCTION

The anterior cruciate ligament (ACL) is a crucial knee stabilizer that prevents the forward movement of the tibia over the femur and maintains rotational stability by restricting internal rotation of the tibia.[1] ACL tear is the frequent type of injury ranging from 11% to 33% of active young people and further leads to instability of the knee resulting in poor athletic performance.[2.] Studies indicate that the annual occurrence of ACL tear is 68.6 per 100,000 person-years. Furthermore, this rate is higher in males compared to females, with 81.7 cases per 100,000 for males and 55.3 cases per 100,000 for females.[3] Non-treatment of ACL tears prone to risk of early degenerative disorders and the conservative management is not effective, hence ACL reconstruction (ACLR) is gold standard surgical procedure for treating ACL tear.[4] A good understanding of biomechanics of native ACL is crucial when choosing ideal graft substitute for the reconstruction of ACL. Even though technique is carried out very frequently, there is lot of variation in ACL graft selected for ACLR, and the best option is still up for debate.

ACLR is usually performed using auto graft and it is the widely used strategy with good surgical outcome.[5] Patellar tendon (PT) and hamstring tendon (HT) autografts are

commonly utilized in clinical management. However, these grafts come with certain drawbacks, including donor site morbidity, postoperative morbidity, scarring, delayed graft incorporation, quadriceps weakness in PT autograft, and decreased HT strength.[6] Alternatively, treating ACLR employing allograft has gained popularity for two decades. Besides, allograft ACLR also faces challenges related to disease transmission, delayed graft incorporation, increased cost of the graft, and poor functional outcomes.[7] Therefore, both the interventions performed for ACLR possess some advantages and limitations. Considering the evidence gathered, orthopaedic surgeons still face a big dilemma when deciding which type of graft to use for ACLR. Therefore, implementing tools of critical analysis, present work emphasizes comparing clinical outcome from randomized clinical trials (RCTs) undergoing ACLR in the adult population using autograft or allograft from 2011 to 2022. In the present investigation, we aim to hypothesize that autograft is a favourable choice of graft for ACLR with min complications, failure rates, and cost-effectiveness.

METHODS

Study selection

The present investigation by one author searched the electronic database: online library of academic institution and PubMed. The search strategy includes all the RCTs carried out in adults (Aged 18 years or more) with symptomatic ACL deficiency, confirmed by magnetic resonance imaging (MRI) that compared allograft with autograft from 2011 to September 2022. The keywords that were applied to search through the databases consisted of (“ACL reconstruction OR ACL reconstruction" AND (“Randomized clinical trials” “autograft" OR “allograft” OR “clinical outcome(s)" OR “cost-effectiveness” OR “graft choice” OR “ACLR complications” to identify all studies about these criteria. The full text of the potential studies included in the review was thoroughly screened.

Eligibility criteria

The author independently screened all the articles using this review’s inclusion and exclusion criteria. Studies were included in the meta-analysis satisfying the following criteria: (1) All the RCTs with adult patients undergoing primary ACLR (2) All the RCTs with ACLR compared with allograft and autograft (3) All RCTs with the usage of any allograft or autograft and (4) The RCTs with ACLR comparing the allograft with autograft indicating one of the functional knee (e.g., International knee documentation committee level, (IKDC), pivot shift test, Lachman test) whereas studies including (1) Published articles below the year 2010 (2) The patients with revision ACLR and (3) Patients below the eighteen years were excluded.

Data collection and analysis

Information was collected from all relevant studies, including details on study design, sample size, patient ages, follow-up duration, surgical technique, graft type, rehabilitation protocols, Lachman testing, pivot-shift testing, IKDC scores, Tegner scores, complications, and failure rates. The obtained data were compared, and any inconsistencies were resolved through consensus.

Assessment of methodological quality

As per the guidelines of the Cochrane Collaboration, the reviewers evaluated the methodological quality of the trials included in the study using a specific tool to determine the risk of bias. A "risk of bias" table consists of a summary and assessment for each component, with each entry specifically addressing a different aspect of the research. Each item was assessed by answering a question, resulting in a score of "low" indicating a low likelihood of bias, "high" indicating a high likelihood of bias, and "unclear" indicating either a lack of knowledge or uncertainty about the potential for bias (Table 1).[21]

Table 1: Risk of assessment of included randomized studies.

Study	Random sequence generator	Allocation concealment	Blinding of outcome	Incomplete data outcome	Free of selective reporting	Other bias
Noh et al[8]	Unclear	Unclear	Unclear	High risk	Low risk	Low risk
Sun et al[9]	Low risk	Low risk	High	Low	Low	Low
Lawhorn et al[10]	Low	Low	High	High	Low	Low
Bi et al[11]	Low	Unclear	High	Unclear	Low	Low
Bottoni et al[12]	Low	Unclear	Low	Low	Low	Low
Jia et al[13]	Low	Low	Unclear	Low	High	Low
Li et al[14]	Unclear	Unclear	Low	Low	Low	Low
Sun et al[16]	Unclear	Low	Low	Low	Low	Low
Yoo et al[15]	Low	Unclear	Unclear	Low	Low	Low

Statistical analysis

MedCalc software was utilized to generate statistical calculations and forest plots. A p value less than 0.05 were considered as statistically significant. The I2 statistics were used to assess the presence of heterogeneity among studies, and were classified as low, moderate, or high heterogeneity based on Thompson's definition.

RESULTS

Study search

Figure 1 provides a concise overview of the study selection process, spanning from 2011 to September 2022. A total of 113 records were found through our searches. A total of ninety-six citations were excluded due to duplication or failure to meet the qualifying requirements. Following a comprehensive examination and confirmation of the remaining 17 publications, 12 research were selected and included in the analysis.

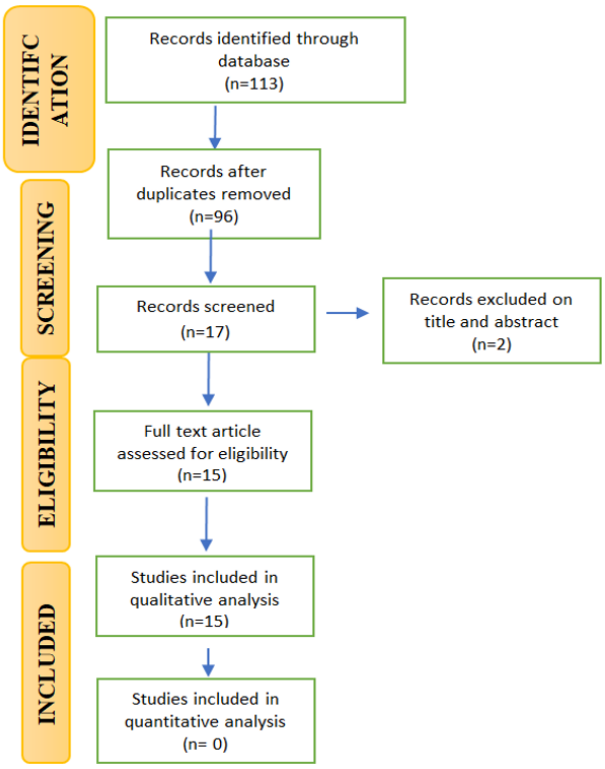


Figure 1: Flow chart.

Study characteristics

Table 1 and 2 display the study characteristics and methodological features of the included research, respectively. The publication dates of these papers range from 2011 to 2022. The sample sizes varied from 64 to 424, with patients being randomized at random to either the autograft group (n = 518) or the allograft group (n = 475). The average age of participants in the studies ranged from 18 to 56 years. Furthermore, the average duration of follow-up was four years. Both the autograft and allograft groups employed comparable surgical techniques and fastening procedures in every study.

Clinical outcomes

In this review, the RCTs with consistent results were included for comparing the choice of graft in ACLR for the adult population. The meta-analysis of the nine individual clinical outcomes demonstrated that incorporating allograft or autograft during ACLR failed to significantly alter parameters such as overall International Knee Documentation Committee (IKDC), pivot shift, Lachman test, and Tegner activity (Table 3-6). Furthermore, the patients of both groups reported nearly normal to ordinary IKDC scores, revealing equal effectiveness of both grafts at the end of the respective follow-up duration. On the contrary, the positive pivot shit test and positive Lachman test having 2+ or higher scores are shown by more patients in the allograft group. However, the study failed to reach a statistically significant level. Furthermore, Tegner's activity score was also found to be non-significant in both the intervention group.

Meta-analysis

For the meta-analysis of clinical outcomes between autograft and allograft groups, nine studies were considered.[8-16] The RCTs evidenced the Tegner activity scale score, the IKDC subjective knee form score, the Lachman score, and the Pivot shift score test preoperatively and at the last follow-up. The following illustrates the well-established knee metrics.

Overall IKDC

All studies comparing autograft and allograft reported overall IKDC data.[8-16] Out of recruited 993 patients, 502 (96.92 %) patients of the autograft group (n=518) and 445 (93.68%) of the allograft (n=475) were respectively reported IKDC scores normal to the nearly average end of the follow-up period. The follow-up period ranges from 2 to 10 years in the included studies. There was no significant difference in the overall IKDC score between the autograft and allograft groups (χ^2=5.67607, p=0.0172, 95% CI=74.66 to 95.27, I^2=0.00%). Moreover, there was no significant difference (OR=1.0325, 95% CI=0.8639 to 1.2339, p=0.7255, Table 3).

Pivot shift test

Five out of the nine studies reported the pivot shift (2+ or more significant) test data.[8-10,14,15] In the autograft group (n=223), four patients (1.79%), whereas in the allograft group (n=223), 11 patients (4.9%) recorded their pivot shift score (2+ or higher). No heterogeneity was detected when the data from the five studies were pooled (χ^2=3.1611, p=0.612, I^2=0%). The overall result showed that the pivot shift test (2+ or higher) was significantly more evident in the allograft group than in the autograft group for 5 of these studies (OR 0.3636, 95% CI=0.847 to 6.464, p=0.0872, Table 4).

Lachman test

Four studies reported Lachman test data. High heterogeneity was detected when the data from the four studies were pooled (χ^2=4.205 p=0.2401, I^2=84.2%).[8,9,14,15] The result showed that the Lachman test was significantly more in the allograft group than in autograft group (OR 0.4654, 95% CI: 0.3346 to 1.6497, p=0.0003, Table 5).

Table 2: General characteristics of studies included in the analysis.

Source	Study design	Level of evidence	Sample size	Sex	Age range (In years)	Intervention		N (auto/ allo)	Follow up Month (range)
						Autograft	Allograft		
Noh et al[8]	Prospective randomized	I	65	56 M 9 F	20-55	HT	FTA	33/32	29.8 (NR)
Sun et al[9]	Prospective randomized	II	67	52 M 15 F	18-54	HT	HT	36/31	42.2 (30-56)
Lawhorn et al[10]	Prospective randomized	II	102	70 M 32 F	16-53	HT	TPT	54/48	24 (NR)
Bi et al[11]	Prospective randomized	NR	86	60 M 26 F	22-56	HT	LET	41/38	39.6 (Autograft) 37.4 (Allograft)
Bottoni et al[12]	Prospective randomized	I	97	NR	20-42	HT	TPT	48/49	120 (120-132)
Jia et al[13]	Prospective randomized	NR	106	54 M 52 F	18-51	HT	BPTB	53/53	81 (28-86)
Li et al[14]	Prospective randomized	II	64	32 M 32 F	28-35	HT	TPT	32/32	60 (NR)
Sun et al[16]	Prospective randomized	I	282	200 M 82 F	19-52	HT	TAT	154/128	36 (NR)
Yoo et al[15]	Prospective randomized	I	132	120 M 12 F	13-52	HT	TT	68/64	24

BPTB: Bone patellar tendon bone, F: Female, FTA: Free tendon Achiles, HT: Hamstring tendon, LET: Lower extremity tendon, M: Male, NR: Not reported, TAT: Tibialis anterior tendon, TPT: Tibialis posterior tendon, TT: Tibialis tendon.

Table 3: OR analysis and forest plot for overall IKDC value.

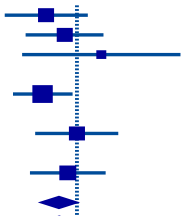
Study	Autograft		Allograft		Weight (%)	OR fixed	OR (M-H, random 95% Cl)
	Events	Total	Events	Total			
Noh et al[8]	30	33	26	32	15.22	0.289 (0.0536 to 1.557)	
Sun et al[9]	33	36	27	31	17.28	0.614 (0.126 to 2.982)	
Lawhorn et al[10]	53	54	48	48	4.15	2.720 (0.108 to 68.352)	
Bi et al[11]	41	41	38	38	-	Not estimate	
Bottoni et al[12]	44	48	36	49	29.79	0.252 (0.0755 to 0.839)	
Jia et al[13]	53	53	53	53	-	not estimate	
Li et al[14]	29	32	29	32	15.28	1.000 (0.186 to 5.371)	
Sun et al[16]	154	154	128	128	-	Not estimate	
Yoo et al[15]	128	68	60	64	18.27	0.692 (0.149 to 3.221)	
Subtotal (95 % Cl)		518		475			
Total events	502		445		100	0.486 (0.259 to 0.912)	
Heterogeneity: I^2=0.00 %; Chi^2 =0.138598; df=5; p=0.6078							
Test for overall effect: Z=0.372 (p=0.7097)							

Table 4: OR analysis and forest plot for pivot shift test.

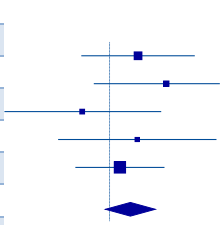
Study	Autograft		Allograft		Weight (%)	OR fixed	OR (M-H, random 95% Cl)
	Events	Total	Events	Total			
Noh et al[8]	1	33	3	32	23.47	3.310 (0.326 to 33.629)	
Sun et al[9]	0	36	4	31	14.39	11.945 (0.617 to 231.31)	
Lawhorn et al[10]	1	54	0	48	12.14	0.401 (0.0159 to 10.083)	
Li et al[14]	0	32	1	32	12.02	3.095 (0.121 to 78.872)	
Yoo et al[15]	2	68	3	64	37.98	1.623 (0.262 to 10.044)	
Subtotal (95% Cl)		223		203		0.3636 (0.929 to 7.112)	
Total events	4		11		100		
Heterogeneity: I^2 =0.00 %; Chi^2=3.82574; df=4; p=0.6249							
Test for overall effect: Z=1.868 (0.1038 to 1.0560)							

Table 5: OR analysis and forest plot for Lachman test.

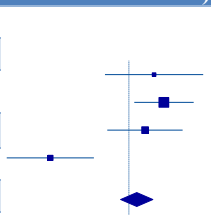
Study	Autograft		Allograft		Weight (%)	OR fixed	Odd ratio (M-H, random 95% CI)
	Events	Total	Events	Total			
Noh et al[8]	1	33	3	32	14.89	3.310 (0.326 to 33.629)	
Sun et al[9]	3	36	10	31	40.74	5.238 (1.290 to 21.272)	
Li et al[14]	2	32	4	32	25.43	2.143 (0.364 to 12.629)	
Yoo et al[15]	4	68	6	64	18.94	0.0246 (0.00315 to 0.192)	
Subtotal (95% Cl)		107		159		1.455 (0.680 to 3.113)	
Total events	10		20		100		
Heterogeneity: I^2=84.22 %; Chi^2 = 0.535766; df = 3; p=0.0003							
Test for overall effect: Z=0.730 (0.3346 to 1.6497)							

Table 6: Tegner score between two interventions (median, range).

Study	Intervention		P value
	Autograft	Allograft	
Noh et al[8]	6 (5-9)	6 (4-9)	>0.05
Sun et al[9]	7.6 (3-9)	7.0 (2-9)	-
Bottoni et al[12]	5.1 (NR)	5.1 (NR)	-
Li et al[14]	7.3 (NR)	7.0 (NR)	>0.05
Yoo et al[15]	5 (2-9)	5 (3-8)	>0.05

Tegner score

The study included five papers that published the Tegner score, including the median and range.[8,9,12,14,15] Nevertheless, the scope encompassed in the particular study varied. No statistically significant difference was found between the two intervention groups, as determined by a student t test followed by a Mann Whitney test. The test result was not statistically significant (p>0.05) (Table 6).

Failure rates

Two studies reported the clinical failure, although the studies had varying definitions of failure.[12,15] Patients who reported failure were 22 among the overall population comparing autograft and allograft. Out of which, 7 (31.81%) patients belong to autograft, and 15 were from allograft (68.18 %) (Figure 2).

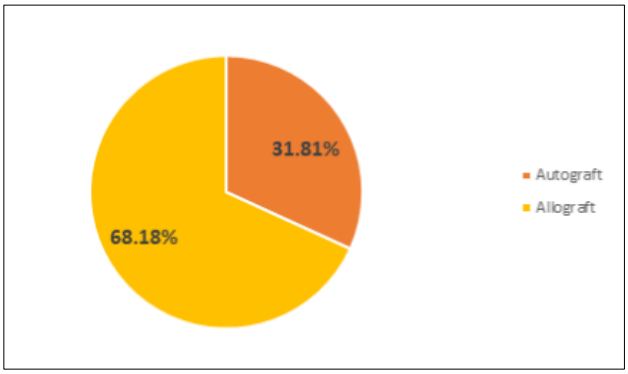


Figure 2: Percentage of cases showing failure rates in the autograft and allograft group.

Complications

Post-operative rehabilitation is essential for maximizing outcomes. 3 out of 12 studies included in the meta-analysis and systematic review reported the complications (Table 7).[9,13,15]

Table 7: Studies showing complications reported at the end of the follow-up period.

Study	Complications
Sun et al[9]	Tenderness or irritation at the graft harvest site (Autograft).
	Hypoesthesia of the medial saphenous nerve territory (Autograft).
Jia et al[13]	Tunnel widening to be significantly less (Autograft).
Yoo et al[15]	Revision (1 Allograft; 1 Autograft)
	+3 or higher Lachman (2 Allograft; 1 Autograft)
	+3 or higher pivot shift (0 Allograft; 2 Autograft)
	Infection (2 Allograft; 0 Autograft)
	Sensory nerve injury (4 Allograft; 3 Autograft)

Cost-effectiveness

The present work demonstrates three studies that directly compare the costs associated with autograft and allograft ACLR (Table 8). The studies in this analysis demonstrated that ACLR using allograft tissue is a costlier procedure than autograft. Three economic evaluations were identified and procured through the abstract screening process.

Of the three cost-comparisons favouring autografts, one of the studies measured a total mean cost of $3,154±704 for an autograft versus $4,147±943 for an allograft. Another two studies involve a cost of $5,375/surgery and supply costs for allograft cases of $1,392 respectively.[17-19]

Table 8: Cost comparison between allograft and autograft ACLR.

Study	Cost		OR time		P value
	Autograft (USD)	Allograft (USD)	Autograft (min)	Allograft (min)	
Oro et al[17]	3154±704	4147±943	91±23	83±32	<0.001
Genuario et al[18]	4072	5195	NR	NR	NR
Greis et al[19]	3848.81±695	4587.27±463	125±21	92±21	<0.001

DISCUSSION

This systematic review aimed to optimize the choice of graft for ACL in the adult population based on clinical outcomes. The review of individual clinical outcomes included in the present study demonstrated that incorporation of either allograft or autograft during ACLR failed to significantly alter any of the parameters such as overall IKDC, pivot shift, Lachman test, and Tegner activity. Moreover, allografts were associated with a higher risk of graft failure than the autograft group. Despite no differences in knee stability and function between the two groups, the allograft group is sensitive to the risk of graft failure. This sensitivity might be attributed to the allograft preparation method, which further affects the structural and mechanical properties. Therefore, graft choices must be made depending on the diagnosis and factors influencing long-term stability, like the patient's age, weight, and level of physical activity.

Many studies project the clinical results between autografts and allografts used for ACLR. Clinical reports have concluded no significant difference between the autograft and allograft groups based on functional, subjective evaluations and activity level testing.[8-16] The clinical outcomes in several earlier comparison studies have shown allograft to be a viable alternative to autograft tissue.[20,21] The main benefit of allograft tissue is the absence of complications at the donor site, reduced surgical duration, enhanced aesthetic outcome, availability of many transplant alternatives and sizes, and decreased overall expenses.[22] In addition to the reported benefits, it is important to highlight the drawbacks of allograft, including the possibility of disease transfer, delayed integration, and potential reduction in graft strength and stiffness depending on the processing method used.[23]

Moreover, graft failure that required revision reconstruction was also more frequent in the allograft group than in the autograft.[12,15,16] The multicentre orthopaedic outcomes network (MOON) study mainly studied failure rates of allografts as compared to autografts at two years follow-ups. They concluded that the two factors responsible for an increased failure rate of ACLR were patient age and graft type. The study concluded that there was an increased ruptured rate in allografts as compared to autograft used, and graft rupture rate increased for the average group; hence, they cautioned that allograft is not an ideal option for the younger population and allografts are more suitable for the older groups of patients.[24.] Bottoni et al reported that graft failure in the allograft group was three times higher than in the autograft group.[12] Another study, which compared double BPTB (dBPTB) allograft with four single hamstrings (SHS) grafts, showed fewer graft failures during three years follow-up period.[25]

Likewise, one of the studies demonstrated that the implementation of double-bundle ACLR resulted in superior anterior and rotational stability, as well as a reduced incidence of arthritic development and tunnel expansion compared to the single-bundle technique.[16] Furthermore, other than graft failure, complications related to either graft are also considered over the past decade. Consequently, there is ongoing debate on the most suitable graft material for ACL replacement. A study conducted on primary ACLR showed that the autograft group had a lower incidence of complications, such as tibial femoral widening.[13] Other complications, such as post-operative infection and sensory nerve injury, were also observed in the patients undergoing ACLR using a tibialis allograft.[15] In the clinical management of PT and HT, autograft remains the most common and traditional choice.[26] Nevertheless, it is linked to certain drawbacks, including pain in the front of the knee after surgery, negative effects on the donor site, weakened quadriceps in the case of PT autograft, reduced strength of the HT, delayed integration of the graft, and increased looseness in the joint when using HT autograft.[27,28] Considering the similar findings depicting the advantages and disadvantages of either graft, the choice of graft to be used in adults for primary ACLR is still a matter of investigation.

Tunnel widening is a problem that occurs during ACLR surgery due to biological and biomechanical factors. Jia and Sun reported significantly less tunnel widening in autograft reconstruction.[13] The phenomenon occurs due to biological and biomechanical variables, specifically the presence of synovial fluid with high levels of cytokines and inflammatory chemicals. This leads to the infiltration of inflammatory cells and enzymes into joint cavity.

In another study conducted by Sun et al no instances of early postoperative problems necessitating reoperation or readmission were recorded in either the autograft or irradiation allograft groups.[9] In addition, two patients in

the autograft group experienced hypoesthesia in the area of the medial saphenous nerve. Conversely, a different patient in the autograft group reported experiencing soreness or irritation at the place where the graft was taken. Nevertheless, none of these problems were incapacitating, but they necessitated the removal of the tibial screw in the irradiated allograft group due to persistent, localized discomfort, which was addressed following the surgical procedure.

Evaluation of the clinical results presented by Yoo et al unveiled that one patient in the HT autograft group and four patients in the tibialis allograft groups exhibited aberrant looseness exceeding grade 2.[15] Two patients in the tibialis allograft group suffered early post-operative infections and required antibiotic therapy, while four patients in the hamstring autograft group and two patients in the tibialis allograft group experienced sensory nerve injury.

In Genuario et al ACLR performed with allograft ($1,585/case additional to HS autograft) is the most expensive and least effective treatment option available.[18] The cost of HS autograft is the least expensive option but with the highest quality-adjusted life years (QALY) (0.912). Likewise in another study conducted by Greis et al the supply costs for allograft cases are higher, $1,392 as compared to autograft procedures which includes $556 only.[19] Our report is in corroboration with the study done by Cooper and Kaeding where the total mean hospital cost for ACLR is $4,072.02 for autograft and $5,195.19 for allograft.[29]

CONCLUSION

ACL tear can lead to repeated instances of knee instability, which can hinder an athlete's capacity to execute sports techniques and perhaps cause additional harm to the knee's cartilage and meniscus. Furthermore, the investigation of ACLR with autograft or allograft in adult patients is ongoing, as they are highly involved in sporting activities that can result in abrupt ligament damage. Hence, the choice between an allograft or autograft is predominantly influenced by the physician and patient's preferences, rather than the intrinsic advantages of the procedure. Thus, the results of the meta-analysis in the present study should be interpreted with caution.

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