

A Network Meta-Analysis of the Efficacy of Four Types of Graft Options for Reconstruction of Posterior Cruciate Ligament Injury

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Abstract:

Anterior cruciate ligament injury research is very mature, but posterior cruciate ligament injury is a less studied content in sports medicine. The purpose of this article is to evaluate and compare the efficacy of four different ligament grafts for reconstruction of posterior cruciate ligament injury. The Cochrane Library, EMbase, PubMed, web of science, and Scopus were searched electronically from the establishment of the database to October 2023. The literatures were screened and the literature information was extracted according to the inclusion and exclusion criteria, and the network among the studies was displayed through Stata16. The relationship, the area under the cumulative ranking probability plot (SUCRA) represents the probability of each option being the best option. Nine articles were included, including four intervention methods, with a total of 398 patients. The results of the network Meta analysis showed that there was no significant difference in the efficacy of the 4 types of ligament grafts ($P>0.05$), while the mixed ligament grafts had a slight advantage over other graft options according to the SUCRA curve analysis. However, due to the small sample size of clinical applications And the cost is high, so the value in clinical application needs to be further considered. At present, there is no more reliable statistical evidence to indicate which graft choice is the best for posterior cruciate ligament reconstruction.

Keywords:

Allograft, Mixed Graft, Autograft, LARS, Randomized Controlled Trial, Controlled Clinical Trial, Posterior Cruciate Ligament Reconstruction

1. Introduction

The cruciate ligament is an important tissue that maintains the structural stability of the knee joint [1], its damage and repair have received more and more attention in recent years. However, from the perspective of injury type, posterior cruciate ligament

injury combined with other knee ligament injuries is the most common [2]. Compare to anterior cruciate ligament injury, the proportion of single posterior cruciate ligament injury is relatively low [3], so studies on the reconstruction of the posterior cruciate ligament (PCL) are relatively rare. Therefore, the selection of ligament grafts for PCL reconstruction has good clinical significance. PCL reconstruction is currently the main method to treat PCL injury and delay knee osteoarthritis. From the current literature data, the selection of PCL ligament grafts [4] are mainly divided into four categories: autologous ligament grafts, such as hamstring tendon; allograft ligament grafts; autologous-allogeneic hybrid grafts; artificial ligament grafts, such as LARS. The four types of ligament grafts each have their own unique advantages and disadvantages.

2. Materials and Methods

2.1. Registration

The purpose of this network meta-analysis is to analyze the comprehensive efficacy of the four types of ligament grafts by indirectly comparing the improvement effects of the four types of ligament grafts in patients with PCL reconstruction after surgery, and to provide a reference for the clinical selection of PCL reconstruction.

2.2. Retrieval strategy

The Cochrane Library, EMBASE, PubMed, Web of Science, and Scopus were searched by computer, and the search time was from the establishment of the library to October 2023. The retrieval method is the combination of subject words and free words “allograft”, “mixed graft”, “autograft”, “LARS”, “randomized controlled trial”, “controlled clinical trial”, “posterior cruciate ligament reconstruction”, and use search engines to find relevant documents on the Internet and retrospective references to included studies.

2.3. Inclusion and exclusion criteria

Inclusion criteria: (1) Patients with posterior cruciate ligament injury who are going to undergo PCL surgery; (2) Interventions: autologous ligament grafts (such as hamstring tendon), allografts (such as Achilles tendon), autologous and allogeneic mixed tendon grafts materials, artificial ligaments (such as LARS ligament augmentation and reconstruction system) (3) Methodological standards: randomized controlled trials, clinical controlled trials.

Exclusion criteria: (1) Patients with other ligament tear or previous surgery on the same knee joint; (2) Patients with ACL injury; (3) The full text of the literature cannot be obtained; (4) The data is unclear, the comparison method is unreasonable or the literature without control 5. Reviews, reviews, abstracts or letters.

2.4. Literature screening and data extraction management

Endnote X9 literature management software was used to manage the literature search records. Two researchers browsed the titles and abstracts in a blinded manner. The literature was preliminarily screened according to the inclusion and exclusion criteria. The literatures that did not meet the inclusion criteria were excluded, and then cross-checked. Exchange opinions or seek third-party opinions to resolve. The included literatures were then independently extracted using Excel, including the

investigators, sample size, gender, average age, follow-up time, intervention measures, and outcome indicators. If there is any disagreement, it will be resolved through discussion or consultation with a third party.

2.5. Publication bias quality assessment

The methodological quality of the included literature was assessed using the risk of bias assessment tool in accordance with the Cochrane Handbook version 5.1.0 tool, including the generation of random order, allocation concealment to randomization, blinding of study subjects and intervention practitioners, and blinding of outcome assessors, completeness of outcome data, possibility of selective reporting of findings, and other sources of bias. Each item is rated as “high risk”, “low risk” and “unclear”.

2.6. Statistical methods

The mean difference (MD) and 95% confidence interval (CI) of the Graft Selection Scheme score table after PCL reconstruction were calculated. Plotting the Cumulative Ranked Undercurve Area (SUCRA) presents the likelihood of each intervention being the best intervention. Identify evidence of small sample effects in the intervention network by plotting a compare-adjusted funnel plot. Stata 16.0 software and Review Manager 5.3 were used for data processing and graph drawing.

3. Result

3.1. Literature search results

In this study, a total of 398 relevant literatures were retrieved, and irrelevant literatures were excluded after removing duplicate literatures, reading titles, abstracts and full texts. Finally, a total of 9 literatures were included [5-13]. The literature screening process and results are shown in Figure 1.

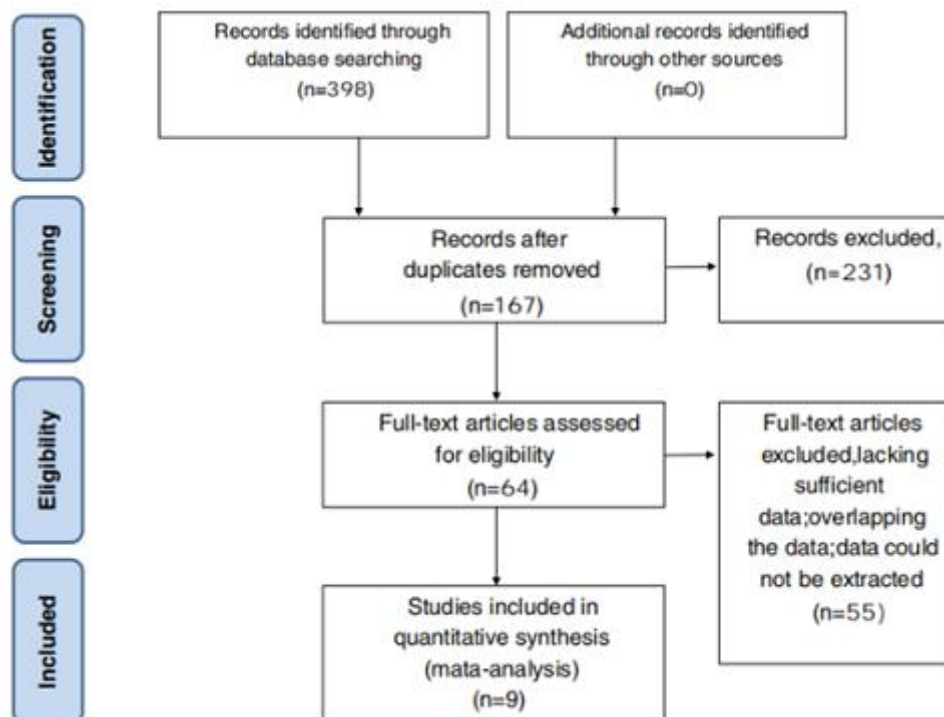


Figure 1. Flowchart of literature screening.

3.2. Basic characteristics of the included literature and methodological quality evaluation

A total of 9 literatures were included, with a total sample size of 398 cases, the maximum sample size of a single study was 71 cases, and the minimum sample size of a single study was 16 cases; all literatures reported the relevant research outcome indicators, and explained the experimental group and the experimental group. Status and comparability of baseline information in the control group; 2 out of 9 were Randomized Controlled Trial (RCT), 7 were Clinical Controlled Trial (CCT), and 5 of them reported Lost to follow-up, the data integrity was good; 7 literatures explained the method of clinical grouping, and there was selection bias in the included literatures. Quality evaluation results: The nine included articles were all grade B, and the included articles are shown in Table 1. The quality of bias assessment of the included studies is shown in Figure 2.

Table 1. Basic information of the included articles.

Include basic information in the literature							
Author/Y ear	Desig n meth od	Case (test group/cont rol group)	Average age (test group/cont rol group)	Sex ratio	follow-up time	Intervention condition	
						test group	control group
Yang 2012	CCT	28/30	27.7/26.8	(24:4)/ (25:5)	5Y	Allogene ic (Achilles tendon)	Hybrid (hamstrin g + tibialis anterior)
Kwon 2014	CCT	27/29	31.3/32.5	(22:5)/ (22:7)	1.5Y	Allogene ic (Achilles tendon)	Hybrid (hamstrin g + tibialis anterior)
Li 2016	RCT	26/27	31.3/30.6	(17:9)/ (17:10)	3Y	Autologo us (hamstrin g tendon)	Hybrid (semi-tendon + tibialis anterior tendon)
Sun 2015	CCT	36/35	31.1/33.4	(27:9)/ (27:8)	5Y	Autologo us (hamstrin g tendon)	Allogene ic (Achilles tendon)
Li 2014	CCT	18/19	31.3/32.5	(13:5)/ (12:7)	2.3Y	Autologo us (hamstrin g tendon)	Allogene ic (tibial anterior tendon)
LUO 2021	CCT	21/15	36.5/39.7	(15:6)/ (10:5)	4.11Y	Autologo us (hamstrin g tendon)	artificial ligament graft(LA RS)
Li 2008	CCT	15/21	18—47	(13:2)/ (17:4)	2.3Y	Autologo us (hamstrin g tendon)	artificial ligament graft(LA RS)
Xu 2014	CCT	16/19	29.1/28.6	(9:7)/(	4.3Y	Autologo	artificial

				8/11)		us (hamstrin g tendon)	ligament graft(LA RS)
Saragaglia 2019	RCT	8/8	24.5/34.0	(8:0)/(7:1)	2Y	Autologo us (hamstrin g tendon)	artificial ligament graft(LA RS)

(RCT=Randomized Controlled Trial; CCT=Clinical Controlled Trial; LARS=ligament-advanced reinforcement system; Y=years)

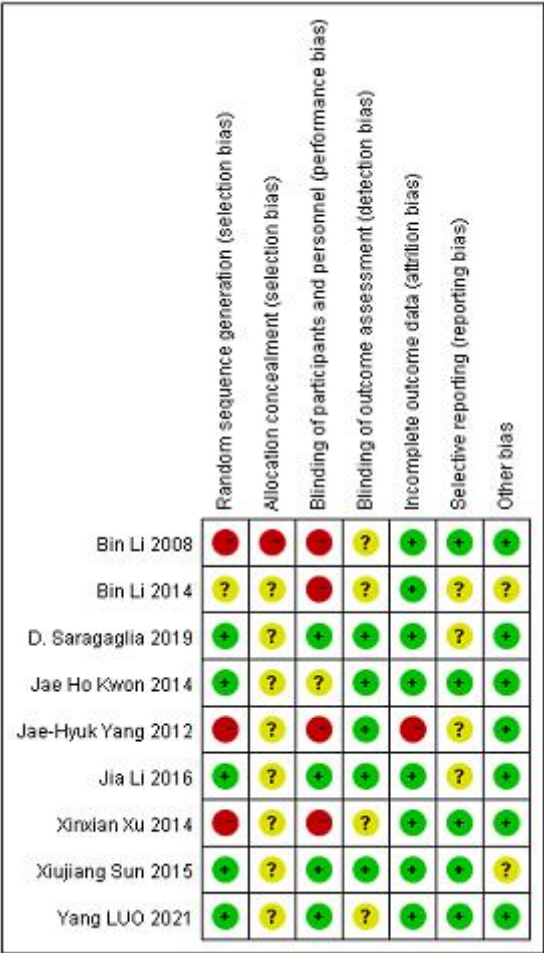


Figure 2. The Cochrane Risk of Bias Tool assesses bias in controlled trials.

4. Network Meta-Analysis Results

4.1. Evidence Network

Based on direct comparison data, relationships between all interventions were formed. Each dot in the network diagram represents different graft intervention methods. The size of the dot represents the sample size of each intervention method. The larger the dot, the larger the sample size. The lines between the dots represent two different methods. Comparisons exist between interventions, with line thickness proportional to the number of studies per intervention pair. There are direct or indirect comparisons between the different intervention methods included in this study, and the basic conditions for conducting a network meta-analysis are met, as shown in Figure 3.

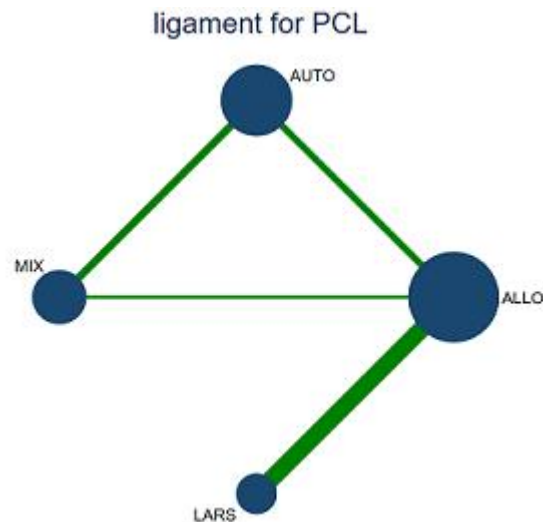


Figure 3. Network Evidence Diagram.

4.2. Network Meta-Analysis Results

4.2.1. Prediction interval graph analysis

The results are shown in Figure 4: A total of 9 literatures were included to analyze and compare various comparison items of each intervention method for posterior cruciate ligament reconstruction and transplantation, 4 direct comparisons and 2 indirect comparisons of 4 graft selection schemes after PCL reconstruction. The study concluded that there was no statistically significant difference in efficacy between the four types of ligament grafts. The 95% CI is the result of the fixed effect model (shown by the black line in the figure), and the 95% PrI is the result of the prediction interval with τ^2 added (shown by the red line in the Figure 4).

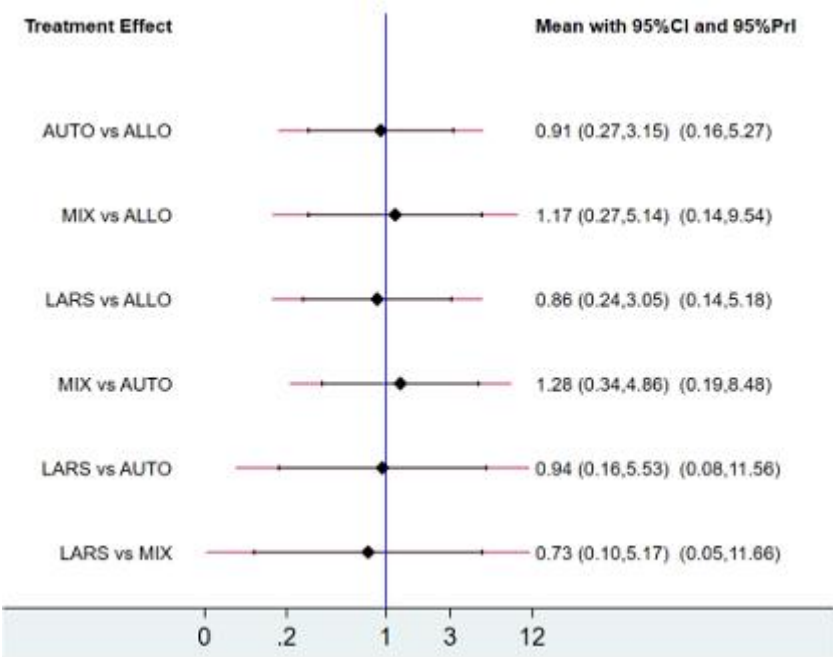


Figure 4. Prediction interval plot of the network meta-analysis.

4.2.2. Lysholm Knee Score

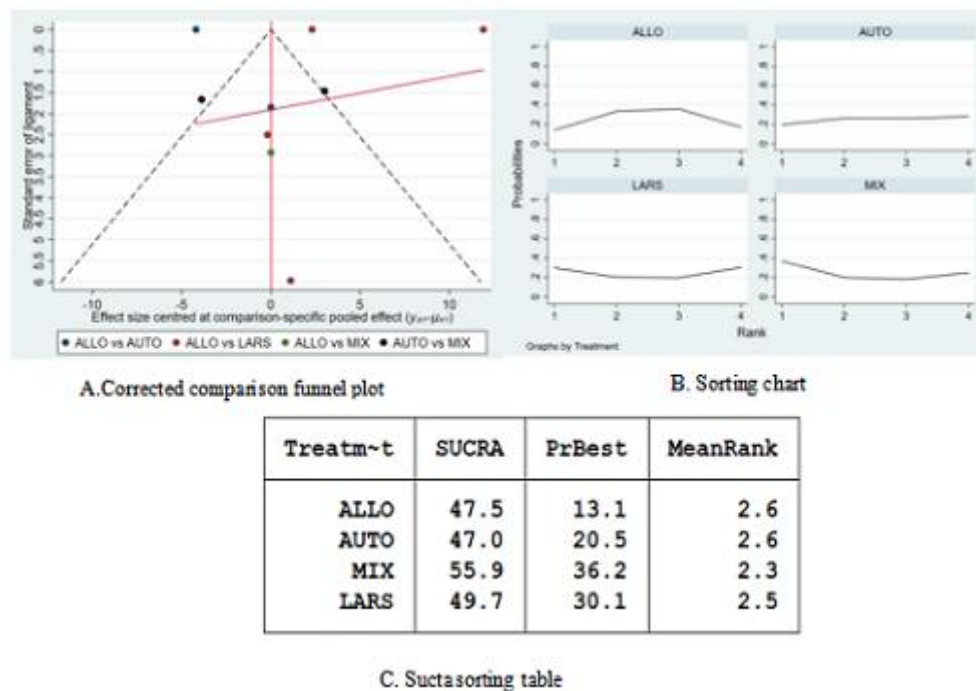


Figure 5. Lysholm Knee Score meta-analysis graph.

The results of Lysholm Knee Score are shown in Figure 5. All 9 reports were included in the network meta-analysis. Panel A shows the adjusted funnel plot for all results. The funnel plot is symmetric, but there are points that fall outside the plot. The results in this study were heterogeneous, and a random effects model was used. analyze. Use STATA 16 to draw probability ordination charts and SUCRA curves, and use the area under the curve to predict the efficacy of various treatment measures. The larger the area under the curve, the better the efficacy. It can be seen from Figure B that the hybrid ligament graft has the highest probability of the best curative effect (36.2%). Figure C is the sucra sorting table, which is the probability of the best cumulative curative effect after 10,000 software simulations, showing the ranking of the hybrid ligament graft. (55.9%)> artificial ligament augmentation and reconstruction system (39.7%)> autologous ligament graft (47.5%)> allogeneic ligament graft (47%).

4.2.3. Tegner Activity Score

For the Tegner Activity Score scoring results, all 9 reports were included in the network meta-analysis, as shown in Figure 6. Panel A shows the corrected funnel plot for all results. The funnel plot is symmetrical and the points all fall within the plot. There was no heterogeneity in the results in this study, and the fixed-effects model was used. It can be seen from Figure B that the hybrid ligament graft has the highest probability of the best curative effect (40.6%). Figure Csucra ranking table shows the curative effect ranking: hybrid ligament graft (61.8%) >S autologous ligament graft (52.6%) > allogeneic ligament Graft (44%)> artificial ligament augmentation and reconstruction system (41.6%).

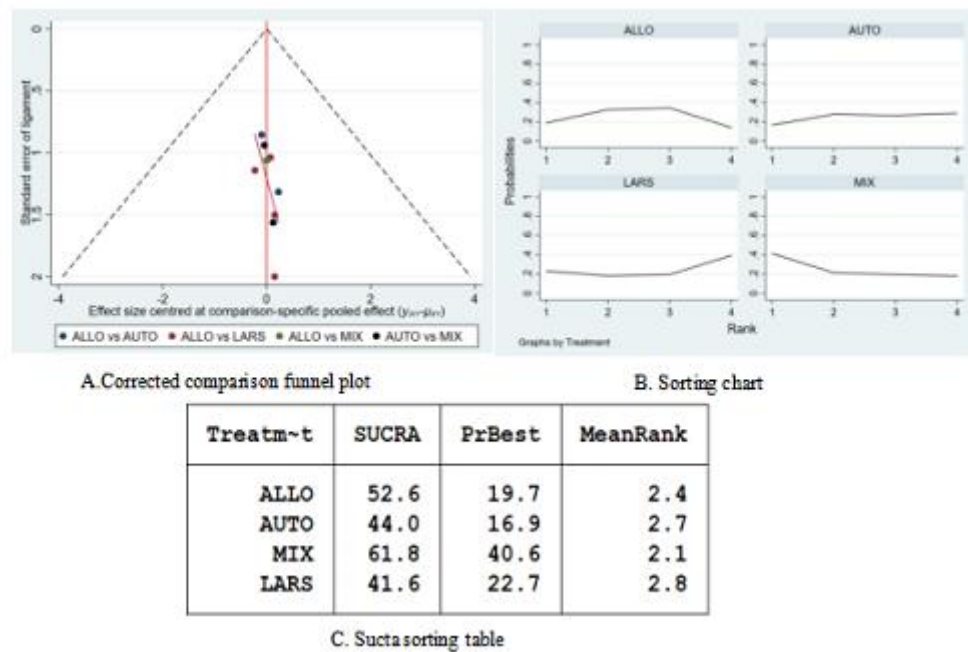


Figure 6. Tegner Activity Score meta-analysis graph.

4.2.4. IKDCS score

For the IKDCS score results, 5 of these reports were included in the network meta-analysis, as shown in Figure 7. Panel A shows the corrected funnel plot for all results. The funnel plot is symmetrical and the points all fall within the plot. There was no heterogeneity in the results in this study, and the fixed-effects model was used. It can be seen from the probability map of Figure B that the artificial ligament augmentation and reconstruction system has the highest probability of ranking first (38.5%); and the ranking table of Figure Csucra shows the efficacy ranking: hybrid ligament grafts (54.3%)> allograft ligament grafts (51.8%) > artificial ligament augmentation and reconstruction system (50.1%)> autologous ligament graft (43.8%).

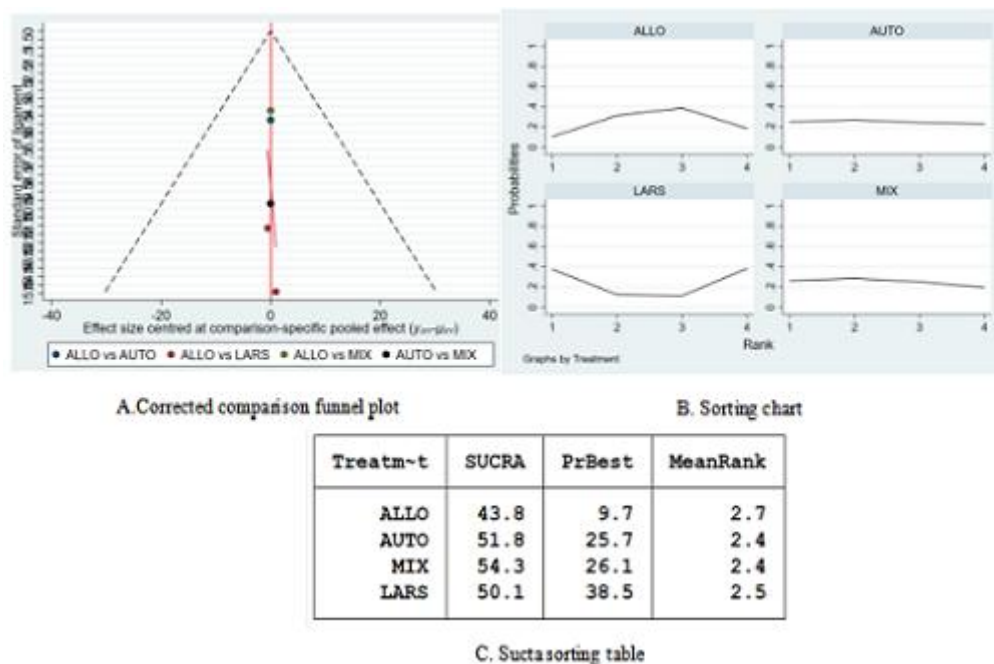


Figure 7. IKDCS score meta-analysis graph

4.2.5. Postoperative complications

Postoperative complications were recorded as binary variable data, and the complication rates were ranked by the mvmeta program, as shown in Figure 8. Blue Best represents the possibility of the highest complication probability, and orange worst represents the possibility of the lowest complication probability. Complications include joint stiffness, thrombosis, synovitis, etc., excluding postoperative numbness. It can be seen that the probability of complications is lowest in mixed ligament grafts and highest in allogeneic ligament grafts.

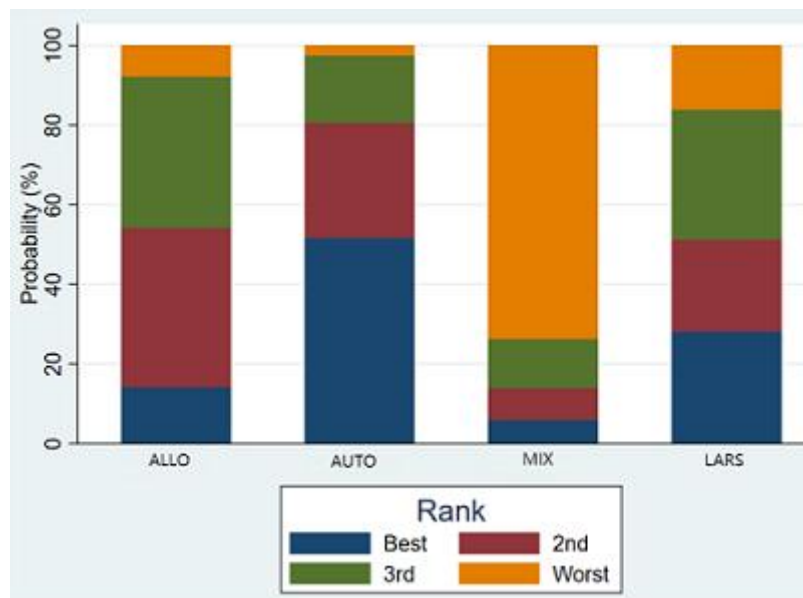


Figure 8. Ranking of complication rates.

5. Discussion

In this network meta-analysis, we combined direct and indirect evidence from 9 randomized and controlled clinical trials, compared 4 different interventions, and reported 398 patients with posterior cruciate ligament injury, a comprehensive analysis of different ligament grafts. The effect of material selection on the efficacy of posterior cruciate ligament reconstruction. First, all studies using different validation indicators (such as secondary arthroscopy, KT1000, side to side test, Telos stress view, Lachman test, etc.) showed that the postoperative stability of the posterior cruciate ligament in patients was significantly improved compared with preoperative, calculated. The differences in the results obtained by MD were small, so the ligament stability after posterior cruciate ligament surgery was not separately analyzed and compared. By comprehensively comparing the Lysholm Knee Score, Tegner Activity Score, IKDCS score, and postoperative complication score of the four different ligament grafts, it can be seen that the four grafts have no significant effect on the postoperative efficacy of PCL, and among them Hybrid ligament grafts outperformed other options by a small, but not statistically significant, advantage.

In the clinical treatment process, when there is no significant difference in the efficacy of several options, some additional factors need to be considered, such as the cost of the transplant, the simplification of the surgical procedure and other factors. The current clinical gold standard for graft selection for posterior cruciate ligament reconstruction is autologous ligament grafts [14]. The advantages of autologous ligament grafts [15] are: it has good histocompatibility, high strength and

easy access, and the probability of complications such as infection of infectious diseases and immune rejection is small. However, the use of autologous graft materials may cause corresponding complications at the site of tendon extraction, and there may be insufficient autologous graft materials for patients with multiple ligament injuries. The advantages of allograft materials [16] are: wide range of sources; fewer surgical incisions, no need to remove other ligaments, and no complications in the donor area; it can significantly shorten the operation time and tourniquet use time, and reduce the risk of surgery. Although no failure cases were mentioned in the included literature reports, other literatures [17] show that its main problem is poor biocompatibility, and the implanted tendon may produce immune rejection, resulting in tendon dissolution and absorption, and tendon strength decreases and relaxation issues. For mixed ligament grafts, there is currently no clear literature data suggesting that it can significantly improve postoperative stability or complications, and combined with its clinical operating costs, it is not the first choice in clinical practice. The artificial ligament is a popular option for ligament grafts in recent years, of which the French ligament augmentation and reconstruction system LARS is the most widely used [10]. It has the advantages of good joint stability and fewer complications in the short term [18], and at the same time, it can simplify the operation process and shorten the operation time. However, its high cost and lack of long-term clinical follow-up results are one of the reasons why it cannot be widely used in clinical practice. In addition, some studies have pointed out that LARS often have problems [12] such as postoperative loosening and fatigue injury failure. Therefore, in a comprehensive discussion, autologous ligament grafts with the lowest cost are still the best choice when there is no significant difference in the selection of grafts between groups.

There are still some limitations in this study: (1) the number of literatures that can be included in the network meta-analysis is small, which may increase the chance of the results and reduce the reliability of the results; (2) there is a lack of evaluation of knee stability after posterior cruciate ligament reconstruction. Uniform evaluation criteria cannot assess the reliability of the results; 3. Due to the influence of the technical level of different researchers, the influence of surgical techniques on the judgment of ligament graft selection cannot be ruled out; 4. There are differences in follow-up time among all reports in this study, and no The unified time standard cannot exclude the influence of various scoring indicators and postoperative recovery time; There is heterogeneity, and benign outcomes are exaggerated. Therefore, the selection of grafts for PCL needs to be further confirmed by randomized or clinical controlled trials with large sample size and high quality.

6. Conclusions

There is no significant difference in the effect of autologous ligament graft, allogeneic ligament graft, hybrid ligament graft and artificial ligament on the efficacy of posterior cruciate ligament reconstruction, which still needs to be further confirmed by large sample size and well-designed randomized controlled trials.

Registration

This systematic review and NMA is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta - Analyses (PRISMA) statement. The study protocol was registered (registration number:

CRD42022333469) with the International Prospective Register of Systematic Reviews (PROSPERO).

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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