

SYSTEMATIC REVIEW

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Efficacy and safety of platelet-rich plasma combined with core decompression and enhanced bone grafting versus core decompression with enhanced bone grafting alone in treating femoral head necrosis: a systematic review and meta-analysis

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Abstract

Background The efficacy and safety of platelet-rich plasma (PRP) combined with core decompression (CD)-enhanced bone grafting for the treatment of osteonecrosis of the femoral head remains controversial. This study aimed to conduct a systematic review and meta-analysis of the efficacy and safety of PRP combined with CD-enhanced bone grafting for treating osteonecrosis of the femoral head and to compare this method with CD-combined bone grafting as a way to provide theoretical bases for future clinical treatments and research.

Objective This study aimed to assess the improved efficacy and safety of core decompression combined with platelet-rich plasma-enhanced bone grafting for osteonecrosis of the femoral head compared to core decompression-enhanced bone grafting.

Method We systematically searched several databases for randomised controlled trials comparing bone graft and core decompression with or without PRP, including 16 studies involving 999 subjects and 1139 hip cases. This meta-analysis followed the Preferred Reporting Items (PRISMA) guidelines. The study is registered with PROSPERO under code CRD42024557968.

Result 16 articles involving 999 patients (1139 hips) were included in this study. Pooled analyses demonstrated that when core decompression-enhanced bone grafting was combined with PRP, the Harris hip score (mean difference [MD]: 5.26, 95% CI:4.81–5.71; $P < 0.00001$), visual analog scale (MD: -0.74, 95% CI:-0.99 – -0.49; $P < 0.00001$) and reduction in the need for THA: (risk ratio [RR]: 0.29; 95% CI:0.16–0.53; $P < 0.0001$) were superior to core decompression-

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enhanced bone grafting alone. Furthermore, a pooled analysis confirmed the safety of PRP [RR:0.33; 95% CI:0.13–0.83; $P=0.02$]. All these results were statistically significant.

Conclusion Compared to CD-enhanced bone grafting, the combination of PRP appears to yield superior therapeutic outcomes in restoring hip function, alleviating pain, preventing THA, and ensuring postoperative safety. Moreover, we require a higher level of randomised controlled trials to evaluate its efficacy and safety.

Keywords Femur head necrosis, Core decompression, Platelet-rich plasma, Total hip arthroplasty, Meta-analysis, Systematic review

Introduction

Femur head necrosis, also called osteonecrosis of the femoral head (ONFH), is a disorder of the blood supply to the proximal femur due to several causes, which in turn triggers bone cell death [1]. Common causes include the use of corticosteroids, hip fractures and dislocations, and chronic alcohol consumption [2]. The common age of onset for patients with ONFH is 20–50 years [3]. According to statistics, the number of cases in the United States is increasing at a trend of 20,000 cases per year, with a cumulative total of approximately 300,000–600,000 patients [4]. In China, there are about 8.12 million ONFH patients over 15 years old [5]. Clinical manifestations of femoral head necrosis include hip pain and a limitation of flexion and extension movements. As the disease progresses to an advanced stage, it can lead to the collapse of the femoral head, resulting in a high rate of disability and making it difficult to cure [6]. Currently, there is a lack of clinical cures, and the function of the hip joint can be restored by total hip arthroplasty. However, the drawback of this method is the limited service life and usually requires a second surgery to repair the replaced artificial hip joint at a later stage, which will impose a considerable psychological burden and economic pressure on ONFH patients, particularly younger individuals, therefore, in clinical practice, it is crucial to find a safe and effective method to treat ONFH [7].

Core decompression (CD) is an effective surgical procedure for treating ONFH and is generally more effective than most non-surgical treatment options [5]. When performed before the hip collapses, core decompression theoretically reduces the intraosseous pressure in the affected area, increases blood flow to the necrotic tissue, and improves the likelihood of new bone formation [2]. However, the therapeutic efficacy of CD is controversial [8], and some studies [8, 9] indicate that approximately 37% of patients who undergo the procedure experience femoral head collapse. This may be due to the reduced biomechanical strength of the femoral head following CD, as the surgical process involves the removal of necrotic bone tissue. Consequently, this increases the risk of femoral head collapse [10].

Bone grafting is considered a method that can compensate for CD by providing mechanical support for the

femoral head, thereby reducing the risk of its collapse [11, 12]. The advantage of platelet-rich plasma (PRP) is that its high concentration of platelets can release a variety of growth and differentiation factors at the site of necrosis, thus promoting bone regeneration and bone healing [13]. Currently, the use of PRP treatment for ONFH is increasingly gaining attention as a trending topic of interest [14, 15]. However, there is a lack of comprehensive assessments regarding its overall effectiveness. Therefore, we will evaluate the efficacy and safety of core decompression, both with and without the addition of PRP, in treating femoral head necrosis.

Materials and methods

This systematic review and meta-analysis followed the guidelines established by the PRISMA [16]. It has been registered with Prospero under registration code CRD42024557968.

Search strategy

We searched for articles published in five databases: PubMed, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), and the Chinese Biomedicine (CBM). We used the following keywords: “femoral head necrosis,” “ischemic necrosis of femoral head,” “femoral head aseptic necrosis,” “avascular necrosis of femur head,” and “platelet-rich plasma” (Additional file 1 for the specific search formula). We aimed to find randomised controlled trials of CD-combined PRP-enhanced bone grafting for treating femoral head necrosis. No language restrictions were applied to our search, covering all articles from the databases’ inception until July 4, 2024.

Inclusion and exclusion criteria

Three responsible researchers (JW, BW and LH) independently reviewed all retrieved literature’s abstracts and full texts. Any disagreements that arose were resolved through discussions with the other researchers involved. The process for including and excluding literature adhered to the PICOS principle. The inclusion criteria were as follows: (1) The researched studies that meet clear diagnostic criteria for ONFH (ARCO or Ficat staging). (2) Studies that involved treatments using CD, PRP,

and bone grafting. (3) Studies need to report at least one of the following four endpoints: improvement in HHS, frequency of THA, improvement in VAS, and postoperative complications. (4). Only randomised controlled trials were included.

Included studies were categorized into two groups: the treatment group, which received CD combined with PRP-enhanced bone grafting, and the control group, which received CD-enhanced bone grafting. The exclusion criteria for literature were as follows: replications, reviews, meta-analyses, case reports, conference papers, unrelated trials (including animal studies, trials with other interventions, retrospective studies, and single-arm trials), mechanistic studies, and literature without full text.

Data extraction

The researchers collected the following information from the included studies: authors, year of publication, age of patients, duration of follow-up, country of study, type of intervention, number of hips involved, staging of ONFH, THA conversion rate, HHS and VAS at postoperative follow-up, postoperative complications, materials used for bone grafting, and methods of PRP preparation, including the number and duration of centrifugation and the rotational speed.

Quality assessment

Researchers utilised the Cochrane Risk of Bias tool [17] to assess the risk of bias, and each study was evaluated for the following types of bias: selection bias (randomised sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete data on outcomes), reporting bias (selective reporting) and other bias.

Statistical analysis

We utilised Review Manager 5.4 to analyse four outcomes: improvement in HHS and VAS, conversion to THA, and postoperative complications. For our comparative analyses, we employed risk ratios (RR) for dichotomous variables and mean difference (MD) for continuous variables.

To assess heterogeneity among the included studies, we applied the I^2 statistic. We considered the results to be statistically less heterogeneous when I^2 was less than 50% ($I^2 < 50\%$), in which case we used a fixed effects model for analysis. Conversely, when I^2 exceeded 50% ($I^2 > 50\%$), we recognised significant heterogeneity and opted for a random effects model for our analysis. In addition, when the number of trials reporting the same outcome was ≥ 10 , a funnel plot was generated to analyse publication bias.

Results

Included studies and the characteristics

We identified 244 relevant articles from our database search. After removing 70 duplicates, we were left with 174 articles. Following our screening and exclusion criteria, we excluded 47 articles, which included reviews, conference papers, and meta-analyses; 36 articles related to animal trials; 6 case reports; and 5 mechanistic studies. Next, we screened the remaining 80 articles again. We excluded 43 articles that involved trials with other interventions, 13 articles from single-arm trials, 3 articles that were retrospective analyses, and 3 articles that had missing required data, 1 article could not be located in full text. We obtained 16 articles [14, 18–32] for the meta-analysis. Figure 1 illustrates the selection process.

The 16 studies in our review involved 999 patients (1,139 hips), all of which utilised Ficat or ARCO staging criteria [33, 34]. The follow-up periods ranged from 6 to 72 months. Of these studies, all but one were conducted in China [18–32], the exception was a study from India [14]. All studies [14, 18–32] reported HHS, fourteen studies [18–29, 31–32] reported VAS, eight studies [14–19, 23, 25–28] documented THA, and ten studies [14, 18, 19, 21, 22, 26, 28–30, 32] reported postoperative complications. Specific study characteristics are detailed in Table 1.

In terms of materials for bone grafting, nine studies [14, 20, 24, 26, 27, 29–32] employed autogenous bone grafting, five studies [18, 19, 23, 25, 28] utilised β -tricalcium phosphate bioceramic bone grafting, one study [22] used allograft fibula grafting, and one study implemented tantalum rod grafting [21]. Regarding the preparation of PRP, ten studies [18, 19, 22–25, 27–30] used a secondary centrifugation method, while two studies [14, 26] applied a single centrifugation method. Additionally, 12 studies [14, 18, 19, 22–30] specified the time for PRP preparation, and 11 studies [14, 18, 19, 22–25, 27–30] reported the rotational speed during centrifugation. Specific characteristics are shown in Table 2.

Data extraction and risk of bias assessment

Figure 2 presents a detailed risk of bias assessment for the included studies. Among them, seven studies [18, 23, 25–29] employed random grouping using a random number table method and were assessed as low risk of bias. Two studies [14, 20] utilised computer-generated randomisation and were evaluated as low risk. One study [30] applied the principle of randomisation and was rated as having an unclear risk, while another study [32] used semi-randomised grouping based on the “order of admission” principle, which was also assessed as having an unclear risk. Additionally, one study [24] used baseline comparable principles for grouping and was deemed to have an unclear risk. Moreover, three studies [21, 22,

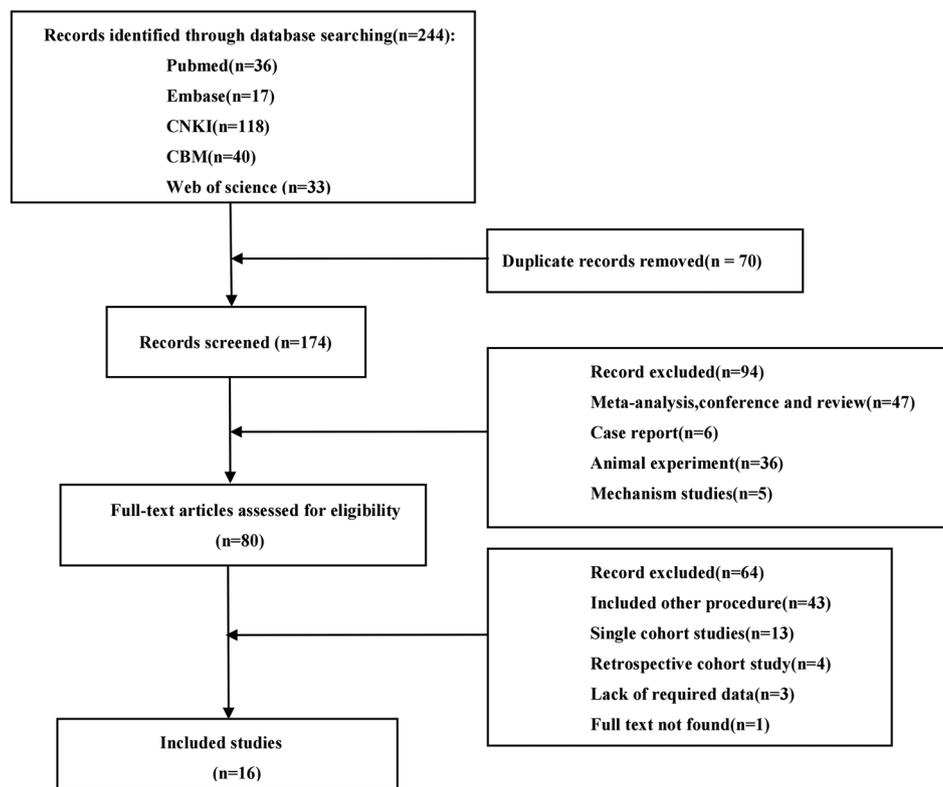


Fig. 1 PRISMA Flowchart for identifying and selecting studies for this meta-analysis

[31] mentioned randomisation but did not provide sufficient methodology details, resulting in an unclear risk assessment. The remaining study [19] was evaluated as high-risk. Regarding blinding, three studies [14, 26, 28] reported double-blinding (where both assessors and participants were blinded), while two studies [18, 27] were labelled as single-blind (where either the participants or personnel were blinded). The other studies [19–25, 29–32] were assessed as having a high risk of bias in this aspect. As for attrition bias, three studies [18, 23, 25] were terminated due to objective factors, such as intertrochanteric femoral fractures caused by car accidents during patient follow-up. The remaining studies [14, 19–22, 24, 26–32] did not exhibit attrition bias. In terms of selective reporting, ten studies [14, 18, 19, 21, 22, 26, 29–32] were assessed as low risk, while the other studies [20, 23–25, 27, 28] were classified with an unclear risk because the ten studies reported postoperative complications, the remaining ones did not provide similar information. Other biases were also considered, including disease stage, postoperative management (such as weight-bearing restrictions, pharmacological rehabilitation, and postoperative functional exercises), and preparation methods for PRP (like centrifugation method and dosage). Therefore, we believe that these factors may create other biases.

Harris hip function score

The 16 studies in the analysis [14, 18–32] all reported HHS. Due to the high heterogeneity observed among the studies, we employed a random-effects model for our meta-analysis. The results of the meta-analysis, illustrated in Fig. 3, indicated that combined PRP appears to be a more effective option for improving hip function (MD = 5.26, 95% CI: 4.81–5.71; $P < 0.00001$).

All studies reported HHS, prompting the generation of a funnel plot (Fig. 4) to assess publication bias. The funnel plot displayed an asymmetrical distribution, which suggests the presence of publication bias. One possible reason for this bias is the variation in follow-up times; however, this does not diminish the significance of our study.

Visual analog scale score

Fourteen studies [18–29, 31, 32] (1015 hips) reported VAS scores, and given the high degree of heterogeneity present ($I^2 = 92%$, Fig. 5), we used a random-effects model. With both using bone grafting, the combined estimate favoured treatment with PRP combined with CD compared with surgery with CD alone. (MD = -0.74, 95% CI: = -0.99 - -0.49; $P < 0.00001$).

Table 1 Essential characteristics of the included studies

Inclusion studies	Country	Sample (patients/hips, Mean age, staging)		Follow-up (month)	Outcomes
		Treatment group	Control group		
Aggarwal 2020 [14]	India	19/25 38.2±10.4 Ficat I-II	21/28 35.2±12.5 Ficat I-II	T:64.3 C:63.7	HHS; THA; postoperative complications
Chai 2021 [18]	China	30/30 43.73±3.25 ARCO II	30/30 44.33±3.17 ARCO II	12	VAS; HHS; THA; postoperative complications
Chen 2020 [19]	China	50/80 43.47±7.23 ARCO II	50/80 45.72±7.43 ARCO II	12	VAS; HHS; THA; postoperative complications
Dai 2019 [20]	China	26/26 46.53±1.25 Ficat I-II	26/26 46.49±1.21 Ficat I-II	6	VAS; HHS
Guo 2022 [21]	China	60/76 51.12±5.86 ARCO II-III	60/84 50.62±5.25 ARCO II-III	12	VAS; HHS; postoperative complications
Jiang 2018 [22]	China	26/35 37.4 ARCO II	24/32 36.7 ARCO II	6	VAS; HHS; postoperative complications
Li 2020 [23]	China	35/35 39.17±6.79 ARCO I-II	35/35 37.06±7.15 ARCO I-II	12	VAS; HHS; THA;
Niu 2021 [24]	China	36/36 37.24±9.81 ARCO I-II	36/36 37.58±9.24 ARCO I-II	6	VAS; HHS
Wang 2019 [25]	China	35/35 39.29±6.67 ARCO I-II	35/35 37.16±7.16 ARCO I-II	12	VAS; HHS; THA
Xian 2019 [26]	China	24/24 28.3±1.4 ARCO II-III	22/22 29.6±1.7 ARCO II-III	36	VAS; HHS; THA; postoperative complications
Yang 2016 [27]	China	15/20 35.6±2.4 Ficat I-II	20/20 37.2±7.1 Ficat I-II	12	VAS; HHS; THA;
Yuan 2019 [28]	China	19/19 45±11 Ficat I-II	20/20 41±14 Ficat I-II	18	VAS; HHS; THA; postoperative complications
Zhang 2021 [29]	China	41/41 37.58±10.26 ARCO II-III	40/40 38.72±11.37 ARCO II-III	6	VAS; HHS; postoperative complications
Zhao 2017 [30]	China	30/32 40.21±5.12 Ficat I-III	30/33 39.25±6.01 Ficat I-III	12	HHS; postoperative complications
Zhao 2023 [31]	China	30/30 30.3±3.04 ARCO II-III	30/30 29.7±4.02 ARCO II-III	12	VAS; HHS
Zhu 2018 [32]	China	22/22 43.23±7.01 ARCO II-III	22/22 44.14±5.67 ARCO II-III	12	VAS; HHS; postoperative complications

ARCO: Association Research Circulation Osseous, T: treatment group, C: control group, HHS: Harris hip score, VAS: visual analog scale, THA: total hip arthroplasty

Conversion to THA

A total of 8 studies [14, 18, 19, 23, 25–28] (538 hips) reported the need for THA, as illustrated in Fig. 6. Due to low heterogeneity ($I^2=0\%$, $P<0.0001$), we employed a fixed-effects model. The pooled analysis results (RR: 0.29; 95%CI:

0.16–0.53; $P<0.0001$) indicate that the rate of THA was lower in the treatment group than in the control group.

Postoperative complications

A total of ten studies [14, 18, 19, 21, 22, 26, 29–32] reported on postoperative complications, as illustrated in Fig. 7. One study [30] identified several complications,

Table 2 Characteristics of interventions in included studies

Inclusion studies	PRP preparation		Interventions		Bone grafting(materials)
	Duration(min)	Rpm(r)	Treatment group	Control group	
Aggarwal 2020 [14]	15	1500	CB + PRP	CB	Autogenous fibular graft
Chai 2021 [18]	20,10	1500	CB + PRP	CB	β -tricalcium phosphate bioceramic bone graft
Chen 2020 [19]	20,10	1500	CB + PRP	CB	β -tricalcium phosphate bioceramic bone graft
Dai 2019 [20]	none	none	CB + PRP	CB	Autogenous iliac bone graft
Guo 2022 [21]	none	none	CB + PRP	CB	Tantalum rod graft
Jiang 2018 [22]	20,10	1500	CB + PRP	CB	Allograft fibula graft
Li 2020 [23]	15, 15	2000, 2200	CB + PRP	CB	β -tricalcium phosphate bioceramic bone graft
Niu 2021 [24]	10, none	1500, none	CB + PRP	CB	Autogenous iliac bone graft
Wang 2019 [25]	10,10	2000,2200	CB + PRP	CB	β -tricalcium phosphate bioceramic bone graft
Xian 2019 [26]	8	none	CB + PRP	CB	Autogenous iliac bone graft
Yang 2016 [27]	10,10	2000	CB + PRP	CB	Autogenous bone graft
Yuan 2019 [28]	15,20	3500	CB + PRP	CB	β -tricalcium phosphate bioceramic bone graft
Zhang 2021 [29]	20,10	1500	CB + PRP	CB	Autogenous iliac bone graft
Zhao 2017 [30]	10,10	2000	CB + PRP	CB	Autogenous iliac bone graft
Zhao 2023 [31]	none	none	CB + PRP	CB	Autogenous iliac bone graft
Zhu 2018 [32]	none	none	CB + PRP	CB	Autogenous iliac bone graft

PRP: platelet-rich plasma, CB: core decompression and bone grafting

including erythema, postoperative infections, hypovolemic shock, and deep vein thrombosis in the lower extremities. In that study, the number of complications reported was 4 in the treatment group and 14 in the control group. The pooled analysis of complications indicates the safety of PRP for ONFH. However, it is challenging to conclude that complications do not exist in other studies. This difficulty arises from various factors, including a lack of uniformity and the subjective nature of the evaluations conducted.

Discussion

Clinicians typically evaluate the effectiveness and safety of an intervention before making treatment decisions. Our pooled analysis indicated that the treatment group is more effective than the control group in restoring hip function ($P < 0.00001$), alleviating pain ($P < 0.00001$), and preventing the need for THA ($P < 0.0001$). Furthermore, of the 10 studies [14, 18, 19, 21, 22, 26, 29–32] reporting postoperative complications, 8 studies [14, 18, 19, 22, 26, 29, 31, 32] found no complications. The remaining 2 studies [21, 30] showed that preserving the hip while using PRP was relatively safe, with complications occurring in 5 out of 60 patients in the treatment group compared to 15 out of 60 in the control group.

PRP platelet counts can be three to six times higher than the baseline whole blood count, ranging from 300,000 to over 1,500,000 platelets/mm³. This concentration is influenced by several factors, including the magnitude of centrifugal force, centrifugation time, total blood

volume, the platelet activation medium used, and the donor's status [35]. It is well established that the platelet concentration in PRP exceeds baseline levels found in whole blood [36]. Therefore, the defining characteristic of PRP is its absolute platelet concentration [37]. The fundamental principle of PRP therapy involves injecting concentrated platelets at the injury site, which can initiate tissue repair by releasing various biologically active factors, including growth factors, cytokines, lysosomes, and adhesion proteins [38]. During the treatment of ONFH, numerous factors released by PRP can promote the proliferation and differentiation of bone marrow mesenchymal stem cells while inhibiting the formation and resorption of osteoclasts. This process provides essential growth factors for femoral head repair, facilitates new bone formation, and accelerates bone tissue healing in the necrotic area [39].

To the best of our knowledge, this is the first meta-analysis exploring the safety and efficacy of PRP combined with CD-enhanced bone grafting for ONFH in the context of VAS, HHS, THA, and postoperative complications. However, several limitations must be considered. Firstly, the quality of the randomised controlled trials included in this study is not high, and various biases may weaken the strength of our findings. For instance, the included studies were primarily conducted in China and India, indicating a potential geographical bias. Furthermore, only three of the included studies [14, 26, 28] reported using double-blinding, meaning that most were either single-blinded or not adequately blinded. This lack of blinding could introduce significant

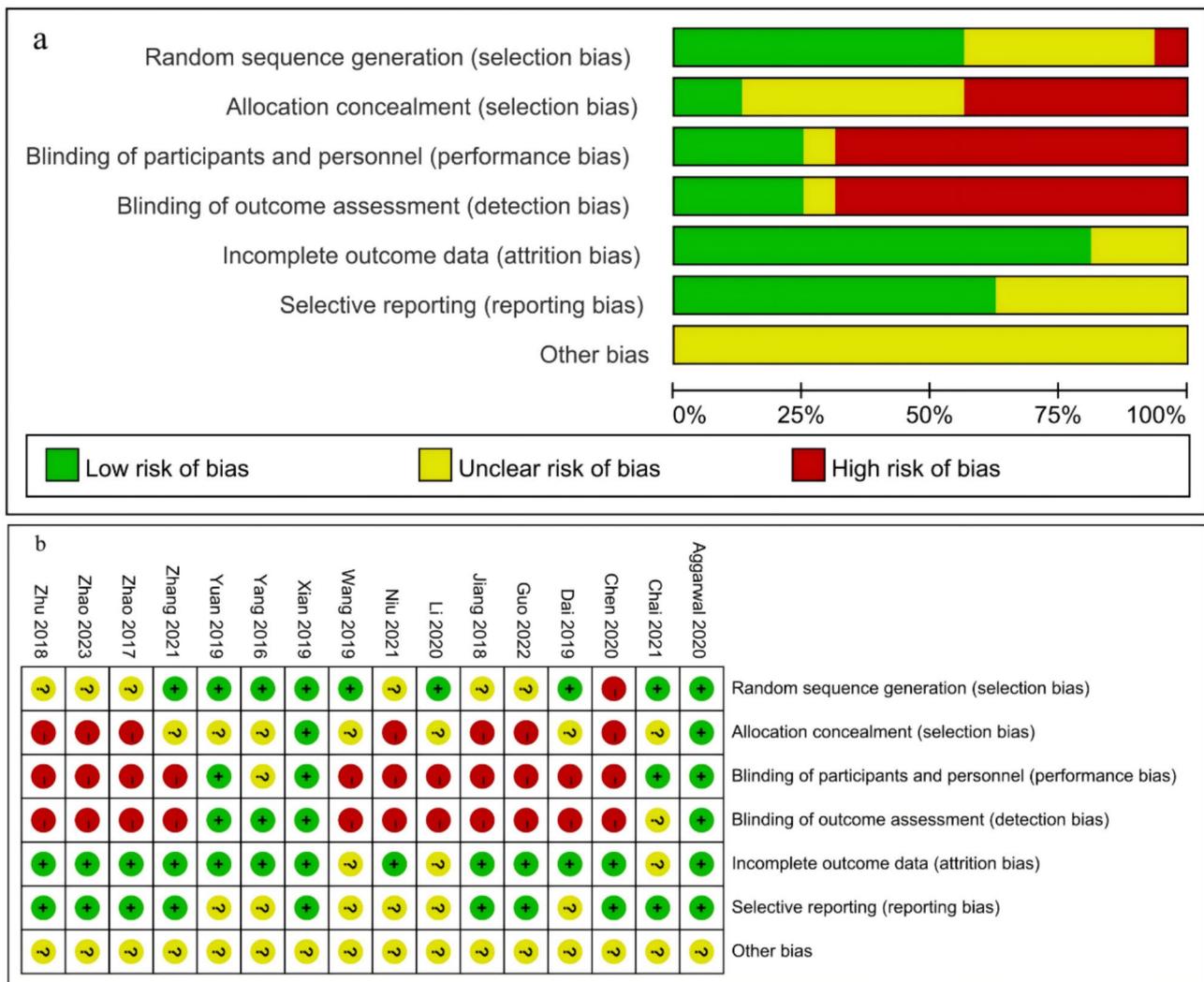


Fig. 2 The Cochrane Risk of Bias Tool assessed the quality of randomised controlled trials (RCTs). **a** Risk of Bias Chart; **b** Risk of Bias Summary

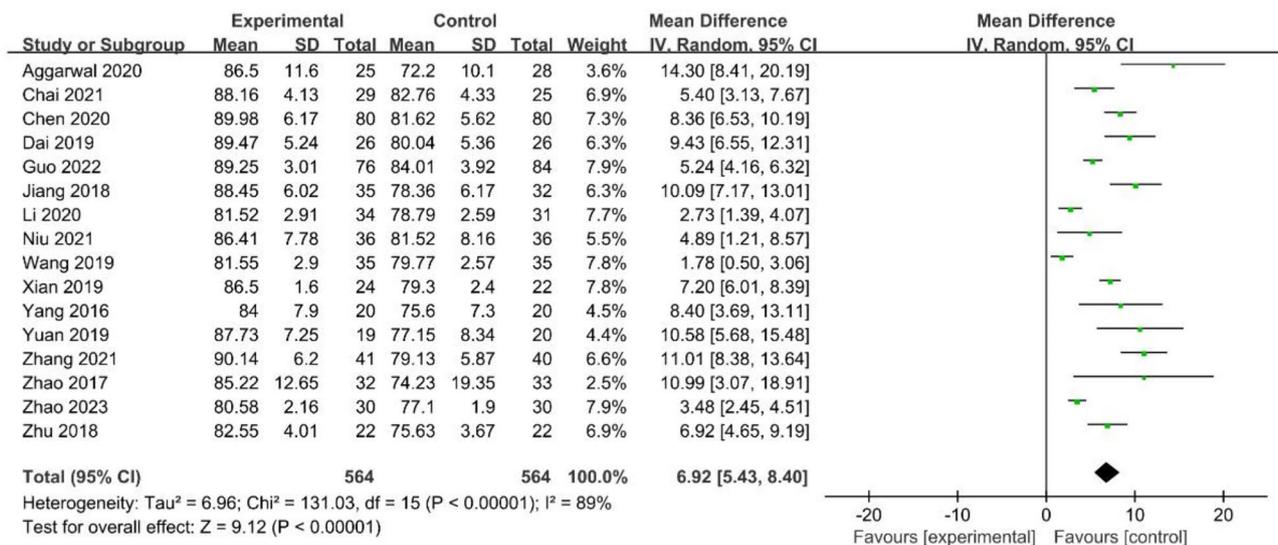


Fig. 3 Forest plot demonstrating HHS in patients undergoing bone grafting and CD, both with and without platelet-rich plasma

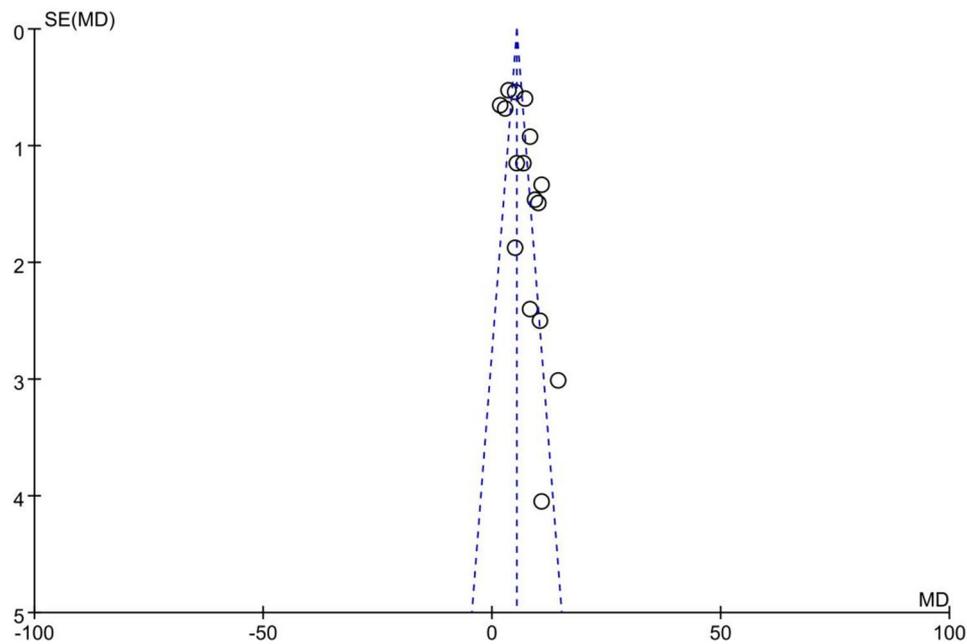


Fig. 4 Funnel plot of HHS in patients undergoing bone grafting and core decompression with and without platelet-rich plasma

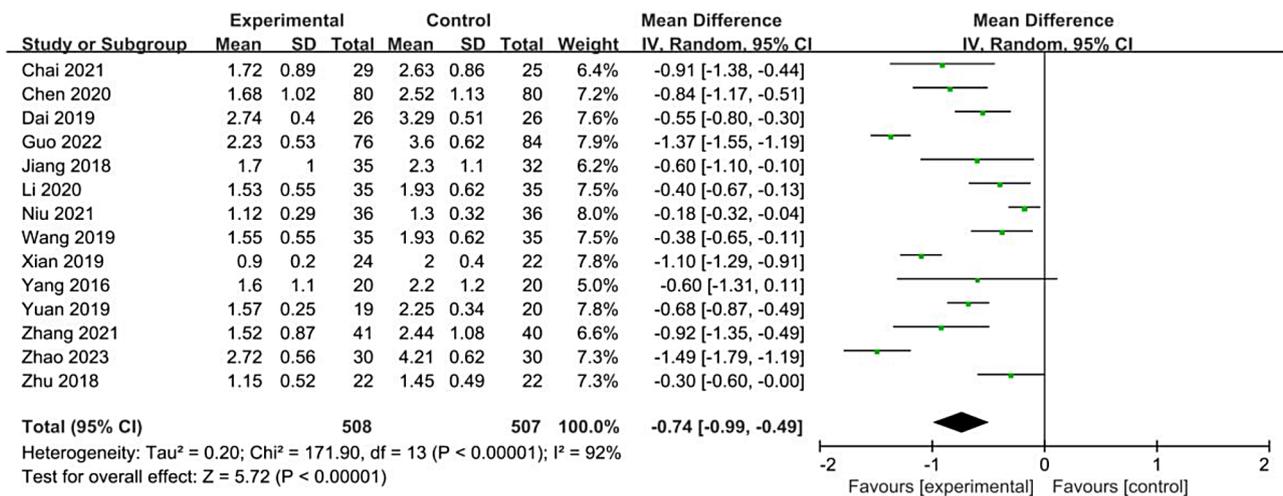


Fig. 5 Forest plot of visual analog scale scores in patients undergoing bone grafting and core decompression with and without platelet-rich plasma

bias into our results, increasing heterogeneity. Additionally, while the number of studies included in this research is 16, the overall number of subjects is relatively low. This limitation may affect the validity of our findings. Therefore, it is crucial to incorporate more high-quality RCTs in future studies to strengthen our conclusions.

Conclusions

In conclusion, our findings suggest that the use of PRP in combination with CD and bone grafting for patients with ONFH leads to improved hip function, pain relief, a decreased likelihood of THA, and a lower risk of postoperative complications. However, further high-quality RCTs are necessary to validate our results.

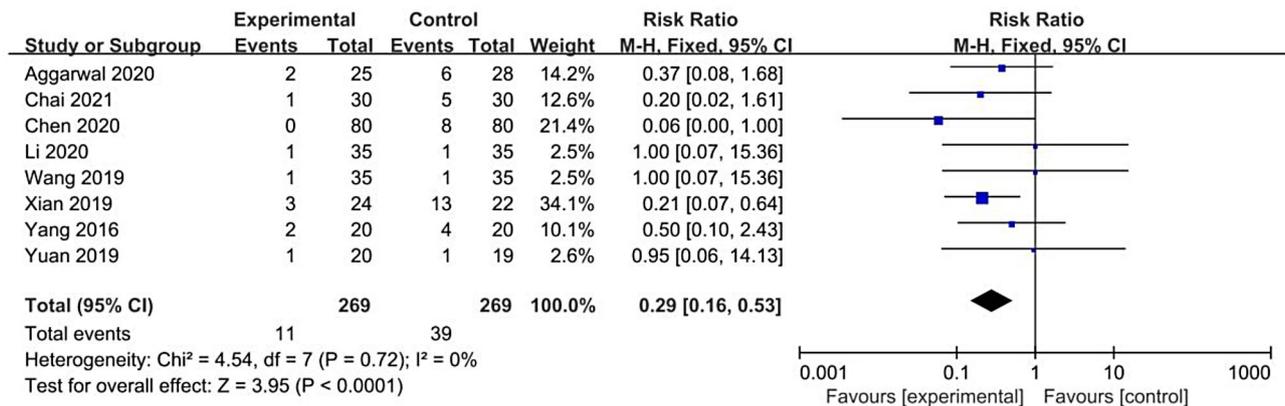


Fig. 6 Forest plot showing patients who underwent core decompression and bone grafting, followed by total hip arthroplasties, with and without platelet-rich plasma

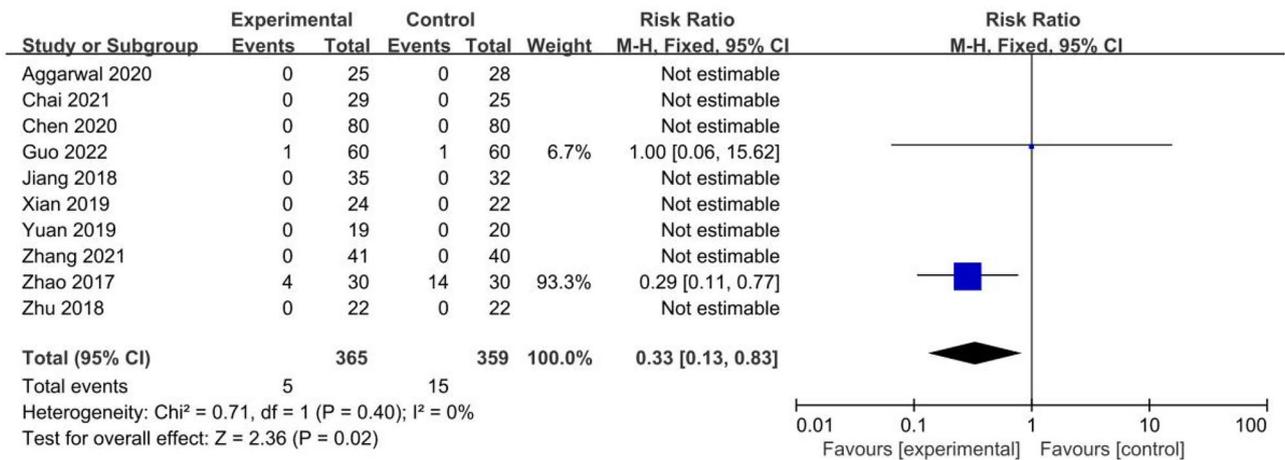


Fig. 7 Forest plot of postoperative complications in patients undergoing bone grafting and core decompression, with and without platelet-rich plasma

Abbreviations

- ONFH Osteonecrosis of the femoral head
- PRP Platelet-rich plasma
- CD Core decompression
- CB Core decompression and bone grafting
- CNKI China National Knowledge Infrastructure
- CBM Chinese Biomedicine
- PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- HHS Harris hip score
- MD Mean difference
- VAS Visual analog scale
- CI Confidence interval
- THA Total hip arthroplasties
- RR Risk ratio
- RCTs Randomised controlled trials

Author contributions

XD contributed to the article’s design and conceptualization and obtained funding for this work. YC and SH were responsible for editing, writing, and revising the manuscript. BW, JW, and LH reviewed the manuscript and were involved in collecting, collating data, and performing the statistical analysis. DH provided resources, technology, and supervision. All authors have read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

All analyses were based on previously published studies; therefore, no ethical approval or patient consent is required.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Supplementary Information

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Supplementary Material 1

Acknowledgements

Not applicable.

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