No difference in postoperative efficacy and safety between autograft and allograft in anterior cruciate ligament reconstruction: a retrospective cohort study in 112 patients

Bin-An Zhao^{1#}, Yi-Yong Yao^{2#}, Qing-Xin Ji^{3#}, Zhen-Yu Li¹, Biao Cheng¹, Jian-Feng Pan¹

¹Department of Orthopedics, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai, China; ²Department of Orthopedics, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, Shanghai, China; ³Department of Pharmacy, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai, China

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[#]These authors contributed equally to this work.

Correspondence to: Jian-Feng Pan, Biao Cheng. Department of Orthopedics, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, 301 Yanchang Road, Shanghai 200072, China. Email: pansmith@163.com; drbiaocheng@163.com.

Background: Arthroscopic anterior cruciate ligament reconstruction (ACLR) is the best treatment choice for returning to pre-injury activities following ACL rupture. Although allografts are considered an effective alternative to autografts, there is still controversy regarding the safety and effectiveness of this procedure, especially concerning the risk of postoperative infection and disease transmission. The purpose of this study was to compare the efficacy outcomes and safety between allografts and autografts in primary ACLR.

Methods: The retrospective analysis involved 112 patients (58 patients received allogeneic tendons and 54 patients received autologous hamstring tendons) who underwent primary ACLR. All patients were followed up and evaluated on admission and at 1 week, 3 months, 6 months, and 1 year postoperatively. The efficacy outcome of the ACLR was evaluated by International Knee Documentation Committee (IKDC) score and physical examinations (Lachman test, anterior drawer test, and pivot shift test). The safety outcome of allografts and autografts was compared by investigating the occurrence of postoperative complications, including postoperative inflammation and potential disease transmission. The benefits of each operation for surgeons and patients were also analyzed, including the length of surgical incision and operative time.

Results: There was no significant difference in the demographic and clinical characteristics between the allograft and autograft groups. The two cohorts proved to be similar in terms of the acute or chronic nature of the cruciate ligament and the incidence of concomitant meniscal surgery. Arthroscopic ACLR was performed in all patients. The physical examinations were all positive before surgery and negative immediately after the operation. The KT-1000 and IKDC scores of two groups significantly decreased than pre-operative ones (P<0.05), but the difference between the two groups was not statistically significant (P>0.05). At final follow-up, all patients had returned to their pre-injury activities. Allografts showed no increased risk for postoperative infection or potential disease transmission relative to autografts.

Conclusions: The outcomes of reconstructed ACL with allografts were similar to those of autographs. Moreover, the safety of allografts showed to be comparable to that of autografts, especially concerning postoperative infection and disease transmission. Therefore, the surgical option should be chosen wisely according to the patient's condition.

Keywords: Anterior cruciate ligament (ACL); allograft; autograft; postoperative inflammation; disease transmission

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Introduction

The anterior cruciate ligament (ACL) is a dense band of tendon tissue that extends from the posteromedial aspect of the lateral femoral condyle to the anterior intercondylar area of the tibia (1). The ACL plays a role in preventing the anterior translation and internal rotation of the tibia, which controls excessive movement of the knee joint. The incidence of ACL rupture is 0.046% in Germany and 0.029% in America (2,3). Magnetic resonance imaging (MRI) and knee arthroscopy are used to make a definite diagnosis, and knee arthroscopy is considered the gold standard but is not commonly used in preliminary examination (3). After ACL injury, a very high prevalence of posttraumatic knee osteoarthritis (OA), life-long knee joint pain, and functional limitations is a reality for young and athletically active patients, which can severely impair quality of life (4). OA is a long-term complication of ACL rupture that is associated with chronic anteroposterior instability in the knee joint (5). Many studies have investigated OArelated biomarkers in ACL-deficient patients, and a systematic review found that elevated collagen turnover may be the most informative biomarker of OA following ACL injury (6,7). To restore the function and stability of the knee joint, resume sport activities, and minimize the risk of further cartilage damage and progression to OA, some patients choose to undergo ACL reconstruction (ACLR).

The surgical treatment for ACL rupture is arthroscopic ACLR using an allograft, hybrid graft, or autograft. For autograft, bone-patellar tendon-bone (B-PT-B) has long been the first choice, accounting for nearly 90% of primary ACLR s in 1992 (8). Over time, the use of hamstring tendon and quadriceps tendon has become more prevalent due to the low incidence of immediate postoperative pain and anterior knee pain compared to B-PT-B (9-12). For allograft, the grafts are obtained from tissue banks and frozen at -70 °C in a sterile environment until the surgery (13). Allograft is associated with some negative outcomes, including disease transmission (13), immune rejection (14), and a high risk of surgery failure (14). A hybrid graft combines allograft (tibialis posterior, tibialis anterior, gracilis tendon, or semitendinosus) with auto hamstring tendons to strengthen the autograft, resulting in a graft with a thicker diameter and a larger graft occupancy than that of autograft (15,16).

Orthopedists tend to prefer allograft in clinical practice, due to the lower relapse incidence, shorter operation time, and the availability of sufficient donor tissue to complete the allograft (17). Although allografts have the potential

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to transmit diseases, including hepatitis C virus (HCV), human immunodeficiency virus (HIV), *Clostridium*, *Neisseria meningitidis*, and *Streptococcus A* (18), improved donor screening and modern harvesting and sterilization techniques such as low temperature chemical sterilization, gamma irradiation, electron beam irradiation, and ethylene oxide have significantly minimized this risk (18-20). However, these methods are not without flaws; ethylene oxide has been related to poor biomechanical integrity and prognosis (18), and the use of gamma irradiation has been reduced in recent years in favor of antibiotic solutions (21).

Allografts have been used extensively in ACLR for decades. ACLR using allografts has several advantages over autografts, including the absence of donor site morbidity, shorter operation time, sufficient graft length and diameter, less hypoesthesia, and shorter recovery time (22-24). The operation time for allograft reconstruction is significantly shorter than that of autograft reconstruction, as there is no need for a second incision to obtain the autologous tendon tissue. When autografts are used in surgery, the length and diameter of the graft tissue varies due to individual differences and may be inadequate for ACLR. Allografts do not face this problem, as there are adequate amounts of patellar, Achilles, and tibialis tendon tissues in tissue banks. Once allografts undergo appropriate sterilization processes, the clinical outcome is comparable to that of autografts (25). Studies have shown that when irradiated grafts were excluded, autografts and allografts showed no significant difference in Lachman test, International Knee Documentation Committee (IKDC) score, and failure risk at short- and long-term follow-up (26,27). Even in revision ACLR, clinical outcomes are similar between autografts and allografts (28). Based on these advantages, allografts are becoming more prevalent in clinical practice. However, there are still concerns about the long-term function, clinical efficacy and safety of allografts compared to autologous tendons. Although many studies have been conducted to compare, the limitations of some of the previous studies have been overcome with the development of tissue repair techniques. Besides, few studies have focused on the potential for disease transmission and immune rejection with allografts. We sought to support the clinical use of allograft ligaments by retrospectively comparing the safety of autologous and allograft ligament reconstruction in terms of treatment outcomes and potential complications. We present the following article in accordance with the STROBE reporting checklist (available at https://atm. amegroups.com/article/view/10.21037/atm-22-1008/rc).

Methods

Inclusion and exclusion criteria

From June 2017 to January 2020, a total of 112 patients were diagnosed with primary ACL rupture in Shanghai Tenth People's Hospital. A retrospective study was conducted on these patients, of whom 58 underwent allograft reconstruction and 54 underwent autograft reconstruction. All patients were followed up for at least 1 year to evaluate the function and safety of allografts and autografts. The function and effectiveness of ACLR were evaluated by IKDC score and physical examinations (Lachman test, anterior drawer test, and pivot shift test). The safety of allografts and autografts was compared by investigating the occurrence of postoperative complications, including postoperative inflammation and potential disease transmission. The benefits of each operation for surgeons and patients were also evaluated, including the length of surgical incision and operative time.

The inclusion criteria were as follows: (I) patients aged between 18 to 60, including both ends of the scale; (II) the unilateral ACL was confirmed as completely torn under arthroscope examination; and (III) subjects were willing to participate in the study after fully understanding the benefits and risks and provided informed consent. The exclusion criteria were as follows: (I) patients who had undergone ipsilateral knee surgery; (II) patients with medial collateral ligament tear assessed at grade II and above or multiple ligament injuries in the knee; (III) patients with open knee joint injury combined with vascular injury, fracture, or other conditions; (IV) patients with an incomplete or bilateral ACL tear; (V) patients who were pregnant; (VI) patients with OA accessed at stage II and above; (VII) patients with severe psychosis.

This study was approved by the Institutional Ethics Committee of Shanghai Tenth People's Hospital (No. SHSY-IEC-4.0/18-11) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study participants provided written informed consent for participation and the use of their clinical data in this study.

Autograft surgery

After routine anesthesia, the leg was disinfected and covered with a tourniquet. The knee joint was examined by arthroscope through an anterolateral and anteromedial approach. The synovium was excised, and the ligament stump was reserved. A longitudinal incision of 3 cm was made in front of the tibia. The semitendinosus and gracilis tendon were harvested and then folded and weaved in 4 strands. One end of the ligament was braided while the other was attached to the endobutton. Next, the tibial tunnel was drilled and positioned at a 55° angle to the coronal plane. The femoral tunnel was drilled according to the femoral ACL insertion site. The autograft was pulled into the femoral tunnel and fixed with a cortical endobutton suspension device. The tibial tunnel was fixed with a resorbable interference screw.

Allograft surgery

Fresh allografts were obtained from the tissue bank and performed in sterile conditions. After anesthetization, the knee joint was examined by arthroscope through an anterolateral and anteromedial approach. The ACL rupture stump was reserved in the allograft group. Then, one end of the allograft was braided into 2 strands, and the other was attached to the endobutton. The tibial tunnel was drilled and positioned at a 55° angle to the coronal plane. The femoral tunnel was drilled according to the femoral ACL insertion site. The allograft was pulled into the femoral tunnel and fixed with a cortical endobutton suspension device. The tibial tunnel was fixed with a resorbable interference screw.

Clinical follow-up

All patients were assessed on admission and at 1 week, 3 months, 6 months, and 1 year after surgery. MRI scanning was performed before and after surgery to diagnose ACL rupture and confirm the complete reconstruction of the ACL. Physical examinations, including Lachman test, anterior drawer test and pivot shift test, were performed on admission and at 1 week, 3 months, 6 months, and 1 year postoperatively. These tests were conducted to evaluate the stability of the knee joint and the effectiveness of the ACLR. The comprehensive functional outcomes were assessed by IKDC score. The length of the surgical incision and the operative time were analyzed. The possibility of postoperative inflammation was evaluated through laboratory examinations, including white blood cell count (WBC), neutrophilic granulocyte percentage (NEUT%), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). The possibility of disease transmission, such as hepatitis B, syphilis, and acquired immunodeficiency syndrome (AIDS), was evaluated. At the final follow-up, all

Parameters	Allograft (n=58)	Autograft HS (n=54)
Male/female	40/18	44/10
Age (years)	31.54±8.13 (18.00–58.00)	32.18±8.96 (18.00-54.00)
Height	170.65±7.64	172.16±8.25
Weight	71.42±11.31	75.74±13.75
Acute reconstruction (<3 months)	28 (48%)	27 (50%)
Chronic reconstruction (>3 months)	30 (52%)	27 (50%)
Subjects with meniscal repairs	19 (33%)	19 (35%)

 Table 1 The demographic characteristics of the patients

HS, hamstring.

patients were evaluated to ascertain if they had returned to their pre-injury activity level.

Statistical analysis

SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis, and a P value less than 0.05 was considered significant. A Wilcoxon test was performed to analyze the difference between the paired groups.

Results

The demographic characteristics of all patients are summarized in *Table 1*. The male/female ratio was 40/18 for the allograft group and 44/10 for the autograft group. The mean age at surgery was 31.54 ± 8.13 (range, 18–58) in the allograft group and 32.18 ± 8.96 (range, 18–54) in the autograft group. There was no significant difference between the 2 groups (P>0.05). The mean height was 170.65 ± 7.64 cm in the allograft group and 172.16 ± 8.25 cm in the autograft group, with no significant difference (P>0.05). The mean weight was 71.42 ± 11.31 kg in the allograft group and 75.74 ± 13.75 kg in the autograft group. There was no significant difference in the level of pre-injury sport activities between the 2 groups.

Arthroscopic ACLR was performed in all patients using autografts or allografts. ACL complete rupture was observed during operation (*Figure 1A*). The gracilis and semitendinosus tendons (*Figure 1B*) were harvested as autologous grafts and prepared in double-strand and four-bundle style (*Figure 1C*₁, 1C₂). The allogeneic grafts were taken from Achilles, tibialis, and patellar donor tendons. They were sterilized after cryogenic freezing, ethanol soaking, and irradiation. Allografts were prepared in single-strand and double-bundle style due to their higher length and diameter than those of autografts (*Figure* $1D_1, 1D_2$). As illustrated in *Figure* 1E, 1F, femoral and tibial tunnels were drilled at ACL footprint zones according to the diameter of the prepared grafts. In all patients, a transverse fixation system was used to conduct femoral fixation, and a resorbable interference screw was used to perform tibial fixation (*Figure* 1G). After surgery, we examined the state of the knee ligaments under arthroscopy (*Figure* 1H). The continuity of the ACL was observed as disrupted in the preoperative MRI scanning, and the integrity of the reconstructed ACL was confirmed in the postoperative MRI scanning.

The results of the physical examinations are shown in Table 2 and Figure 2. In all patients, Lachman test, anterior drawer test, and pivot shift test were positive before surgery and negative immediately after arthroscopic ACLR. During the follow-up, there was no recurrence of any positive physical examination in the allograft and autograft groups, indicating that the reconstructed ACL was effective. To further compare the degree of laxity between allografts and autografts after ACLR, the KT-1000 instrument was used to determine the magnitude of anterior translation in millimeters. Before surgery, the mean translocation distance of the anterior drawer test was 8.29±2.67 mm in the allograft group and 7.66±1.94 mm in the autograft group, indicating complete tear of the ACL in the patients of both groups. At 3 months postoperation, the mean translocation distance of the anterior drawer test was 0.39±1.03 mm in the allograft group and 0.18±0.82 mm in the autograft group, with no significant difference (P=0.419). At 6 months, the mean translocation distance of the anterior drawer test was 0.41±0.95 mm in the allograft group and 0.23±0.74 mm in the autograft group, with no significant difference (P=0.391). Similarly, at the final 1 year follow-up,

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Figure 1 Arthroscopic ACL reconstruction was performed in all patients. ACL complete rupture was observed under arthroscopic examination (A). The gracilis and semitendinosus tendons were harvested through an oblique incision of 3-5 cm in the autograft group (B). The autografts were prepared in double-strand and four-bundle style (C_1, C_2). The allografts were prepared in single-strand and double-bundle style (D_1, D_2). The femoral tunnel was drilled according to the diameter of the prepared grafts (red arrow) (E). The tibial tunnel was drilled at ACL footprint zones (red arrow) (F). Transverse fixation system (red arrow) was used to conduct femoral fixation, and a resorbable interference screw (black arrow) was used to perform tibial fixation (G). The integrity of the reconstructed ACL (white arrow) was confirmed under arthroscopic examination while retaining the remnant of the original ACL (black arrow). The red arrow shows the posterior cruciate ligament (H). ACL, anterior cruciate ligament.

Functional performance tests -	Preoperative		3 months		6 months		12 months	
	Allo	Auto	Allo	Auto	Allo	Auto	Allo	Auto
Lachman test	58	54	0	0	0	0	0	0
Anterior drawer test	58	54	0	0	0	0	0	0
Pivot shift test	58	54	0	0	0	0	0	0

Table 2 During the follow-up, physical examinations were performed to assess the effectiveness of the reconstructed ACL

"Allo" represents allograft; "Auto" represents autograft. ACL, anterior cruciate ligament.

there was no significant difference in the mean translocation distance of the anterior drawer test between the allograft and autograft groups (*Figure 2*).

During the follow-up, clinical outcomes were assessed by IKDC score (*Table 3*). The mean score at 3 months was 54.03 ± 8.39 (range, 40.93-61.62) in the allograft group and 57.14 ± 8.23 (range, 49.43-66.22) in the autograft group. Over time, the mean IKDC score gradually increased. At the 6-month follow-up, the mean IKDC score had significantly increased to 65.53±4.03 (range, 61.62–71.97) in the allograft group and 67.94±4.74 (range, 63.92–73.11) in the autograft group. These results demonstrated that the function of the reconstructed ACL was recovering step by step over time. Moreover, there was no significant difference in IKDC score between the allograft and autograft groups at different points in time after the surgery. This indicated that primary ACLR using allografts resulted in similar clinical outcomes to autografts.

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Figure 2 The magnitude of anterior translation was determined in millimeters by the KT-1000 instrument. The KT-1000 instrument was used to determine the magnitude of anterior translation in millimeters. The test was considered positive if there was more than 2 mm of anterior translation relative to the contralateral side (*, P>0.05; **, P<0.05). P<0.05 is two-sided.

Table 3 The IKDC score

Parameters	Allograft	Autograft		
3 months				
IKDC score	54.03±8.39	57.14±8.23		
Range (min-max)	40.93–61.62	49.43–66.22		
6 months				
IKDC score	65.53±4.03	67.94±4.74		
Range (min-max)	61.62–71.97	63.92–73.11		

IKDC, International Knee Documentation Committee.

Table 4 The risk of postoperative infection was compared betweenthe allograft and autograft groups at 1 week and 3 months aftersurgery

Parameters —	1 w	veek	3 months			
	Allo (%)	Auto (%)	Allo (%)	Auto (%)		
WBC	6.89	12.96	1.72	3.70		
NEUT%	3.45	1.85	3.45	3.70		
ESR	65.52	77.78	0	1.85		
CRP	58.62	64.81	3.45	5.56		

"Allo" represents allograft; "Auto" represents autograft. WBC, white blood cell count; NEUT%, neutrophilic granulocyte percentage; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

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To explore the difference between the 2 groups with respect to postoperative inflammation, laboratory examinations were performed, including WBC, NEUT%, ESR, and CRP (Table 4). For WBC count, there were 4 patients in the allograft group and 7 patients in the autograft group whose indicator turned abnormal at 1 week after surgery (6.89% vs. 12.96%). For NEUT%, there were 2 patients in the allograft group and 1 patient in the autograft group whose indicator turned abnormal at 1 week after surgery (3.45% vs. 1.85%). For ESR and CRP, respectively, there were 38 and 34 patients in the allograft group compared with 42 and 35 patients in the autograft group (65.52% vs. 77.78%, 58.62% vs. 64.81%). Three months after surgery, the number of patients whose laboratory indicators remained abnormal declined dramatically. For WBC count, there was only 1 patient in the allograft group and 2 patients in the autograft group with abnormal indicators. For NEUT%, there were 2 patients in the allograft group and 2 patients in the autograft group. For ESR, there were no patients in the allograft group and only 1 patient in the autograft group. For CRP, there were 2 patients in the allograft group and 3 patients in the autograft group. Although some laboratory indexes turned abnormal following surgery, no patients had clinical symptoms of postoperative inflammation or infection such as clinical fever or surgical site infection. Thus, these indexes were nonspecific, and the changes had no clinical significance. Compared with autograft tissue, ACLR with allograft tissue showed no increased risk of postoperative infection.

The risk of potential disease transmission, including hepatitis B, HCV, syphilis, and AIDS, was also evaluated between the allograft and autograft groups (*Table 5*). There was only 1 patient in the allograft group and 1 patient in the autograft group whose HBV surface antibody (HBsAb) turned positive at 3 months after surgery. HBsAb is a protective antibody that is beneficial to patients. Except for this item, there were no positive indicators of potential disease detected 3 months after surgery that were negative before the operation. Therefore, compared with autografts, allografts showed no increased risk of disease transmission in arthroscopic ACLR.

Discussion

ACL rupture is one of the most common musculoskeletal

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Parameters —	(–	(-/-)		(+/+)		(+/-)		(-/+)	
	Allo	Auto	Allo	Auto	Allo	Auto	Allo	Auto	
HIV antibody	58	54	0	0	0	0	0	0	
HCV	58	54	0	0	0	0	0	0	
TPPA	57	54	1	0	0	0	0	0	
HBsAg	55	53	3	1	0	0	0	0	
HBsAb	36	32	19	21	2	0	1	1	
HBeAg	57	54	1	0	0	0	0	0	
HBeAb	54	52	4	2	0	0	0	0	
HBcAb	51	51	6	2	1	1	0	0	

Table 5 The risk of potential disease transmission was evaluated between the allograft and autograft groups at 3 months after surgery

"Allo" represents allograft; "Auto" represents autograft. HIV, human immunodeficiency virus; HCV, hepatitis C antibody; TPPA, treponema pallidum antibody; HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B e antigen; HBsAb, hepatitis B e antibody; HBcAb, hepatitis B core antibody. (-/-) represents a negative clinical result both before and 3 months after surgery; (+/+) represents a positive clinical result both before and 3 months after surgery; (+/-) represents a positive preoperative result that turns negative three months after surgery; (-/+) represents a negative preoperative result that turns positive three months after surgery.

injuries in sports medicine. In terms of therapy, both operative and nonoperative treatments are available according to the severity of the ACL injury. When the ACL tear is incomplete, nonsurgical treatments such as exercise training, rehabilitation, and platelet-rich plasma (PRP) injection are preferable (29,30). When the tear is complete or the ACL has disappeared, ACLR is the best choice for most patients to return to their pre-injury activities.

ACLR has evolved over the last 50 years. Initially, the femoral fascia lata was utilized in ACLR to limit the gliding movement of the knee joint, followed by the use of B-PT-B, hamstring tendons, and quadriceps tendons (31,32). All of these tendons originate from autologous tissue, which ensures no immune rejection after transplantation. However, the required length and diameter of autografts varies greatly among patients of different heights and genders, and the autograft tissue might be limited. For skeletally immature patients, hamstring autografts are insufficient in thickness and stretchability, and so allografts are recommended for ACLR in teenagers (33). Moreover, the autograph surgical process is lengthy, and additional incisions are needed to prepare the autologous tendon tissue during the operation. In this study, allografts for primary ACLR resulted in clinical outcomes equal to those of autografts using autologous four-strand hamstring tendons.

Preservation methods for allografts include fresh freezing, freeze-drying, and cryopreservation. Fresh freezing, the simplest preservation method, requires that fresh tendons be frozen for several weeks, soaked in an antibiotic solution, and subsequently frozen to -80 °C for storage (34). In freeze-drying, also known as lyophilization, the harvested tendons are frozen, soaked, and then lyophilized to reduce the moisture content to less than 5% for storage. Both fresh frozen and freeze-dried allografts have no viable donor cells. However, compared with fresh tissue, the strength of freezedried allografts may be decreased (35). In cryopreservation, allografts are created by extracting cellular water with the aid of the cryoprotectant dimethyl sulfoxide and storing it in liquid nitrogen at -196 °C (36). The use of cryoprotectants allows for the viability of donor cells, while fresh frozen and freeze-dried allografts do not. This may lead to host immune rejection and is not conducive to the ligamentization of allografts, although cryopreservation improves the biomechanical characteristics of allografts (37).

In this study, we focused on the efficacy and safety of allografts in primary ACLR. The allografts were preserved through the fresh freezing procedure. A total of 112 patients were included in this retrospective study, including 58 patients with allografts and 54 patients with autografts. There were no significant differences in demographic information, IKDC score, anterior drawer test, disease transmission, or deep infection between the 2 groups. Therefore, we concluded that allografts are an equally safe and valid reconstruction method.

Although there are concerns about disease transmission in allografts, our study has confirmed that there is no risk

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of disease transmission when reconstructing ACL with allografts. The safety of allografts is controversial, as some previous studies have indicated the allografts might lead to disease transmission, while others have stated that the risks of autografts and allografts were similar (14,33). We ascribe these heterogeneous findings to the preparation of allografts, including donor screening, tissue processing, and storage. A large cohort study found that the incidence of deep infection, such as coagulase-negative Staphylococcus, methicillinsensitive Staphylococcus aureus, and Peptostreptococcus micros, was only 0.15% regardless of whether the allograph was sterilized (38). To decrease the risk of disease transmission in ACLR, strict procedures should be adopted in tissue banks, such as low dose non-gamma irradiation, strict microbiological evaluation, transportation in temperatures below zero, aseptic operation, and soaking the graft in an antibiotic solution (39). The BioCleanse sterilization process, which combines mechanical and chemical methods to kill or inactivate microorganisms, has recently been proposed as another option, as it decreases the risk of disease transmission but has no effect on the biomechanical or physiological properties of the allograft (40).

Conclusions

In this study, ACLR using allographs showed comparable efficacy to autografts. Allographs had no increased risk of disease transmission when compared to autografts. If the surgical process is strictly aseptic, there is no postoperative infection associated with allografts or autografts. Therefore, allografts are safe, effective, and time saving and can be recommended in clinical practice.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm. amegroups.com/article/view/10.21037/atm-22-1008/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.

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amegroups.com/article/view/10.21037/atm-22-1008/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by The Institutional Ethics Committee of Shanghai Tenth People's Hospital (No. SHSY-IEC-4.0/18-11) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study participants provided written informed consent for participation and the use of their clinical data in this study.

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