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Review Article

Autografts promote post-operative activity level compared to allografts in posterior cruciate ligament reconstruction: a systematic review and meta-analysis

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Abstract: Objective: To compare the clinical outcomes of autografts with allografts in PCL reconstruction. Methods: Data bases including Pubmed, Cochrane Library databases, Web of Science, and Grey literature were searched from their inception to January, 2017. Literature search, quality assessment, and data extraction were independently conducted by two investigators. The data were analyzed by using the Cochrane Collaboration Review Manager software (RevMan, version 5.3). The primary outcomes were overall IKDC levels and subjective IKDC scores. The secondary outcomes included Lysholm scores, TAS, instrumented knee laxity test and complications. Results: A total of 5 studies containing 130 patients in autograft groups and 122 patients in allograft groups were included. Study quality was evaluated by using the Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analyses. The results of meta-analysis revealed that autografts can significantly promote the level of TAS (MD: 0.46, [95% CI: 0.03 to 0.90]; P=0.04) compared to allografts for patients after PCL reconstruction. As for complication aspect, paresthesias or pains at donor-site or incision were higher frequency of occurrence in autograft groups compared with allograft groups (OR: 4.46 [95% CI: 1.81 to 10.96]; P=0.001). There was no significant difference between autografts and allografts with respect to overall IKDC levels, subjective IKDC scores, Lysholm scores, and instrumented knee laxity test. Conclusions: Autografts can provide a higher level of postoperative activity than allografts for patients after PCL reconstruction. The finding is limited by the quantity of included literatures and the lack of randomized controlled trials.

Keywords: Autograft, allograft, posterior cruciate ligament, reconstruction, systematic review/meta-analysis

Introduction

Posterior cruciate ligament (PCL) injuries are common injuries of all knee ligament injuries [1, 2]. Traffic accidents and athletic injuries were the most common injury causes according to the clinical epidemiology analysis in German and China [3-5]. PCL reconstruction showed a better satisfactory and knee stability compared with conservative treatment for patients with isolated PCL injury [6]. However, there still exists some controversies and challenging areas in orthopedic practice of PCL reconstruction [7]. Which graft (allograft or autograft) to use in PCL reconstruction is one of the most controversial issues. Autograft has advantages in certain aspects, such as availability, free tissue rejection, free disease transmission and faster graft incorporation. The common disadvantages of autograft include longer surgical time, graft size limitations and donor-site complications [8-11]. Most of these disadvantages are derived from the harvest process. As for allograft in comparison, its advantages contain reduction of surgical time, without donor-site morbidity, the ability to have grafts of sufficient length and diameter, being more appropriate for revision surgery, and shorter rehabilitation time [12-14]. However, its disadvantages are also obvious, such as disease transmission, possible immune rejection response, delayed incorporation, poorer stability, and increased failure rate [15-21].

There was only one systematic review published in 2013 on allograft versus autograft in PCL

reconstruction. This article has draw a conclusion that the available evidence cannot determine which graft showing more effect due to the lack of article directly comparing allograft with autograft in PCL reconstruction [22]. Recently, direct comparison articles between allografts and autografts in PCL reconstruction have become increasingly more available. Since there is no consensus on this topic, so we performed this meta-analysis to explore which graft is better for PCL reconstruction.

Materials and methods

Protocol

This study abided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) [23].

Search strategy

The search strategy was made according to the guidance of the Cochrane Handbook. We electronically searched the following databases: PubMed, Cochrane Library databases, Web of Science, and Grey literature. All studies comparing allograft with autograft for PCL reconstruction were searched in electronic databases by two authors independently. The key words included "posterior cruciate ligament", "reconstruction", "allograft", and "autograft". The search time was set from inception to January, 2017. We also manually searched the reference lists of all retrieved studies and published systematic reviews/meta-analysis, and included all identified relevant articles.

Eligibility criteria

Inclusion criteria for the study were as follows: (1) studies comparing allograft with autograft for PCL reconstruction, (2) pubulished in English, (3) human subjects, (4) patients with isolated grade II/III PCL injuries, (5) patients had failed conservative treatment and were deemed clinically and functionally unstable, (6) available outcomes of clinical and functional, (7) follow-up time more than 24 months, (8) randomized controlled trials (RCTs), prospective and retrospective non-randomized trials, and case series.

Exclusion criteria were: (1) technique articles, (2) case reports, (3) studies including knee multi-ligament injuries (including posterolateral corner injuries), PCL bony avulsion, revision PCL surgery, or associated fracture of the ipsilateral lower extremity.

Study identification and data extraction

All titles of searched articles were firstly viewed by two authors independently. Secondly, article abstracts associated with the topic were reviewed. Full articles were reviewed if information in the abstracts were insufficient. Data extraction was performed by two authors independently. If there was discrepancy in these procedures, the third investigator was consulted to resolve it.

Assessment of methodological quality

Study quality was evaluated by using the Newcastle-Ottawa Scale (NOS) [24] (range, 0 to 9 stars) for assessing the quality of non-randomized studies in meta-analyses according to the recommendation of the handbook Cochrane Library. This measure assessing the methodological quality enrolled observational is consist of three parts, including selection of cases, comparability of populations, and ascertainment of exposure to risks.

Outcome measures

The primary outcomes were the IKDC (International Knee Documentation Committee) level, including the overall IKDC level and the subjective IKDC score. The secondary outcomes were Lysholm score, TAS (Tegner activity score), the instrumented knee laxity test (KT-2000/1000 or a Telos stress device) and complications.

Statistical analysis

Data analysis was conducted by using the Review Manager statistical 5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Continuous variables were conducted by using mean difference (MD) or standard mean difference (SMD) with 95% confidence intervals (CIs). Dichotomous outcomes were conducted by using odds ratios (ORs) with 95% CIs. When there was no statistical significance ($P>0.1$ and $I^2<50$) of heterogeneity test, a fixed-effect model was adopted in the meta-analysis. Otherwise, a random-effect model was used.

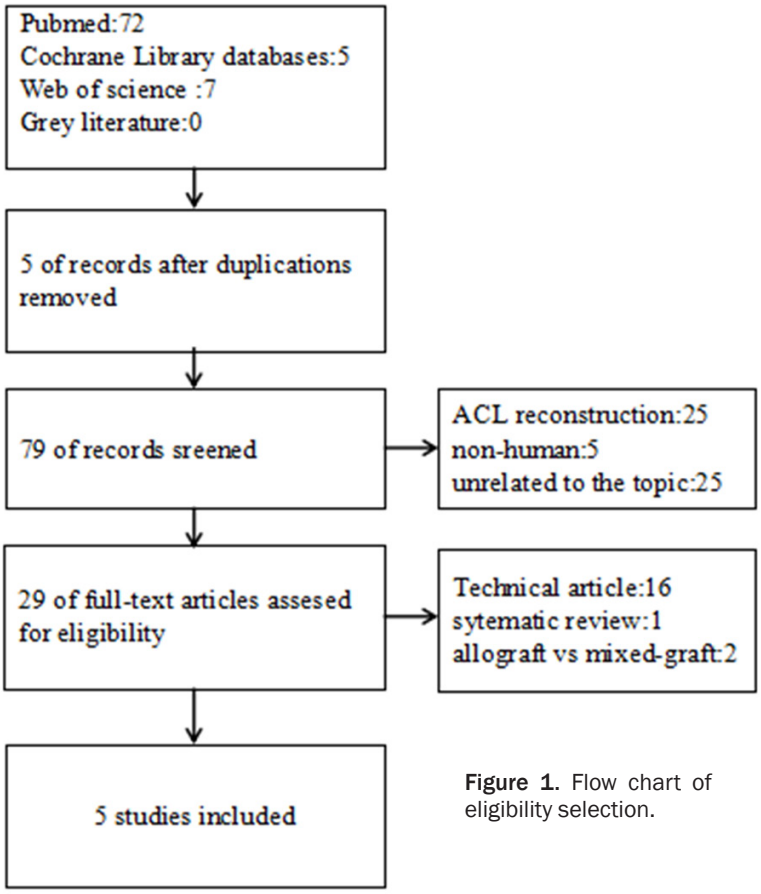

Figure 1. Flow chart of eligibility selection.

Results

Study selection

A total of 84 studies were searched, 5 studies were removed after duplication, then 79 studies remained to be reviewed. The remained studies were excluded for the following reasons: 25 anterior cruciate ligament reconstruction, 16 technical aspect, 5 non-human, 1 systematical review, 2 comparing allograft with mixed graft, and 25 obviously unrelated to the topic. Finally, a total of 5 studies were available for meta-analysis. See flow chart of study selection, **Figure 1**.

Study description

There were 5 studies [25-29] enrolled in this study. All the studies were non-randomized comparative studies. Among these studies, 2 studies [25, 29] were prospective non-randomized comparative study, and evaluated as level II evidence; 3 studies [26-28] were retrospective case-control study, and evaluated as level III evidence. 3 studies [26, 28, 29] have reported the time from injury to surgery which was ranged from 3.5 months to 9.2 months. All these studies set the follow-up period from 24 months to 68 months (**Table 1**).

Participants

The included studies reported 252 participants, including 130 patients in the autograft groups and 122 patients in the allograft groups. The gender proportion, mean age, and time from injury to surgery between autograft groups and allograft groups showed no significant difference except for the follow-up interval in the article of Ahn [26] showing a significant difference (**Table 1**).

Intervention

All the 5 studies reported the comparison between autografts and allografts in PCL reconstruction. As for autograft groups, 4 studies [26-29] adopted hamstring tendon as their graft source, and 1 study [25] used quadriceps tendon or hamstring tendon as their graft source according to the patient's specific situation. With regard to allograft groups, 2 studies [28, 29] adopted anterior tibial tendon as their graft source; 1 study [26] used achilles tendon as graft source; 1 study [25] employed achilles tendon or anterior tibial tendon as graft source according to the patient's specific situation; and 1 study [27] did not reported the specific graft category (**Table 1**). In the allograft groups, 2 studies [27, 29] reported that allografts used in their studies have been received an irradiation dose of 2.5 Mrad before distribution (**Table 1**).

Outcomes

In regard to the overall IKDC level, 4 studies [25, 26, 28, 29] adopted this assessment criteria. There also exists 2 studies [27, 29] used the subjective IKDC score as their assessment criteria. As for the Lysholm score, all of the 5

Table 1. Demographics of allograft versus autograft in PCL reconstruction (auto/allo)

Study	Study type	Level of evidence	Auto	Allo	Mean age	Sample size	Gender M, F	TIS (mo)	Follow-up interval (mo)
Wang 2004 [25]	PNS	Level II	Quadriceps, hamstring	Achilles, anterior tibial	29±12/30±12	32/23	25, 7/16, 7	NR	33±12 (24-71)/34±11 (24-71)
Ahn 2005 [26]	RCS	Level III	Hamstring	Achilles	30 (16-58)/31 (17-60)	18/18	15, 3/12, 6	9.2 (5-18)/8.4 (4-21)	35 (28-55)/27 (24-36)
Sun 2015 [27]	RCS	Level III	Hamstring	NR	31.1±5.7/33.4±6.4	36/35	27, 9/27, 8	NR	38.4±2.4/39.6±7.2
Li 2015 [28]	RCS	Level III	Hamstring	Anterior tibial	31.3±6.8/32.5±7.4	18/19	13, 5/12, 7	8.9±2.4/9.3±2.9	24/24
Li 2016 [29]	PNS	Level II	Hamstring	Anterior tibial	31.3±6.2/32.2±7.8	26/27	17, 9/16, 11	3.7±2.3/3.5±1.9	66.0±2.4/68.4±3.6

Abbreviations: PNS, prospective non-randomized comparative study; RCS, retrospective case-control study; Auto, autograft; Allo, allograft; TIS, Time from injuryto surgery; NR, not reported; M, male; F, female; mo, months.

Table 2. Results of allograft versus autograft in PCL reconstruction (auto/allo)

Study	Overall IKDC level	Subjective IKDC	Lysholm score	TAS (mm)	IKLT (mm)
Wang 2004 [25]	N: 11/5, NN: 12/9, A: 5/5, SA: 4/4	NA	87.8±9.6/92.3±6.8	4.73±1.66/4.70±1.66	3.16±2.60/2.83±1.70
Ahn 2005 [26]	N: 7/2, NN: 9/12, A: 2/3, SA: 0/1	NA	90 (78-100)/85 (70-95)	NA	2.2±1.8/2.9±1.9
Sun 2015 [27]	NA	81±9/80±10	82±9/84±8	7.7±1.2/7.1±1.6	2.7±1.7/3.6±2.0
Li 2015 [28]	N: 5/6, NN: 9/8, A: 3/4, SA: 1/1	NA	84 (36-100)/85 (38-100)	6 (1-9)/6 (1–9)	4.1±1.7/3.3±1.8
Li 2016 [29]	N: 12/8, NN: 13/16, A: 1/3, SA: 0/0	83.5±6.3/80.2±6.8	87.8±3.6/85.2±3.9	6.8±1.1/6.2±1.7	2.1±1.0/3.5±1.1

Abbreviations: IKDC: International Knee Documentation Committee; N: Normal; NN: Nearly normal; A: Abnormal; SA: Severely abnormal; TAS: Tegner activity score; IKLT: instrumented knee laxity test; NA: No application.

Table 3. Quality indicators from Newcastle-Ottawa scale

Study	Quality Indicators From Newcastle-Ottawa Scale									
	1	2	3	4	5A	5B	6	7	8	Total
Wang 2004 [25]	★	★	×	★	★	★	★	★	×	★★★★★★★
Ahn 2005 [26]	★	★	×	★	★	×	★	★	×	★★★★★★★
Sun 2015 [27]	★	★	×	★	★	★	★	★	★	★★★★★★★★
Li 2015 [28]	★	★	×	★	★	★	★	★	★	★★★★★★★
Li 2016 [29]	★	★	×	★	★	★	★	★	★	★★★★★★★★

Notes: For case-control studies: 1 indicates cases independently validated; 2, cases are representative of population; 3, community controls; 4, controls have no history of PCL reconstruction; 5A, study controls forage; 5B, study controls for additional factor(s); 6, ascertainment of exposure by blinded interview or record; 7, same method of ascertainment used for cases and controls; and 8, non-response rate the same for cases and controls.

studies adopted it as an important evaluation index. But 2 of the 5 studies [26, 28] reported the scores in the form of median (minimum-maximum values) which cannot execute a meta-analyses. In these situation, we asked the author (Ahn JH and Li, B) by email to provided the raw data or data in the form of mean ± standard deviation (M ± SD), but did not get response. So we abandon these data when executed a pooled analyses. With respect to the TAS, 4 studies [25, 27-29] employed it an important factor to evaluate the postoperative knee activity level. 1 of the 4 studies [28] reported the scores in the form of median (minimum-maximum values). We dealt with it like the situation of Lysholm score, and also did not get response from the author (Li, B). All the 5 studies reported the instrumented knee laxity test. All of the 5 studies have adopted the arthrometer side to side difference. But the force and angle used in the the process of instrumental measurement were different. 1 study [25] adopted the force of KT-1000; 1 study [26] adopted the Telos stress machine without reported the specific force and angle, 1 study [27] adopted the force of KT-2000 and angle of 90° flexion; 1 study [28] adopted the force of 132 N and angle of 90° flexion; and 1 study [29] did not report the specific force and angle (**Table 2**).

There existed some complications in both groups. With respect to the postoperative infection, 1 study [25] reported 2 cases in autograft group and 1 suspicious case in allograft group. 2 studies [26, 27] reported the complication of joint stiffness or arthrofibrosis, and all these 2 studies demonstrated no significant difference between graft types. 1 study also reported the complication of reflex sympathetic dystrophy (RSD) in autograft group [25]. 1 study reported the complication of leg muscle thrombosis, 8 cases in autograft group and 7 cases in allograft group [27]. 1 study reported the complications of uncomfortable on the medial side of the knee during activities (auto/allo: 3/4), and stage I radiographic degeneration (auto/allo: 2/1) [28]. 3 studies [25, 27, 28] evaluated paresthesia or pain at donor-site or incision.

Assessment of methodological quality

The treatment method was determined on the preference of patient in 2 studies [27, 28], hospital randomly assigned but limited by allograft availability in 1 study [25], randomly allocated by sealed envelopes in 1 study [29]. Only 1 study [25] utilized an independent examiner. All the 5 studies reported the baseline demographic characteristics of mean age of patients, gender distribution and follow-up interval. There was no significant difference on these demographic characteristics except the follow-up interval in the article of Ahn JH [26] showing a significant difference. 3 studies [26, 28, 29] reported the time from injury to surgery showing no significant difference. 4 studies [26-29] reported the baseline of measurement index, and all showing no significant difference in each study. Within each study, the surgical approach, fixation technique, and postoperative rehabilitation were consistent for every patient.

Two reviewers evaluated the quality of included studies by using the Newcastle-Ottawa Scale (NOS) according to the recommendation of the handbook Cochrane Library. 1 study [26] got 6 stars, 2 studies [25, 26, 28] got 7 stars and 2 studies [27, 29] got 8 stars (**Table 3**). There was

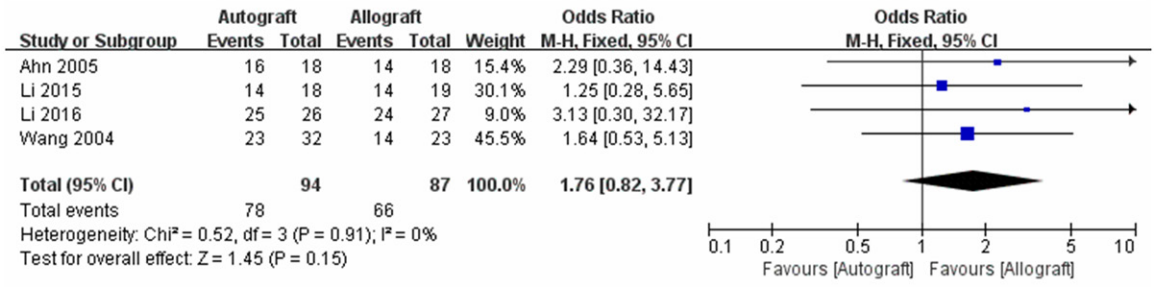

Figure 2. Forest plot of follow-up Overall IKDC level (auto vs allo).

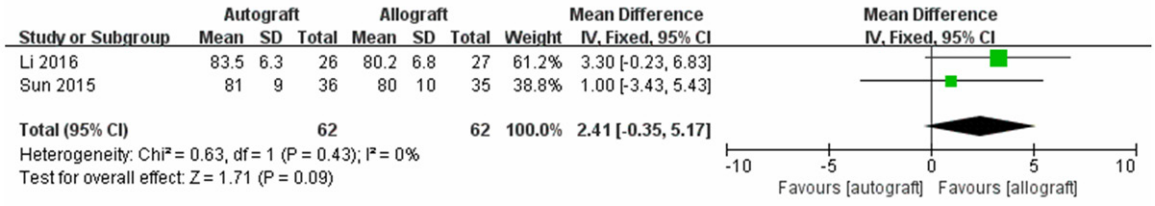

Figure 3. Forest plot of follow-up Subjective IKDC score (auto vs allo).

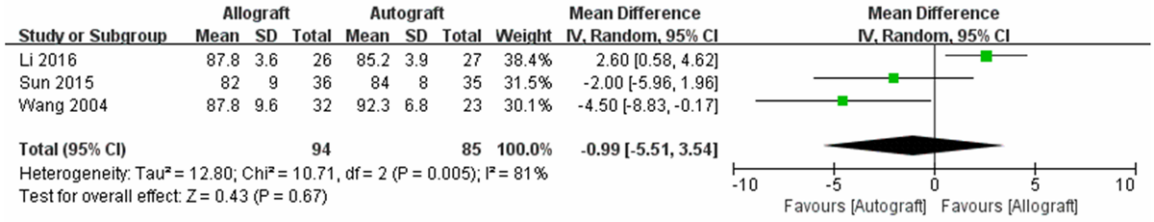

Figure 4. Forest plot of follow-up Lysholm score (auto vs allo).

no validated criteria to define the methodological quality based on the Newcastle-Ottawa Scale (NOS). In Yuhara's article, he considered a study awarded seven or more stars as a high-quality study [30]. So 4 of the 5 included studies [25, 27-29] could be thought as high-quality studies according to this statement.

Meta-analysis of outcomes

Overall IKDC level: 181 patients from 4 studies were received a meta-analysis. The results showed no significant difference between autograft and allograft (OR: 1.76 [95% CI: 0.82 to 3.77]; P=0.15) with no heterogeneity (I^2=0%) (**Figure 2**) [25, 26, 28, 29].

Subjective IKDC score: 124 patients from 2 studies were received a meta-analysis. There was no statistically significant difference between autograft group and allograft group (MD: 2.41, [95% CI: -0.35 to 5.17]; P=0.09) with no heterogeneity (I^2=0%) (**Figure 3**) [27, 29].

Lysholm score: 179 patients from 3 studies were accepted a pooled analysis. The results manifested that there was no significant difference between autograft groups and allograft groups (MD: 0.99, [95% CI: 5.51 to 3.54]; P=0.67) with high heterogeneity (I^2=81%) (**Figure 4**) [25, 27, 29].

Tegner activity score (TAS): 179 patients from 3 studies were included in the pooled analysis. The results indicated that there was a significant difference in favor of autograft groups compared with allograft groups (MD: 0.46, [95% CI: 0.03 to 0.90]; P=0.04) with no heterogeneity (I^2=0%) (**Figure 5**) [25, 27, 29].

Instrumented knee laxity test: All the 5 studies adopted the instrumented knee laxity test as

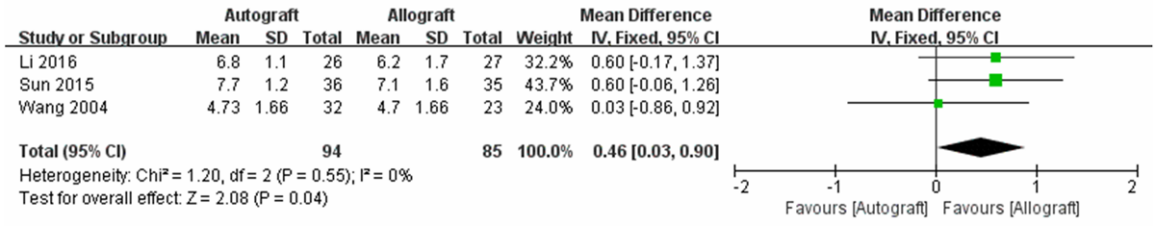

Figure 5. Forest plot of follow-up Tegner activity score (auto vs allo).

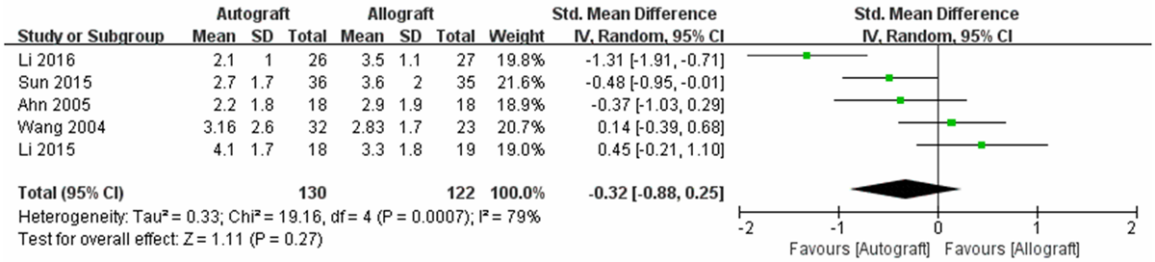

Figure 6. Forest plot of follow-up instrumented knee laxity test (auto vs allo).

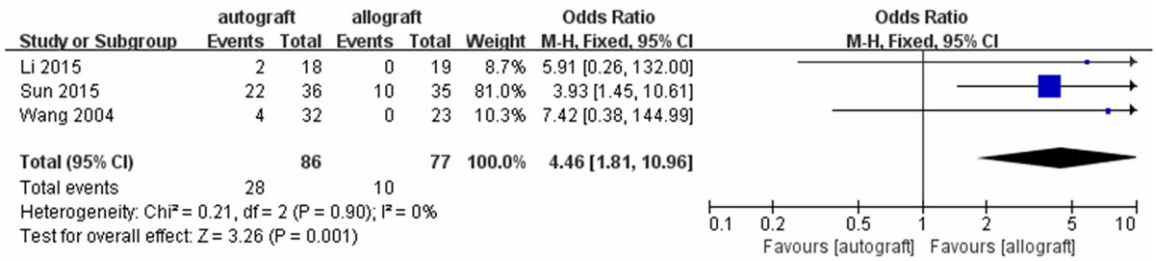

Figure 7. Forest plot of the complications of paresthesia or pain (auto vs allo).

an important factor to evaluate the stability of the knee joint. But the force and angle used in the the process of instrumental measurement were different between the studies. So we adopted the standard mean difference effect measure when executed a pooled analysis. 252 patients from 5 studies received a pooled analysis. The result revealed that there was no significant difference between autograft groups and allograft groups (SMD: -0.32, [95% CI: -0.88 to 0.25]; P=0.27) with high heterogeneity (I^2=79%) (**Figure 6**) [25-29].

Complications: The result of pooled analysis revealed that autograft groups have higher frequency of paresthesia or pain at donor-site or incision compared with allograft groups (OR: 4.46 [95% CI: 1.81 to 10.96]; P=0.001) with no heterogeneity (I^2=0%) (**Figure 7**) [25, 27, 28].

Discussion

This study is an updated systematic review and first meta-analysis on comparing the clinic outcomes of autografts with allografts for PCL reconstruction. The main findings of this study indicate that autografts have advantage over allografts for PCL reconstruction on TAS. And the subgroup analysis based on whether the allograft received gamma irradiation or not, revealed that autografts can significantly decrease the level of instrumented knee laxity test compared with γ-irradiated allografts. There was no significant difference between autografts and allografts with respect to the overall IKDC level, subjective IKDC score, and Lysholm score.

The function of the IKDC level/score is to detect improvement or deterioration in symptoms,

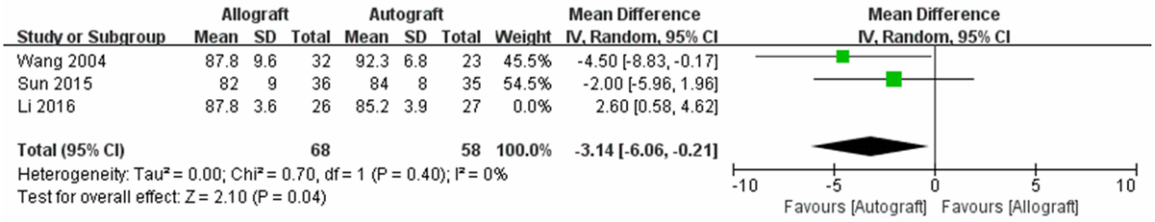

Figure 8. Forest plot of sensitivity analysis of follow-up Lysholm score (auto vs allo).

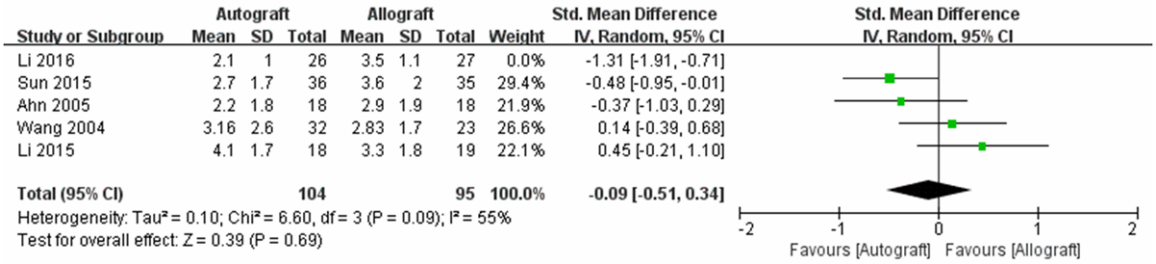

Figure 9. Forest plot of sensitivity analysis of follow-up instrumented knee laxity test (auto vs allo).

function, and sports activities due to knee impairment [31, 32]. 4 studies [25, 26, 28, 29] used the overall IKDC level and 2 studies [27, 29] adopted the subjective IKDC score as their important assessment criteria of the knee function. The Lysholm Knee Scoring Scale is designed to evaluate outcomes of knee ligament surgery, particularly symptoms of instability [32]. In this meta-analysis, we found that there was no significant difference between autografts and allografts for patients' PCL reconstruction with respect to the overall IKDC level, subjective IKDC score, and Lysholm score.

And the purpose of the TAS is to provide a standardized method to grading work and sporting activities after knee injury [33]. The original design of TAS was regarded as a complement the Lysholm scale, so it always been used in conjunction with the Lysholm Knee Scoring Scale to describe the patients' current level of activity [32, 33]. The result of our meta-analysis indicated that autografts can provide a higher level of postoperative activity than allografts for patients after PCL reconstruction.

With respect to the complications, this study found the similar outcomes like many previous studies on the problem of paresthesia or pain at donor-site or incision. The sensory disturbance postoperatively was mainly located at the anteromedial and anterolateral of the knee, where the infrapatellar branch of the saphenous nerve was supplied. Since the nerve is on the surface of gracilis tendon [34], the hamstring harvesting process might damage the branches of the saphenous nerve [35]. Particularly worth pointing out is about the complication of reflex sympathetic dystrophy (RSD) in autograft group [25]. The authors in the study also adopted the fever time and the white blood cells and neutrophils as the index to predict postopertive infection [27]. The fever time after operation in allograft group was significant longer than it in autograft group, and the postoperative white blood cells and neutrophils in the allograft group significant higher than those in the autograft group. But there was no postoperative infection case found in these 2 groups [27]. So the longer fever time and increased white blood cells and neutrophils were considered associated with immune rejection.

Statistical tests of heterogeneity revealed that there were high heterogeneity on the Lysholm score aspect (I^2=81%) (**Figure 4**) and instrumented knee laxity test aspect (I^2=79%) (**Figure 6**). We found that the study published by Li, J [29] may be the source of the high heterogeneity when we performed a sensitivity analysis for Lysholm score and instrumented knee laxity test. When we removed the study published by Li, J [29] from the pooled analysis of Lysholm

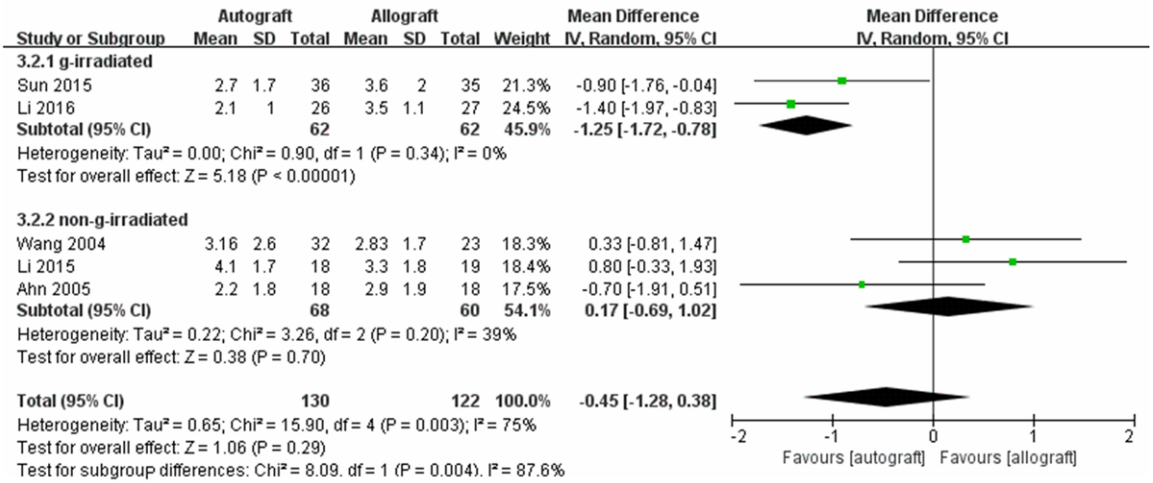

Figure 10. Forest plot of the subgroup analysis of follow-up instrumented knee laxity test (auto vs allo).

score and instrumented knee laxity test we got the I^2=0% (**Figure 8**) and I^2=55% (**Figure 9**), respectively. This might be because the study published by Li, J [29] was a prospective study and adopted random and blind method in some part of the study. As for instrumented knee laxity test aspect, when removed the study published by Li, J [29], there still exist a relative high heterogeneity (I^2=55%) (**Figure 9**). So we executed a subgroup analysis on instrumented knee laxity test aspect based on whether the allograft received gamma irradiation or not. We divided the allograft groups into 2 subgroups, γ-irradiated allograft subgroups (including Sun 2015 [27] and Li 2016 [29]) and non-γ-irradiated allograft subgroups (including Wang 2004 [25], Ahn 2005 [26], and Li 2015 [28]). The subgroup analysis revealed that there was significant difference in favor of autograft groups compared with γ-irradiated allograft subgroups on instrumented knee laxity test (MD: -1.25, [95% CI: -1.72 to -0.78]; P<0.00001) with no heterogeneity (I^2=0%); and there was no significant difference between autograft groups and non-γ-irradiated allograft subgroups (MD: 0.17, [95% CI: -0.69 to 1.02]; P=0.70) with low heterogeneity (I^2=39%) (**Figure 10**) [25-29]. This result revealed that γ-irradiated allograft subgroups showed a more laxity knee than autograft groups. The associations between graft choice and clinical outcome may be distorted by biological of the allograft. According to previous research, gamma irradiation has the features of bactericidal and killing virus, which can be used in the sterilization of allografts. But the process of gamma irradiation may change internal structure biomechanical properties of the allograft tendon [36]. Prodromos et al. reported that irradiated grafts had an abnormal stability rate of 31% vs 12% for non-irradiated grafts [37].

As for the internal validity, the non-randomized design of the included studies limits the validity of clinical conclusions. In particular, selection bias may have been produced by the determination of treatment on the basis of patient preference. In our study, the treatment method was determined on the preference of patient in 2 studies [27, 28], hospital randomly assigned but limited by allograft availability in 1 study [25], randomly allocated by sealed envelopes in 1 study [29]. Furthermore, dropout bias may have been introduced because the patients in retrospective study only reported the patients who received follow-up. Additionally, four studies [26-29] did not involve independent examiners, which may have contributed some observer bias, a distortion, conscious or unconscious, in the perception or reporting of measurements [38].

RCT is the ideal study design for meta-analysis of comparing autograft with allograft in PCL reconstruction. However, in clinical practice, the ethical consideration and allograft availability concern limited the execution of RCT. Forthmore, different patients have a different preference on graft choice. Consequently, a well-designed and high-quality prospective comparative study is the next-best option.

There also exists some limitations among this study. Firstly, the follow-up period was relatively short except 1 study [29] having a 5-years-follow-up (**Table 2**). Secondly, 3 of 5 were retrospective studies, 2 of 5 were prospective studies, and there was no RCTs. The patients were not assigned randomly except 1 study [29], but mainly according to the patients preference, which may increase selection bias. Thirdly, we did not conduct publication bias and meta regression of the published articles due to the limitation of trial number and information.

Conclusion

Autografts can provide a higher level of postoperative activity than allografts for patients after PCL reconstruction. Autografts have advantages over γ-irradiated allografts with respect to the knee stability for patients after PCL reconstruction. Postoperative paresthesias or pains at donor-site or incision in autografts were higher frequency of occurrence compared with allografts for patients after PCL reconstruction. The finding is limited by the quantity of included literatures and the lack of randomized controlled trials.

Disclosure of conflict of interest

None.

Authors' contribution

L Chen, YT Wang, YF Wu, DW Gao, GP Xie contributed equally to this study; GP Xie and DW Gao contributed to study design, data analysis and statistical analysis support; L Chen and YT Wang contributed to literature search, data acquisition and analysis, manuscript drafting and revision; YF Wu contributed to inspect the data, methodology assessment, heterogeneity analysis, sensitivity analysis and subgroup analysis.

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