Review Article

The long-term outcomes of different grafts in anterior cruciate ligament reconstruction: a network meta-analysis

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ABSTRACT

Objectives: To compare the long-term prognosis of patients with different types of grafts used in anterior cruciate ligament reconstruction (ACLR).

Methods: PubMed, Ovid (MEDLINE and Embase) and the Cochrane library were searched up to Feb 2020. Eligible studies about different grafts in ACLR were searched for identifying the evidence comparing the long-term (mean or median follow-up time or the general description of the follow-up time ≥2 years) knee outcomes of different grafts for ACLR. The final included articles and evaluation criteria were confirmed by the authors and senior clinicians to ensure the validity of the included articles. Lysholm score, the results of pivot shift test, Lachman test and International Knee Documentation Committee (IKDC) evaluation were selected as prognostic indicators. A Bayesian network meta-analysis was conducted.

Results: A total of 30 articles were included in our network meta-analysis. Finally, we found that artificial graft or augmentation can provide the not bad Lysholm score but the worse result of IKDC evaluation for patients with ACLR compared with other types of grafts. Double-bundle hamstring autograft can provide a good Lysholm score as well as lower positive rate of pivot shift test and Lachman test. Patellar tendon autograft can provide the better result of IKDC evaluation. The patients with allogeneic tendon graft may get the higher positive rate of pivot shift test and Lachman test. Patients with single-bundle hamstring autograft may get the ordinary result of IKDC evaluation and Lysholm score.

Conclusions: Double-bundle hamstring autograft may be a better choice because of more items of good prognosis for the patients with ACLR. Patellar tendon autograft is a right choice which only shows the disadvantage on the Lysholm score. The prognosis of patients with single-bundle hamstring autograft is ordinary. The effect of artificial graft or augmentation needs more evidence to prove. Allogeneic tendon graft is not a better choice when compared with other grafts referred in our network meta-analysis.

Translational potential statement: In this study, we made a comprehensive comparison of the grafts commonly used in anterior cruciate ligament reconstruction. The evidence presented in this study provides a reference for clinicians to select a suitable anterior cruciate ligament graft.

Introduction

Anterior cruciate ligament (ACL) injury is a very common disease in sports medicine [1]. This kind of injury often occurs in athletes or in common people who are doing the improper exercise or fitness. When patients are diagnosed with ACL injury, clinicians often perform anterior cruciate ligament reconstruction (ACLR) to help patients recover [2]. The number of ACLR surgery is enormous. According to the statistics of the United States, there are more than 200,000 patients with ACL injury each year and at least 100,000 patients are received ACLR surgery [3,4]. In ACLR, the choice of grafts is very important. At present, the common clinical grafts include single-bundle hamstring autograft, double-bundle hamstring autograft, patellar tendon autograft, artificial graft or augmentation and allogeneic tendon graft. Each kind of graft is supported by some clinicians. There is still debate about which graft might be best suited for ACLR. All of grafts have their own advantages and disadvantages in clinical surgery.

Patellar tendon autograft is a kind of the commonly used ACLR grafts...
which is usually used in the form of bone–patellar tendon–bone in ACLR surgery [5]. This graft provides the stable fixation point with the screw and may be beneficial to rapid healing because of both sides of the bone plugs (if use) [6,7]. However, the use of patellar tendon autograft (often bone–patellar tendon–bone) has also been reported to be associated some donor-site morbidities such as knee pain and knee discomfort, etc. [8]. Nowadays, clinicians start to use single-bundle multi-strand (4-strand most) hamstring tendon autograft to finish the ACLR [9]. The hamstring tendon autograft is usually a combination of the semitendinosus tendon and gracilis tendon [10]. Some studies have reported that fewer complications with hamstring tendon autograft occurred [11,13]. However, in most cases, there is lack of bone plug on both sides of hamstring tendon autograft [14], the rigidity of graft may reduce. There have been many clinical studies comparing the two autografts, but the results are not completely consistent [15,16]. Double-bundle hamstring autograft is another kind of graft in ACLR, which means anteromedial and posterolateral bundles are built respectively and become ‘double bundles’ [17,18]. Thus, double-bundle hamstring autograft may better restore the anatomical structure and function of the ACL, but its clinical effect is controversial. Its disadvantages are that the operation is difficult, bone loss exists and the requirements for clinicians are high [19,20].

Allograft tendons are also the choice of many clinicians for ACLR, for that the selection of allograft tendons allows patients to avoid additional trauma from obtaining autograft tendon and reduces the morbidities or complications at the donor site [21]. The most commonly used allograft tendons in ACLR come from certified tissue banks. Both the patellar tendon allograft and the hamstring tendon allograft are used in ACLR [21]. In addition, the Achilles tendon allograft [22] and the tibialis tendon allograft [23] are used. Although the use of allograft tendons avoids some of the problems associated with the use of autograft tendons, the allogeneic tendons mentioned above are not perfect. Allograft tendons may have problems such as disease transmission [24]. And there are different clinical opinions on the application of allogeneic grafts, which is not conducive to the implementation of clinical decisions and the development of clinical guidelines. Artificial grafts or augmentations, such as Leeds-Keio ligament, have been reported to have been used. There are some relevant meta-analyses [25], but there are still lack of studies on the effect of artificial grafts or augmentations.

As mentioned above, the variety of ACLR surgical grafts is numerous, and each has its advantages and disadvantages. Clinicians consider a number of criteria when selecting ACLR surgical grafts, for example, patients' subjective feelings, objective evaluation of knee status, results of knee physical examination, revision surgery, consideration of return-to-play, patients' satisfaction and failure rate, etc [11,26,27]. During follow-up after ACLR surgery, knee scores are the common ways to follow-up after ACLR surgery, knee scores are the common ways to evaluate the status of knee joint function after ACLR. We can infer that patients with better scores and physical examination results above are more likely to get the successful ACLR surgery, lower failure rate and more likely to return to the playground.

The purpose of this study is to compare the long-term prognosis of different types of grafts in ACLR using the scores and examinations described above. It is well known that patients undergoing ACLR surgery are mainly young and middle-aged. Although there is concern about the short-term effects of ACLR surgery because people want to get back to normal life or go back to the playground as soon as possible. However, whether the function of graft used in ACLR surgery can approach the original ACL in the long run remains a very important question. If the knee scores and knee physical examinations of patients are poor after long-term observation of ACLR, which means that the graft function is poor and the ACLR surgery is not successful after long-term observation, the probability of patients suffering from diseases such as knee osteoarthritis may be increased, because the successful ACLR surgery may reduce the risk of arthritis in patients [31]. Patients are at a higher risk of subsequent ACL injury within 2 years after ACLR compared with healthy people without ACL injury history, and after 2 years of ACLR surgery, the knee joint function of patients will probably be recovered, and the probability of injury may be reduced [32,33]. The revision rate approaches to the peak at 1 to 2 years after primary ACL reconstruction [34]. So the results from 2 years or more follow-up may reflect long-term and stable outcomes for patients. Therefore, the results of studies with the mean, median or the general description of the follow-up time of 2 years or more were considered to reflect the long-term effect in this network meta-analysis.

In the absence of a ‘gold standard’ for ACL graft selection, the use of network meta-analysis to compare and rank different grafts is an appropriate method. Network meta-analysis, also usually called as the multiple treatment comparison meta-analysis, provides a set of visual approaches to explain the pros and cons of existing intervention ways [35]. The advantage of a network meta-analysis is that indirect evidence can be used to obtain certainty for all treatment comparisons, and the two interventions can be compared in a network meta-analysis even if there is no direct evidence to compare them [36]. The network meta-analysis can not only compare interventions directly or indirectly but also rank the existing interventions and provide help for the establishment of guidelines and clinical decision-making [37]. The purpose of our network meta-analysis is to compare different types of grafts in ACLR. Lysholm score, IKDC evaluation result and the results of Lachman test and pivot shift test were selected as indicators to evaluate the prognosis of patients undergoing ACLR. We hypothesized that with the network meta-analysis, we could clarify and rank the prognosis of various grafts under the condition of controlling errors and biases. Therefore, we designed this network meta-analysis. Our analysis provides a relatively reliable evidence for the selection of grafts in ACLR surgery and helps sports medicine clinicians in their work.

Method

Articles search strategy

Our network meta-analysis was designed and reported based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [38]. We conducted searches on Ovid (MEDLINE and Embase), PubMed and Cochrane Library from the earliest record to Feb 2020. Take the article search process in PubMed as an example to describe the search strategy used in our research. We searched in PubMed using the following way: (((((Reconstructive) OR Reconstruction)) AND (((((Transplant) OR graft)) OR (((Auto) OR Autologous) OR Auto-transplant)) OR (((Allograft) OR Allogeneic) OR Homograft) OR Homologous)) OR hybrid) OR (((((Hamstring) OR Semitendinosus) OR gracilis) OR Tibialis) OR Achilles) OR Calcaneal)) OR Artificial Ligament)) AND (((((RCT(MeSH Terms)) OR RCT(Title/Abstract)) OR randomized controlled trial(Title/Abstract))) OR randomized controlled trial(MeSH)

| Table 1 |
|-----------------------------------------------|
| **Inclusion and exclusion criteria.** |
| **Inclusion criteria** | **Exclusion criteria** |
| Randomized trials and prospective studies | 1. Duplicate articles; |
| using randomized allocation (pseudo-random methods allowed and will be showed in the risk of bias) that related to the comparison of different kinds of grafts | 2. Conference abstracts or letters; |
| 3. The types of studies didn’t match; |
| 4. Unable to obtain the full text; |
| 5. The studies with irrelevant titles; |
| 6. Retractions; |
| 7. Group dividing or measures did not meet the purpose of meta-analysis; |
| 8. No available or relative data for the meta-analysis; |
| 9. Incomplete data for meta-analysis; |
| 10. Short-term follow-up; |
| 11. Other inappropriate studies (such as using the same observation subjects, etc) that needed to be excluded. |
Terms). Manual method was used to filter the found articles. The final included articles and evaluation criteria were confirmed by the authors and senior clinicians to ensure the validity of the included articles. Eligible studies comparing two or more different types of ACL grafts were included in this network meta-analysis. Duplicate articles, conference abstracts or letters, unmatched types of studies like cohort studies, retractions, articles with irrelevant title or group dividing, no relative data, short-term follow-up (the general description of the follow-up time < 2 years, and mean or median follow-up time < 2 years if recorded) or incomplete data were excluded. If the general description of the follow-up time of a study was 2 years, but the mean follow-up time of a subgroup or more in the study was slightly less than 2 years, the study was not excluded because we could infer that the follow-up time of this study was 2 years according to the general description of the follow-up time, the results of this study could reflect the long-term outcomes and could be used in our meta-analysis. If some studies used the same observation subjects, we only included one of these studies to avoid duplication, and others were excluded. Other inappropriate studies were also excluded. As for types of grafts (group dividing) in our inclusion and exclusion criteria, the patellar tendon autografts with or without bone, single-bundle or double-bundle were analyzed as a group. As for single-bundle hamstring autograft, we mainly chose the studies that related to the common 4-strand (quadrupled) hamstring tendon autograft with single-bundle. The types of hamstring tendons (no matter single-bundle or double-bundle, autograft or allograft) included semitendinosus tendon and the combination of semitendinosus tendon and gracilis tendon, etc. Artificial grafts or augmentations were integrated into a class included common artificial ligaments, LAD and others had been reported. As long as the intervention of one of the groups in a study was using the artificial synthetic as the ligament or augmentation for ACLR, then the group would be analyzed as artificial graft or augmentation. Here we marked augmentation in the group dividing, but we didn’t specify it in many places of the article, for that augmentations such as LAD are artificial synthetics and used for augmentation. Allogeneic tendon grafts were integrated into a class no matter single-bundle or double-bundle or different specific types of grafts such as patellar tendon allograft or others. Some details are reflected in our study. The inclusion and exclusion criteria are shown in Table 1.

**Table 2**
The types of grafts and the corresponding letters.

| Letter | The type of graft                      |
|--------|--------------------------------------|
| A      | Patellar tendon autograft             |
| B      | Artificial graft or augmentation      |
| C      | Single-bundle hamstring autograft     |
| D      | Allogeneic tendon graft               |
| E      | Double-bundle hamstring autograft     |

**Data collection and assessment of risk of bias**

The author extracted the following data from the 30 included studies: (1) study characteristics: the first author’s name, publication year and follow-up time; (2) patient details: number of patients at follow-up, the type of patients (recorded as athletes or not), age, gender, causes of injury, the time to surgery and comorbidities such as meniscal comorbidities, etc.
| Study | Year | Graft type | Patients at follow-up (N) | Age (year) | Gender (male%) | Comorbidities recorded in studies | The time to surgery (months) | Follow-up (years) | Type of patients (directly recorded as athletes or not) | Causes of injury recorded in studies | Outcomes |
|-------|------|------------|--------------------------|-----------|----------------|----------------------------------|-----------------------------|----------------|------------------------------------------------|---------------------------------|-----------|
| Marjan Sajovic [79] | 2018 | Patellar tendon autograft | 28 | 45.5 ± 8.7 | 62.9% | Meniscal surgery: 18 | Mean time to surgery: patellar tendon autograft: 22.1 ± 28.8 months; single-bundle hamstring autograft: 27.5 ± 43.5 months. Both groups: Acute reconstruction (< 12 weeks): 4 patients (17%); Chronic reconstruction (< 12 weeks): 20 patients (83%). Acted (3 months) chronic: 16:94 (patellar), 16:94 (single), 17:95 (double) | 17 years | Not directly recorded as athletes | Not mentioned | Lysholm Knee Score, Lachman test, pivot shift test, IKDC instrumented anteroposterior translation, IKDC Knee Joint Arthritis Grade, Overall IKDC Score |
| Nicholas G. Mohanlal [73] | 2019 | Patellar tendon autograft | 103 | 33.8 ± 9.8 | 58.3% | Medial meniscus abnormal: 79; Lateral meniscus abnormal: 85; Cartilage abnormality: 54 (at the time of surgery) | Mean time to surgery: patellar tendon autograft: 22.1 ± 28.8 months; single-bundle hamstring autograft: 27.5 ± 43.5 months. Both groups: Acute reconstruction (< 12 weeks): 4 patients (17%); Chronic reconstruction (< 12 weeks): 20 patients (83%). Acted (3 months) chronic: 16:94 (patellar), 16:94 (single), 17:95 (double) | 50.8 ± 2.0 months (patellar), 60.0 ± 3.1 months (single), 59.8 ± 1.8 months (double) | Not directly recorded as athletes | Not mentioned | AQL-QOL scores, pivot shift test, IKDC subjective and objective scores, passive extension deficit, single-leg hop, Cincinnati occupational rating, Tegner activity level |
| Marek Masere ch Elweos [60] | 2018 | Patellar tendon autograft | 46 | Mean age: 25 years (range: 16–42 years) | 45.0% | Meniscal resections before operation: 15; non-augmented 20; Meniscal resections or re-resections: 14 (at the time of surgery) | 40 months (range, 1-180 months) | 25 years | Not directly recorded as athletes | Not mentioned | Range of motion, Lachman test, pivot shift test, side-to-side difference, Tegner score, Lysholm score, IKDCS, AHS, Backs Score |
| Hermann O. Mayer [72] | 2016 | Single-bundle hamstring autograft | 28 | 39.0 ± 10.0 | 46.4% | Articular cartilage damage: 92.8%; Meniscal tears: 25%; Meniscal tears: 25%; Lateral meniscus tear: 3.3% | Mean time to surgery: patellar tendon autograft: 22.1 ± 28.8 months; single-bundle hamstring autograft: 27.5 ± 43.5 months. Both groups: Acute reconstruction (< 12 weeks): 4 patients (17%); Chronic reconstruction (< 12 weeks): 20 patients (83%). Acted (3 months) chronic: 16:94 (patellar), 16:94 (single), 17:95 (double) | Median: 3.1 months | Not directly recorded as athletes | Not mentioned | IKDC subjective score, IKDC objective score, rotation angle, detailed Lachman measurement |
| Ze-song Tu [89] | 2016 | Double-bundle hamstring autograft | 60 | 28.8 ± 6.8 | 66.7% | May have a meniscus or medial collateral ligament, the medial collateral ligament damage degree no more than II degrees. | 2 years | Not directly recorded as athletes | Not mentioned | Lachman test, Lysholm score, Tegner score, Immune rejection |
| Shaoqi Tian [88] | 2016 | Single-bundle patellar tendon autograft | 40 | 29.2 ± 6.9 | 80.0% | Meniscal tears: 16; Lateral meniscus tears: 15; Cartilage damage: 2 Medial ligament injuries: 2 | 1.5 ± 1.1 months | 7.0 ± 0.7 years | Not directly recorded as athletes | Not mentioned | Overall IKDC score, Range of motion, Hamer vertical jump test, Daniel 1-legged hop test, side-to-side difference, pivot shift test, Anterior drawer test, Lachman test, Subjective IKDC score, Cincinnati knee score, Lysholm score, Tegner score, Kellgren-Lawrence grade |
| Hideyuki Koga [67] | 2015 | Single-bundle hamstring autograft | 25 | 24 (range: 14–44) | 28.0% | Combined meniscal injuries 17 | 16 months (range: 1-110) | 71 months (range: 36–140) | Not directly recorded as athletes | Not mentioned | KT Measurement, Lachman test, anterior drawer test, pivot shift test, mean muscle strength, mean Lysholm score, mean Tegner score, mean patient satisfaction, mean sports performance level, Overall IKDC score, pivot shift test, Lachman test, knee laxity, Tegner activity score, Lysholm score, Subjective IKDC score |
| Xia Li [71] | 2015 | Single-bundle hamstring autograft | 32 | 29.8 ± 7.9 | 53.3% | Meniscal injury: 17, Lateral Meniscus injury: 15 | 2.2 ± 1.3 months | 5.8 ± 0.9 years | Not directly recorded as athletes | Not mentioned | Sports injury: 25; falls: 4; taffic accident: 3 |

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| Study                      | Year | Graft type               | Patients at follow-up (N) | Age (year) | Gender (male%) | Comorbidities recorded in studies | The time to surgery | Follow-up | Type of patients (directly recorded as athletes or not) | Causes of injury recorded in studies | Outcomes                                                                 |
|---------------------------|------|--------------------------|---------------------------|------------|----------------|----------------------------------|-------------------|-----------|--------------------------------------------------------|-------------------------------------|--------------------------------------------------------------------------------|
| Ran Sun [85]              | 2015 | Double-bundle hamstring autograft Allogeneic tendon graft | 154 | 27.5 (range: 19-52) | 68.8% | Not mentioned meniscus or collateral ligament injuries | Not mentioned | 3 years | Not directly recorded as athletes | Not mentioned | Side-to-side difference, pivot shift test, Lysholm score, Subjective IKDC score, objective IKDC score, range of motion |
|                           |      |                          |                           |            |                |                                  |                   |           |                                         |                                      |                                                                                |
|                           |      |                          |                           | 270 | 27.7 (range: 19-52) | 72.2% |                                |                   |           |                                         |                                      |                                                                                |
| Lars Peterson [87]        | 2014 | Artificial graft or augmentation | 85 (LOCF method used, actual follow up patients:74) | 27 ± 8 | 63.5% | Cartilage injuries allowed | 16 ± 24 months | 4 years (We mainly used 4 years follow-up data.) | Nearly 80% are active athletes | Not mentioned | Side-to-side difference, Lambach test, pivot shift test, IKDC subjective assessment, Tegner score |
|                           |      |                          |                           | 102 | 27 ± 7 | 53.3% |                                  |                   |           |                                         |                                      |                                                                                |
| Sahnghoon Lee [89]        | 2012 | Single-bundle hamstring autograft | 18 | 29.4(range: 17-56) | 85.7% | Meniscal injury: Medial: 6; Lateral: 7; Both: 4; Medial collateral ligament injury: 1 | 13.1 months (range: 1-65) | Single-bundle: 27.6 months (range: 24-31) | Most are recreational players | Not mentioned | Anterior drawer test, Lachman test, pivot shift test, Side-to-side laxity, Lysholm score, IKDC score, Subjective satisfaction score, Lysholm score, Tegner activity score, Knee strength |
|                           |      |                          |                           | 19 | 31.2(range: 18-58) | 90.5% | Meniscal injury:Medial: 8; Lateral: 4; Both: 1; Medial collateral ligament injury: 1 | 10.2 months (range: 1-57) | Double-bundle: 29.2 months (range: 27-38) | Soccer: 13; basketball: 1; ski: 1; football: 2; volleyball: 1; fall/Slip: 1; traffic accident: 1; others: 1 | Not mentioned |                                                                                |
|                           |      |                          |                           | 60 | 32 ± 10 | 69.2% | Meniscal rupture: Medial: 15; Lateral: 17; Both: 9 | Not mentioned | 28 ± 4 months | Not directly recorded as athletes | Not mentioned | Side-to-side difference, pivot shift test, IKDC score |
|                           |      |                          |                           | 61 | 32 ± 10 | 74.7% | Meniscal rupture: Medial: 20; Lateral: 19; Both: 4 | 36 ± 2 months | Not directly recorded as athletes | Lachman test, pivot shift test, IKDC score, Lysholm score, Tegner activity scale, Side-to-side difference, Tannusel diameter |
|                           |      |                          |                           | 33 | Median age: 23 (20-51) | 90.9% | Single-bundle hamstring autograft: medial meniscus tears: 5; lateral meniscus tears: 3; MCL injuries: 4; Allograft group: medial Meniscus tears: 4; lateral meniscus tears: 3; MCL injuries: 3 | 7.2 ± 10.3 weeks | Not directly recorded as athletes | Sports: 28; fall down: 2; traffic accident: 2; unknown: 1 | Not mentioned | Cynthia knee score, Lysholm score, visual analogue scale, side-to-side difference, Hamstring strength 60 deg/s, Hamstring strength 240 deg/s, Quadriceps strength 60 deg/s, Quadriceps strength 240 deg/s, Triple-jump test involved side, static hop test, Kellgren and Lawrence Classification, pain, Tegner score |
|                           |      |                          |                           | 32 | Median age: 22 (20-55) | 81.3% | Allogeneic tendon graft | 6.5 ± 8.2 weeks | 31.6 ± 10.0 months | Sports: 25; fall down: 4; traffic accident: 3; unknown: 0 | Not mentioned |                                                                                |
|                           |      |                          |                           | 29 | 27 ± 9 | 58.7% | Meniscal damage and other comorbidities allowed | 40.5 ± 41.6 months | 10.7 ± 0.4 years | Not directly recorded as athletes | Not mentioned |                                                                                |
|                           |      |                          |                           | 28 | 25 ± 7 | 64.3% | Meniscal damage and other comorbidities allowed | 41.3 ± 41.0 months | 10.2 ± 0.4 years | Not directly recorded as athletes | Not mentioned |                                                                                |
| S.R.A. Ghalayini [83]     | 2010 | Artificial graft or augmentation | 22 | 31.7(95%CI 29.0-34.5) | 87.5% | Meniscal pathology: 44; degenerative change existed | 36 months (95%CI 35-75) | 5 years | Not directly recorded as athletes | Not mentioned |                                                                                |
|                           |      |                          |                           | 24 | 30.9(95%CI 28.1-33.6) | 73.1% |                                | 33 months (95%CI 19-47) | Not directly recorded as athletes | Auto: 0; Sports: 27; Work-related: 2; Traffic accident: 3; Other/combinations: 1 | Not mentioned |                                                                                |
| Kang Sun[A] [82]          | 2009 | Patellar tendon autograft | 33 | 29.7 ± 72 | 72.7% | Meniscal tears: Medial: 15; Lateral: 17; cartilage damage: 6; Medial ligament injuries: 4 | 1.5 ± 1.2 months | 24.2 ± 5.8 months | Not directly recorded as athletes | Not mentioned | Anterior drawer test, Side-to-side difference, Tannusel diameter, Patellar tendon autograft, Subjective IKDC, Cincinnati knee score, Lysholm score, Tegner score |
|                           |      |                          |                           | 32 | 301 ± 61 | 75.0% | Meniscal tears: Medial: 15; Lateral: 17; cartilage damage: 6; Medial ligament injuries: 4 | 1.6 ± 1.3 months | 25.6 ± 6.7 months | Not directly recorded as athletes | Not mentioned |                                                                                |
| Dean C. Taylor [87]       | 2009 | Patellar tendon autograft Single-bundle hamstring autograft | 24 | 21.7 (range: 18-37) | 78.1% | Meniscal injuries: 16; articular cartilage lesions existed | <3 months: 23;≥3 months: 9 | Not directly recorded as athletes | BTT group: 27 years (95% CI (2.2-3.11); HS group: 32 years (95% CI (2.6-3.77) | Not directly recorded as athletes | Femoral tunnel position, Tibal Tunnel, Single Assessment Numeric score (SANES) Score, Lysholm Score, KOOS Score, Subjective IKDC, Cincinnati knee score, Lysholm score, Tegner score |
|                           |      |                          |                           | 29 | 22.1 (range: 17-44) | 87.5% | Meniscal injuries: 17; articular cartilage lesions existed | <3 months: 24;≥3 months: 8 | Not directly recorded as athletes | Not mentioned | (Continued on next page) |
| Study                     | Year | Graft type                  | Patients at follow-up (N) | Age (year) | Gender (male%) | Comorbidities recorded in studies | The time to surgery | Follow-up | Type of patients (directly recorded as athletes or not) | Grading of injury recorded in studies | Outcomes                                                                 |
|--------------------------|------|-----------------------------|---------------------------|------------|----------------|-----------------------------------|---------------------|-----------|---------------------------------|---------------------------------|--------------------------------------------------------------------------------|
| Nikolaus A. Streich     | 2008 | Single-bundle hamstring autograft | 25                        | 29.2 ± 6.3 | 100%           | Meniscal injury: 12               | 4.2 ± 2.1 months    | 24 months | Athletes                        | Not mentioned                        | Tegner Activity Scores, KT-2000 Anthrometer Results, BDC Score, Lysholm Score, Side-to-Side difference, pivot shift sign |
|                          |      | Double-bundle hamstring autograft | 24                        | 30.0 ± 6.5 | Meniscal injury: 14                      | 5.9 ± 2.3 months    |                       |                   |                                 |                                |                                                                                  |
| Stefano Zufflaggini      | 2006 | Patellar tendon autograft    | 25                        | 30.5(range: 22–47) | 64%            | No meniscal injury, chondral injury and the signs of joint degenerative changes | 8 months(range: 3–13) | 5 years | Not directly recorded as athletes | Not mentioned                        | BDIC, Tegner score, Anterior knee pain, Resisting pain, pivot shift test, Lachman test, Evaluation of stability, range of motion, time of returning to sport, evaluation of tunnel enlargement |
|                          |      | Single-bundle hamstring autograft | 25                        | 31.3(range: 26–49) | 60%            | Meniscal injury: 12               | 9 months(range: 2–12) |          |                                |                                | Lysholm score, Tegner activity level, 1-leg hop test, side-to-side difference, BDIC score, Knee-Walking Test, Subjective Anterior Knee Pain |
| Gauti Lavadl            | 2006 | Patellar tendon autograft    | 40                        | 28 (range: 16–52) | 72.5%          | Meniscal injuries allowed         | 14.5 months (range: 2–240) | 25.5 months (range: 23–33) | 26 months (range: 24–43) | Not directly recorded as athletes | Not mentioned                        |                                                                                  |
| Samir Abdul-Kaïs Hammam | 2005 | Single-bundle hamstring autograft | 45                        | 22.3 (range: 17–34) | 100%           | Meniscal tears Medial: 20; Lateral: 10; Chondral lesions of the medial femoral condyle: 6; The softening and fuzzing articular surfaces of the patella: 18 | 9.7 months (range: 4–13) | 81 months (range: 60–96) | PT group: 30 recreational athletes, 10 competitive athletes; STG group: 32 recreational athletes, 13 competitive athletes; All patients are not professional athletes | Not directly recorded as athletes | Lysholm score, Tegner activity level, Lysholm score, Side-to-side difference, BDIC score, Kneewalking Test, Subjective Anterior Knee Pain |
| K. Eriksson             | 2001 | Patellar tendon autograft    | 80                        | 25.7 ± 6.9 | 58.5%          | Meniscal lesions in 82 patients at initial arthroscopy: medial 47; lateral 53; both 16; Of the 21 sutured meniscal injuries: 16 patients healed at reconstruction; 36 patients presented with 38 new meniscal injuries: medial: 25; lateral: 13; Mild arthritis changes on intraoperative radiographs: 1 patient in semimembranosus group. | 16 ± 24 months | 33 ± 7 months | Athletes                        | Not directly recorded as athletes | Tegner activity level, Lysholm score, VS, BDIC score, extension deficit, flexion deficit, Lachman test, pivot shift test, side-to-side difference |
| Olle Muren              | 1995 | Artificial graft or augmentation | 20                        | 25 (range: 18–36) | 65.0%          | Mean duration of symptoms: 2.5 (0.5–9) years | 4 (range: 3–5) years | Most are recreational athletes | Not mentioned                        | Lysholm score, Side-to-side difference, pivot shift test, Extension deficit 3–5°, Moderate effusion |
|                         |      | Patellar tendon autograft    | 74                        | 25.7 ± 6.9 | 58.5%          | Mean duration of symptoms: 2.5 (0.5–9) years | 4 (range: 3–5) years | Most are recreational athletes | Not mentioned                        | Lysholm score, Side-to-side difference, pivot shift test, Extension deficit 3–5°, Moderate effusion |
| Alberto Gobbi          | 2012 | Single-bundle hamstring autograft | 30                        | 31.9 ± 1.92 (SE) | 50.0%          | 1–2 medial collateral ligament sprain: 3 Meniscal lesions: 10 1–2 chondroplasty: 2 Meniscal lesion + chondroplasty: 4 1–2 medial collateral ligament sprain: 4 Meniscal lesions: 8 1–2 chondroplasty: 2 Meniscal lesion + chondroplasty: 5 | AGL injury reported within 5 months | Mean: 46.2 months; range:36-60 months | Athletes | All sports related: pivoting in playing a sport such as skiing, soccer and karate; 82% a fall during sports such as motocross: 18% In the study’s series, the injuries occurred: playing soccer: 38%, skiing: 33%, motocross: 18%, tennis: 10%, and karate: 3% | BDIC Subjective score, BDIC objective score, Tegner score, Marx, Noyes, Lysholm score, DLarity (mm) Rollimeter, pivot shift test, side-to-side difference, range of motion |
|                         |      | Double-bundle hamstring autograft | 30                        | 28.9 ± 1.89 (SE) | 60.0%          | Mean duration of symptoms: 2.5 (0.5–9) years | 4 (range: 3–5) years | Most are recreational athletes | Not mentioned                        | Lysholm score, Side-to-side difference, pivot shift test, Extension deficit 3–5°, Moderate effusion |

(continued on next page)
| Study                          | Year   | Graft type                      | Patients at follow-up (N) | Age (year) | Gender (male%) | Comorbidities recorded in studies                                                                 | The time to surgery | Follow-up | Type of patients (directly recorded as athletes or not) | Causes of injury recorded in studies | Outcomes                                                                 |
|-------------------------------|--------|--------------------------------|--------------------------|------------|----------------|-----------------------------------------------------------------------------------------------|--------------------|-----------|---------------------------------------------------------|-------------------------------------|--------------------------------------------------------------------------------|
| Johannes Leitgeb [76]         | 2014   | Patellar tendon autograft       | 56                       | 28.4       | 80.4%          | Minor associated injuries: 57 (59%) patients: isolated meniscal tears: 32 patients (33%); isolated cartilage lesions: 14 patients (13%); combination of both injuries: 11 patients (11%). | Within 12 days after injury: 31 patients (32%); After 12 weeks: 65 patients (68%). | Mean: PT:5.2 years; HT:5.4 years | Athletes                                              | Not mentioned                        | IKDC score, IKOS results, Kneeing pain, Range of motion |
| Kang Sun [84]                 | 2011   | Single-bundle hamstring autograft | 36                       | 30.9 ± 8.7 | 77.8%          | Medial meniscus tear: 15; Lateral meniscus tear: 14; Cartilage damage: 8; Medial ligament injury: 4 | 1.6 ± 1.3 months   | 41.5 ± 7.6 months                                             | Not directly recorded as athletes | Automobile: 0; sports: 32; work related: 1; traffic accident: 2; other/missing: 1 | Overall IKDC, Hamner vertical jump test, range of motion, Daniel I, leg hop test, pivot shift test, anterior drawer test, Lachman test, side-to-side difference, Subjective IKDC score, Cincinnati knee score, Lysholm score, Tegner score |
| Allogeneic tendon graft       | 31     |                                |                          | 30.3 ± 7.9 | 77.4%          | Medial meniscus tear: 14; Lateral meniscus tear: 13; Cartilage damage: 7; Medial ligament injury: 3 | 1.8 ± 1.3 months   | 43.0 ± 7.1 months                                             |                                                                 | Automobile: 0; sports: 27; work related: 2; traffic accident: 2; other/missing: 0 |                                                                 |
| Kang Sun [83] [85]            | 2009   | Patellar tendon autograft       | 76                       | 31.7 ± 6.3 | 80.3%          | Medial meniscus tear: 32; Lateral meniscus tear: 36; Cartilage damage: 18; Medial ligament injury: 14 | 1.9 ± 1.0 months   | 5.6 ± 1.2 years                                             | Not directly recorded as athletes | Automobile: 0; sports: 65; work related: 7; other/missing: 4 | Overall IKDC, Hamner vertical jump test, range of motion, Daniel I, leg hop test, pivot shift test, anterior drawer test, Lachman test, Lysholm score, Tegner score |
| Allogeneic tendon graft       | 80     |                                |                          | 32.8 ± 7.1 | 78.8%          | Medial meniscus tear: 32; Lateral meniscus tear: 40; Cartilage damage: 20; Medial ligament injury: 12 | 2.1 ± 1.1 months   | 5.6 ± 1.3 years                                             |                                                                 | Automobile: 2; sports: 66; work related: 6; other/missing: 6 |                                                                 |
| Julian A. Feller [62]         | 2003   | Single-bundle hamstring autograft | 31                       | 26.3 ± 6   | 70.6%          | Chondral lesions: 5; Medial meniscal treatment: 12; Lateral meniscal treatment: 6 | 14.2 ± 15 weeks   | 3 years                                                  | Not directly recorded as athletes | Participating in sports: 56, Australian Rules football and basketball are the most; Injured at work: 5; Injured accidentally: 4 | Subjective pain measurement, range of motion, side-to-side difference, isokinetic torque deficits, Cincinnati Knee Score, IKDC score, pivot shift test |
| Patellar tendon autograft     | 26     |                                |                          | 25.8 ± 6   | 74.2%          | Chondral lesions: 8; Medial meniscal treatment: 16; Lateral meniscal treatment: 9 | 19.8 ± 23 weeks   |                                                                 |                                                                 |                                                                 |                                                                 |
| BJORN ENGSTROM [61]           | 1993   | Patellar tendon autograft       | 26                       | 23.8 ± 5.9 | 46.7%          | Medial collateral ligament ruptures: 4; medial meniscus injuries: 7; lateral meniscus injuries: 3; medial meniscus–lateral meniscus injuries: 1 | 33.9 ± 30.4 months | 28.5 months (range, 12–50 months) | Not directly recorded as athletes | Most during playing soccer: 24; other pivoting sports: 19; | Pivot shift test, instrumented laxity test, Lysholm Knee Score, IKDC score |
| Artificial graft or augmentation | 29     |                                |                          | 23.4 ± 5.8 | 70.0%          | Medial collateral ligament rupture: 1; medial collateral ligament rupture + medial meniscus injuries: 2; medial meniscus injuries: 10; lateral meniscus injuries: 3 | 31.0 ± 25.1 months |                                                                 |                                                                 |                                                                 |                                                                 |
| Mark D. Shaieb [70]           | 2002   | Single-bundle hamstring autograft | 37                       | 30 (range, 14 to 53) | 56.8%          | Medial meniscus/partial resection: 7; Lateral meniscus/partial resection: 5; Medial and lateral meniscus/partial resection: 2; Lateral meniscus/repair: 4; Patients with Chondromalacia 10 | 18.9 weeks | Average: 23 months; range: 24 to 45 months | Competitive athletes: patellar tendon group: 7; hamstring group: 11. The remaining athletes are recreational. | Soccer: 2; skiing: 3; basketball: 1; baseball; 2; football; 3; volleyball: 5; softball: 2; martial arts: 0; work: 2; motor vehicle accident: 3; other: 2 | Lysholm score, patellofemoral pain and loss of motion, side to side difference, pivot shift test |
| Patellar tendon autograft     | 33     |                                |                          | 32 (range, 14 to 48) | 78.8%          | Medial meniscus/partial resection: 8; Lateral meniscus/partial resection: 7; Medial and lateral meniscus/partial resection: 2; Lateral meniscus/repair: 9; Patients with Chondromalacia 7 | 19.5 weeks |                                                                 |                                                                 |                                                                 |                                                                 |

* Statement: Table 3 shows the basic information of the included studies and corresponding patients. For the sake of rigor, many contents in Table 3 are the same as the records of the included studies. The references are shown in Table 3 and the corresponding places in the article. Some of the data in Table 3 were recorded from the earlier reports of the corresponding studies and we indicated the references in the article.

ACLR = anterior cruciate ligament reconstruction; VAS = visual analogue scale; IKDC = International Knee Documentation Committee.
(3) the type of graft; (4) outcome details: IKDC evaluation results, pivot shift test results, Lachman test results and Lysholm scores in included studies were collected. According to some studies [91], different versions of scores were allowed because their functions are similar, and units and data types are same, which could be used together in the network meta-analysis. For example, the different versions of IKDC evaluation such as overall/final IKDC (mostly old version of IKDC), IKDC score (recorded as grades and numbers of patients, the IKDC version was not specified and not considered as only subjective IKDC) and the objective IKDC(mostly new version of IKDC) were used together in our analysis because they are all in form of count data and objectively reflect the knee status. The subjective IKDC was not used for analysis. Possible different ways of ligament examination(Lachman test and pivot shift test) or different forms of recording the results were allowed and relevant data would be extracted and pooled. Only the extracted complete data would be pooled.

The risk of bias was assessed using the Cochrane collaboration tool [39]. The tool was used to detect the following potential biases in included studies: (1) the selection bias. The evaluation of the selection bias is mainly based on the evaluation of random sequence generation and allocation concealment; (2) the performance bias and the detection bias. The evaluation of these two biases is mainly based on the evaluation of blinding method of the included studies; (3) the attrition bias. The evaluation of this bias is mainly based on the evaluation of incomplete outcome data; (4) the reporting bias. The evaluation of this bias is mainly based on that whether the results of the studies were selectively reported or not; (5) other bias. The evaluation result of each item may be high risk of bias, low risk of bias or unclear risk of bias, and the final results are presented in figures.

Data processing and statistical analysis

The data for analysis in included studies were extracted as recorded. We also extracted data by inferring from the descriptions in the studies (such as “no lost”). We didn’t abandon studies or data on account of some factors unrelated to the topic of our network meta-analysis, like different previous histories, different operation procedures such as whether to use the arthroscopy or different fixation methods, patients with different complications, re-operation or others, we didn’t consider them as the exclusion or classification criteria. Generally, the longest observation results in included studies were used in analysis. Lysholm score was analyzed as the continuous variable, and the results of pivot shift test, Lachman test and IKDC evaluation were analyzed as count data. However, some articles recorded results in different ways. For example, in different articles, Lysholm score was recorded by most authors in the form of mean ± standard deviation or standard error, but some authors recorded it in the form of interval-number of people or median-range. If the latter two forms of records were abandoned, it would bring a large error and bias to our meta-analysis. Therefore, it is necessary to unify the reasonable data form. For the data recording method of interval—number, the weighted mean and weighted standard deviation were calculated by using the median of each interval. When a study showed the mean (no standard deviation or standard error), and the interval—number, we used the interval—number to calculate the weighted mean and the weighted standard deviation, which made the standard deviation match the mean. For the median-range data recording method, we calculated the standard deviation using the formula SD = range/4(15<n<70) or SD = range/6(n>70), and estimated the mean with the median (n>25) or use the formula m ≈ (a + 2M + b)/4(n ≤ 25) mentioned in Stela Pudar Hozo et al.’s study [40]. Only when the statistical methods of the results of IKDC evaluation, pivot shift test as well as Lachman test in included studies were in the form of count data, then we chose and recorded data. We counted the numbers of people with not normal or not A in the IKDC evaluation and counted the numbers of people with not normal, not 0, not negative, or not A in the Lachman test and pivot shift test as indicators of bad prognosis.

We used GeMTC, rjags, meta and other necessary packages in R 3.5.1 software (JAGS 4.3.0 software should be installed) to complete all the network meta-analysis [41,42,97]. Random effects model was used to analyze. The network plot was used to represent the relationships among the direct comparisons of various grafts. The more that a graft is mentioned in included studies, the larger the node area is. The more comparisons between the two grafts are, the thicker the line between the nodes is. The relative effect forest plot was used to represent the relationship between the effect values (such as mean difference (MD) and risk ratio (RR)) of different grafts. Then, the surface under the cumulative ranking curve (SUCRA) was used to rank different grafts. The larger the SUCRA is, the better prognosis the graft will be [43,44].

Convergence is a characteristic that must be calculated and verified in the process of network meta-analysis, for Markov Chain Monte Carlo (MCMC) method was used in the network meta-analysis to estimate the distribution of parameters [45]. A very important property of MCMC is convergence. Any inference based on the MCMC depends on the assumption that the Markov chain has reached convergence [46]. Because convergence is very important, we used three types of plots: trace plot, density plot and Brooks–Gelman–Rubin diagnosis plot to verify the convergence of the network meta-analysis. Potential scale reduction factor (PSRF) was also used to verify the convergence. We can know whether each chain achieves stationary distribution and good overlapping with other chains in the calculation process through the trace plot, so as to judge whether the model convergence is satisfactory [47]. The satisfactory convergence depends on enough iterations, which is shown in the trace plot as each chain overlaps with other chains, and the iteration process of any chain cannot be identified [48]. Density plot is also used to diagnose the

Figure 2. Network plots of the comparisons of Lysholm score and IKDC evaluation. (A) Lysholm score. (B) IKDC evaluation. The node area represents the number of studies containing each graft, and the line thickness represents the number of studies between the two grafts. The size of the nodes and the thickness of the lines are only used to compare the relative sizes, and only the nodes and lines in a same network plot can be compared. The same as below. The letters corresponding to the grafts are shown in Table 2. IKDC = International Knee Documentation Committee.
convergence of the model. The bandwidth value in density plot can be used as a quantitative assessment. The smaller the value is, the smaller the difference between the distribution range of the parameter's posterior value and the preset distribution range is. The bandwidth value becomes stable and approaches 0 after sufficient iterations [49]. A smooth curve with stable bandwidth indicates good convergence [50]. Brooks–Gelman–Rubin diagnosis plot and potential scale reduction factor (PSRF) are the methods of combining graphical and quantitative to verify convergence [51,52]. Median shrink factor close to 1, 97.5% shrink factor close to 1 and PSRF close to 1 mean that the convergence is good according to Brooks and Gelman's suggestion [53].

Heterogeneity and publication bias were presented by $I^2$ and funnel plot, respectively [54,55]. The heterogeneity of each comparison is shown by corresponding forest plots. Another important parameter of the network meta-analysis is consistency, which refers to the similarity between the results of direct and indirect comparisons [56,57]. The node-splitting method is a method to prove the consistency [58]. Using the node-splitting method, $p$ values are provided to verify the consistency.

Figure 3. Relative effect forest plots of the comparisons of Lysholm score and IKDC evaluation. (A) Lysholm score. (B) IKDC evaluation. The position of the invalid line in the forest plot represents the position of the effect value corresponding to the graft being compared. Each forest plot shows the effect value (Mean difference or RR) and 95% confidence interval of the other grafts compared to the grafts being compared. We didn't conclude as significant statistical difference when both corresponding 95% confidence intervals of the two interventions (e.g., the 95% confidence intervals of A vs B and B vs A) are 1 (RR) or 0 (MD) at one side. The same as below. The letters corresponding to the grafts are shown in Table 2. IKDC = International Knee Documentation Committee.
between direct and indirect comparisons [59]. Inconsistencies mean there are differences between direct and indirect evidence that we need to interpret the results cautiously.

Results

Features of included articles

Fig. 1 shows the process of searching and selecting studies. A preliminary search was conducted from PubMed, Ovid (MEDLINE and Embase) and the Cochrane Library. The search date was set to February 2020, and a total of 2000 studies were obtained. After excluding duplicate articles, conference abstracts or letters, articles with unmatched type (for example a cohort study actually), studies unable to obtain the full text, irrelevant articles and retractions, 1858 studies were excluded. One hundred forty-two studies were considered relative to our meta-analysis. We further screened these studies and excluded unmatched group dividing studies, studies with no available or relative data, studies with incomplete data, studies with short-term follow-up and other studies needed to be excluded according to the search strategy. Finally, 30 studies were included [12,60–73,75–79,81–89,92].

A total of five different graft types were included in the included studies, and the corresponding letters used in this study are shown in Table 2. Table 3 summarizes the basic characteristics of the included studies and patients. The basic data were recorded in accordance with the included studies and some referred to earlier reports of these studies [74,80,90]. Some basic data, such as age, gender, comorbidities, causes of injury, the time to surgery and others, may come from different observation points and patient groups such as at time of surgery or end of follow-up, according to the authors’ records in the studies. Some related details of patients groups and record time are shown in table S1-4, which show age related patient group was the group at the beginning of the trial or at follow-up, the age of the patients was the age at the surgery, at follow-up or not stated clearly (probably at the time of surgery), and the details of gender, comorbidities and causes of injury related patient groups. Some data, such as age and time, may be recorded as general description, median or mean, with no other parameters, range, SD, SE or 95%CI, etc. The forms of data records are not specific in Table 3. Some of the time data in Table 3 were recorded as general descriptions like “3 years”, which represented general follow-up time, the final follow-up time or the minimum follow-up time, etc. More specific information is showed in the included studies. The numbers of patients recorded in table 3 are the numbers of followed up patients mentioned in included studies, but in the process of data extraction for each analysis, the sample sizes were determined according to the specific records of the included studies. Not all results in the Outcomes in Table 3 were used. In records of Outcomes in Table 3, the items referred “Lysholm”, “IKDC”, “Lachman” and “pivot shift” were checked and we chose the available data according to the data collection methods. The items referred IKDC in Outcomes in Table 3 such as IKDC score, IKDC assessment, IKDC and other items referred IKDC were all checked and we selected available data according to the data collection methods as the IKDC evaluation data. Some studies’ data, which are though indicators used in our network meta-analysis, were not used when we couldn’t extract the available or definite data in a study. And some results not used are not mentioned in the Outcomes in Table 3. We recorded the numbers of followed up patients of corresponding groups in

Figure 4. SUCRA plots of the comparisons of Lysholm score and IKDC evaluation. (A) Lysholm score. (B) IKDC evaluation. The SUCRA can be compared in each plot. The letters corresponding to the grafts are shown in Table 2. IKDC = International Knee Documentation Committee; SUCRA = surface under the cumulative ranking curves.

Figure 5. Network plots of the comparisons of Lachman test and pivot shift test. (A) Lachman test. (B) Pivot shift test. The letters corresponding to the grafts are shown in Table 2.
each study, but the records of followed-up patients in some studies didn’t include patients such as patients with re-rupture, etc. More details about followed-up patients are shown in included studies. Only one of the included studies is a three-arm trial [73], and the rest are dual-arm trials. One or more outcomes of each study might be included in the network meta-analysis. The patients included in the 22 studies are not specifically mentioned as athletes. Here although some studies did not directly indicate that the patients were athletes, but some or all patients may have reached the athletic level of athletes. Sixteen studies recorded the causes of injury. Comorbidities mainly included meniscus-related comorbidities and others. The main comorbidities were recorded in sum, and more specific information of comorbidities may be presented in the included studies. The most common treatments are single-bundle hamstring autografts (21 studies) and patellar tendon autografts (18 studies) as shown in Table 3. More detailed information about the contents of table 3 is in the included studies.

A summary of the risk of bias and risk of bias for each study are shown in Figs. S1A and S1B. Some studies that used pseudo-random sequences in random sequence generation, such as the date of birthday or other ways, were evaluated as high risk, which caused that the allocation might not be hidden. Many of the included studies were evaluated as uncertain or high risk of allocation concealment. The method of blinding in many of the included studies is unsatisfactory. We didn’t set the performance bias as high risk on account of the doctors who performed the operations knowing the protocol (it’s almost inevitable), unless we judged that the relevant outcomes of the studies needed to be used in our analysis would

Figure 6. Relative effect forest plots of the comparisons of Lachman test and pivot shift test. (A) Lachman test. (B) Pivot shift test. The letters corresponding to the grafts are shown in Table 2.
Network meta-analysis of knee scores outcomes

The knee scores used in this network meta-analysis mainly included Lysholm score and IKDC evaluation. Lysholm score is designed for knee function and measured in the form of questionnaire. The IKDC evaluation objectively evaluates the status of the knee joint. The full score of Lysholm score is 100. IKDC evaluation is classified as four classes: normal (A), nearly normal (B), abnormal (C) and severely abnormal (D). The network plots of the comparisons of Lysholm score and IKDC evaluation are shown in Fig. 2A and Fig. 2B, showing the number of studies related to each graft and the number of studies between the two of five grafts. The relative effect forest plots of Lysholm score and IKDC evaluation are shown in Fig. 3A and Fig. 3B. We can find that using patellar tendon autograft can obtain a better IKDC evaluation result, and the difference is statistically significant when compared with artificial graft or augmentation as shown in Fig. 3B. There is no other significant statistical difference among the different grafts in the comparisons of Lysholm score and IKDC evaluation. The SUCRA plots of Lysholm score and IKDC evaluation are shown in Fig. 4A and Fig. 4B. As shown in Fig. 4A, double-bundle hamstring autograft ranks first in Lysholm score, and the last is patellar tendon autograft. As shown in Fig. 4B, patellar tendon autograft ranks first in IKDC evaluation, which means the best result of IKDC evaluation. And the last is artificial graft or augmentation.

Network meta-analysis of knee physical examination outcomes

In the knee joint physical examination, pivot shift test and Lachman test are two physical examinations that can determine the injury of the ACL and can be used to determine the long-term recovery effect after the ACL reconstruction. The network plots of the comparisons of the results of pivot shift test and Lachman test are shown in Fig. 5A and Fig. 5B, showing the number of studies related to each graft and the number of studies between the two of five grafts. The relative effect forest plots of the results of pivot shift test and Lachman test are shown in Fig. 6A and Fig. 6B. The comparison result of Lachman test shows that the positive rate of the double-bundle hamstring autograft corresponding to Lachman test is the lowest, and the differences are statistically significant compared with other grafts except patellar tendon autograft and artificial graft or augmentation. Allogeneic tendon graft corresponds to the highest positive rate of Lachman test. The differences are statistically significant except compared with artificial graft or augmentation. The comparison result of the pivot shift test shows that the double-bundle hamstring autograft has the lowest positive rate of pivot shift test, and the difference is statistically significant when compared with allogeneic tendon graft. Allogeneic tendon graft corresponds to the highest positive rate of pivot shift test. The difference is statistically significant when compared with double-bundle hamstring autograft. The SUCRA plots of the results of pivot shift test and Lachman test are shown in Fig. 7A and Fig. 7B. As shown in Fig. 7A and Fig. 7B, double-bundle hamstring autograft ranks first in Lachman test and pivot shift test, which means the best results of Lachman test and pivot shift test. And the last is allogeneic tendon graft.

Convergence, consistency and heterogeneity of network meta-analysis

The convergence tests of network meta-analysis are shown in Fig. S2 (A-D). In the trace plots of the four comparisons, the iteration process of any chain cannot be identified, and each chain in each trace plot achieves stationary distribution and good overlapping with other chains. The curves in each density plot are relatively smooth. All band-width values are stable. All Brooks–Gelman–Rubin diagnostic plots and calculation results showed that the median shrink factors, 97.5% shrink factors and PSRF values are close to 1. It can be inferred from the above that the convergence of our network meta-analysis is acceptable. The heterogeneity forest plots and funnel plots of the comparisons in network meta-analysis are shown in Figs. S3 (A–D). As can be seen from the heterogeneity forest plots and funnel plots, there is no obvious heterogeneity or bias in IKDC evaluation. However, some subgroup comparisons of Lysholm score, Lachman test and pivot shift test may have heterogeneity and bias for I² > 50%, and asymmetric funnel plots of Lachman test and pivot shift test may be related to publication bias or heterogeneity. The sources of heterogeneity may be differences in the clinicians’ assessments of physical examinations or other aspects. According to the Cochrane handbook [93], the random effects model was used to analyze in this meta-analysis. Then, we used the node-splitting method to verify the consistency of the network meta-analysis, as shown in Fig. 54 (A–D). No significant inconsistency is shown in all the comparisons for all p > 0.05, so it is feasible to conduct network meta-analysis. Generally, the acceptable consistency, heterogeneity and convergence make our network meta-analysis have less limitations that affect its validity.

Discussion

In this study, we used a kind of new method, network meta-analysis, to compare the long-term outcomes of different ACL grafts. This method has been used in several studies, but no study on the same topic has been found. Conventional meta-analyses of the prognosis of different ACL grafts have been performed but only for direct comparisons of the two kinds of interventions [94]. It is not rigorous to directly rank the grafts based on the existing conventional meta-analysis, because there is no evaluation of the consistency of evidence and other. Doing a network meta-analysis can make a systematic review of all included studies. We
can analyze and rank more than two treatment measures by a network meta-analysis, which is beyond the scope of general meta-analysis [95].

In this network meta-analysis, we selected a total of five common grafts to rank and evaluate the five grafts from four items: Lysholm score, IKDC evaluation, Lachman test and pivot shift test. The results of the ranks shown in different items are not exactly the same, suggesting that different types of grafts may have different advantages. We can find that the Lysholm score is obtained when artificial graft or augmentation is used, but the results of other items are not satisfactory. A good Lysholm score is obtained by using double-bundle hamstring autograft, and the results of Lachman test and pivot shift test are also satisfactory, which means that the prognosis of double-bundle hamstring autograft is satisfactory. Patellar tendon autograft is a right choice which only shows the disadvantage on the Lysholm score. The prognosis of patients with single-bundle hamstring autograft is inferior, the differences between single-bundle hamstring autograft and some superior ranking grafts are small. Therefore, we could consider that the prognosis of patients with single-bundle hamstring autograft is ordinary. But it should be noted that we mainly used the studies related to 4-strand(quadrupled) hamstring autograft for network meta-analysis, for that 4-strand(quadrupled) hamstring autograft is common used in clinical. Allogeneic tendon graft may not be a good choice because it does not show any advantage in comparisons. The evidence supporting the artificial graft or augmentation is insufficient, and more studies are needed. Therefore, according to the results of this network meta-analysis, it is more recommended to use double-bundle hamstring autograft in ACLR. However, it should be noted that graft selection is based on the clinician and the patients. Although double-bundle hamstring autograft shows advantages in this network meta-analysis, it may cause the opposite effect if the more difficult surgery failed.

One of the advantages of network meta-analysis is to combine the direct and indirect evidence to analysis [96], and network meta-analysis preserves randomization of original evidence when pooling the original studies. The network meta-analysis is not complicated in calculation, and the mathematical model used is also clear. However, there are also some defects in the network meta-analysis: first, the data of three-arm and above studies are special in statistics, and sometimes, they need to be divided into two arms and second, when the consistency is not satisfactory, the interpretation of the results should be cautious, because the authenticity of the indirect evidence is questionable. In this network meta-analysis, the three-arm study was reasonably divided, and the consistency is satisfactory.

The limitations of this network meta-analysis are reflected in some aspects. First, some studies didn’t realise the randomization, allocation concealment and double blindness, which may cause the outcome bias. Although it is very difficult to use double blindness because the placebo method does not exist during surgery. However, we are able to cover both the control and experimental incision sites with sterile dressings in all patients and tell the patients not to remove the dressings without permission. Although the pain sites are different, patients can no longer easily determine whether they are in the experimental or control group. This may reduce the bias of studies. Second, there is heterogeneity and bias in some comparisons. The data finally included in the analysis may have heterogeneity. In addition to the related description in the study, other possible sources of heterogeneity may exist, for example, in some studies, though the mean or median or general description of follow-up time is 2 years or more, the follow-up time for some patients may be less than two years. We chose these studies because we thought that overall results from mean or median 2 years or more follow-up could reflect long-term outcomes. Some studies excluded the influence of complications or other factors, some studies didn’t exclude, and some studies obtained the results through some statistical methods such as LOCF method, etc. When extracting data, we made subjective analysis when necessary to extract data that we thought were correct and appropriate. So heterogeneity is inevitable. Although the random effects model was used to analyze, the heterogeneity will still affect the credibility of evidence. Third, during the analysis, we found that when using the GeMTC package to repeat calculation on the same set of data, although the ranking results were relatively stable, there were some slight differences between the results of repetitive calculations such as relative effect forest plot results, etc. When the effects of the two interventions are very close, the results of the SUCRA plot and the relative effect forest plot may not be completely consistent. Using a better-featured computer may get more accurate results because more iterations can be performed. So in summary, it is necessary for us to be careful to interpret the results of our network meta-analysis.

To sum up, our network meta-analysis may be an appropriate analysis method to provide clinical evidence. The available studies were used for evaluation of therapeutic efficacy to analyze the long-term prognosis of different ACL grafts. We finally ranked the grafts based on four items as referred and stated our opinions.

Author contributions

All authors have made a contribution to the article and also read and approved the submission of the manuscript.

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This article does not contain any studies with human participants or animals performed by any of the authors.

Data sharing statement

No additional unpublished data are available.

Conflicts of Interest Statement

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jot.2020.03.008.

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