Review

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# Bone grafting for femoral head necrosis in the past decade: a systematic review and network meta-analysis

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**Background:** Bone grafting is considered a method that can provide mechanical and structural support to the femoral head and prevent the collapse of the femoral head after core decompression (CD). However, there are no consensus guidelines on which bone grafting method is best after CD. The authors assessed the efficacy of various bone grafting modalities and CD through a Bayesian network meta-analysis (NMA).

**Materials and methods:** Ten articles were retrieved from PubMed, ScienceDirect, and Cochrane Library searches. Bone graft modalities are categorized into four, and CD is the control group: (1) CD, (2) autologous bone graft (ABG), (3) biomaterial bone graft (BBG), (4) bone graft combined with bone marrow graft (BG + BM), and (5) free vascular bone graft (FVBG). The rates of conversion to total hip arthroplasty (THA), femoral head necrosis progression rate, and Harris hip score (HHS) improvement were compared among the five treatments.

**Results:** A total of 816 hips were included in the NMA: specifically, 118 hips in CD, 334 in ABG, 133 in BBG, 113 in BG + BM, and 118 in FVBG. The NMA results show no significant differences in preventing conversion to THA and improving HHS in each group. All bone graft methods are better than CD in preventing osteonecrosis of the femoral head (ONFH) progress [ABG: odds ratio (OR) = 0.21, 95% CI: 0.07–0.56; BBG: OR = 0.13, 95% CI: 0.03–0.52; BG + BM: OR = 0.06, 95% CI: 0.01–0.24; FVBG: OR = 0.11, 95% CI: 0.02–0.38]. The rankgrams indicate that BG + BM is the best intervention in preventing conversion to THA (73%), preventing ONFH progress (75%), and improving HHS (57%), followed by the BBG in preventing conversion to THA (54%), improving HHS (38%), and the FVBG in preventing ONFH progress (42%).

**Conclusions:** This finding indicates that bone grafting after CD is necessary to prevent ONFH progression. Moreover, bone grafts combined with bone marrow grafts and BBG seem to be effective treatment methods in ONFH.

**Key Words:** Bayesian network meta-analysis, bone graft, femoral head necrosis, systematic review

## Introduction

Osteonecrosis of the femoral head (ONFH) is a typical bone joint disease, usually caused by various causes of blood circulation disorders[1,2] and leading to the death of femoral head-related cells and trabecular bone microfractures. Clinical manifestations of ONFH include hip pain, limited hip joint flexion and extension activities, and femoral head collapse in the late stage of necrosis[3]. Therefore, protecting the hip joint from the collapse of the femoral head in ONFH is vital in clinical practice.

Core decompression (CD) is considered the most commonly used procedure technique in ONFH treatment[4]. CD can reach the osteonecrosis lesion and release the pressure intramedullary by drilling. Furthermore, the CD can contribute to revascularization and bone formation in the necrotic femoral head, prompting bone tissue and vessel creep substitution in the necrotic area and remodeling the bone structure. However, some

### HIGHLIGHTS

- The Bayesian network meta-analysis reviewed the literature of bone grafting in osteonecrosis of the femoral head (ONFH) treatments over the past decade.
- Bone grafting after core decompression is necessary to prevent ONFH progression.
- Bone grafts combined with bone marrow grafts and biomaterial bone grafts seem to be effective treatment methods in ONFH.

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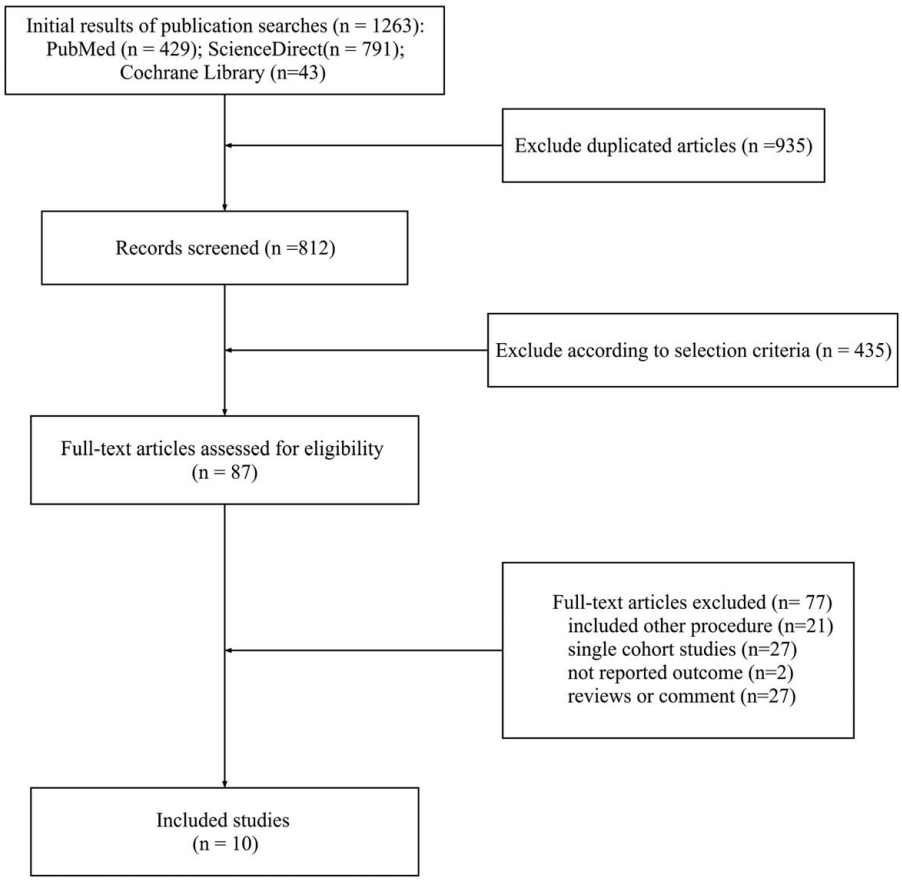


**Figure 1.** PRISMA flow diagram details the process of relevant clinical study selection.

research suggests that 37% of cases after CD progressed to femoral head collapse[5,6], and the possible reason is that the bone defect caused by CD might destroy the mechanical support structure of the femoral head and the subchondral bone plate, which added the risk of femoral head iatrogenic collapse for advanced ONFH[7]. Bone grafting is considered a method to fill up the bone defect formed by CD, which can provide mechanical and structural support to the femoral head and prevent the collapse of the femoral head[8].

Currently, the mainstream bone grafts include autologous bone graft (ABG), biomaterial bone graft (BBG), bone graft combined with bone marrow graft (BG + BM), and free vascular bone graft (FVBG). However, which bone graft method is the best choice after CD remains controversial. Therefore, we use Bayesian network meta-analysis (NMA) to assess the efficacy of different bone graft methods based on three outcomes: (1) conversion to total hip arthroplasty (THA), (2) ONFH progression, and (3) Harris hip score (HHS) improvement.

NMA is a technique to meta-analyze more than two treatments simultaneously[9]. In an entire Bayesian evidence network, all indirect comparisons are considered to arrive at a single, integrated, estimated effect of all treatments based on all included studies[10]. However, to our knowledge, there is no NMA about the efficacy of different bone grafts in femoral head necrosis treatments.

## Materials and methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[11–13] for performing and reporting systematic reviews and NMA, Supplemental Digital Content 1, http://links.lww.com/JS9/A55, Supplemental Digital Content 2, http://links.lww.com/JS9/A56 and methodological quality complied with AMSTART 2[14], Supplemental Digital Content 3, http://links.lww.com/JS9/A57. The study review protocol was registered at PROSPERO (CRD42022357624) (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=357624).

### *Literature search*

We used the keywords 'femoral head necrosis' OR 'femoral head avascular necrosis' AND 'bone graft' in PubMed, ScienceDirect, and Cochrane Library, and relevant literature published during the decade 2012–2022 was searched.

### *Study selection*

First, two researchers independently reviewed all retrieved abstracts and full texts. Any disagreement will be resolved through discussion and consultation with the other researcher.

The inclusion criteria for studies were as follows: Studies concerning patients with nontraumatic femoral head necrosis.

Studies include at least two of the following treatments: CD, ABG, BBG, BG + BM, and FVBG. The included studies should report at least one of the three outcomes: the improvement of HHS, the frequency that hips required THA, and the frequency that the femoral head necrosis stage progressed after the intervention. Randomized controlled trial and retrospective cohort study. Full-text. English language.

Exclusion criteria are (1) reviews, protocols, and basic science articles, (2) studies that included traumatic ONFH, (3) non-English.

### Data extraction

The extracted data were as follows: author, year of publication, enrollment period, country, age, number of hips, stage of ONFH, intervention comparison, follow-up, HHS preoperation and at the last follow-up, conversion to THA, femoral head necrosis progression, and study types.

### Quality assessment

Two authors independently performed the quality assessment. The Newcastle-Ottawa scale, a scale based on selection, comparability, and exposure/outcome, was applied to measure the methodological quality of all studies[15]. Studies scoring 8 and 9 were considered high quality, and scores equal to 6 and 7 were considered medium quality.

### Statistical analysis

We analyzed three outcomes separately (HHS improvement, conversion to THA rates, and femoral head necrosis progressed rates). The odd ratio, mean difference, and 95% CIs were estimated for dichotomous and continuous outcomes, respectively. The possibility of publication bias was assessed by a comparison-adjusted funnel plot using Stata software (version 11.0; StataCorp, College Station, TX). A pairwise meta-analysis was performed by ADDIS software (version 1.16.8, https://addis.drugis.org/) to calculate the odds ratio and heterogeneity[16]. The heterogeneity was tested by $I^2$, and $I^2$ greater than or equal to 50% was considered heterogeneous. Besides, node-splitting analysis was used to assess inconsistency by a particular comparison based on direct and indirect evidence, in which $P$ greater than 0.05 was regarded as insignificant[17].

ADDIS was used to perform the random-effects Bayesian NMA. As described in the ADDIS user manual, the Markov chain Monte Carlo simulation method was used to calculate the posterior distributions of the nodes in the Bayesian network frame, and convergence was assessed using the Brooks–Gelman–Rubin method. This method compares within-chain and between-chain variance to calculate the potential scale reduction factor. A potential scale reduction factor close to one indicates that approximate convergence has been reached[18]. Besides, the Bayesian approach ranked the probability of each treatment being the best to assess the efficacy comprehensibly.

## Results

### Studies selection and characteristics

Figure 1 shows the process of included research. A total of 1263 records were retrieved from the databases. Eight hundred and twelve records were included after removing duplications. Then 482 records were excluded according to selection criteria, and 87 full-text articles were assessed for eligibility. Finally, 10 studies were included in this research. The details of the included studies are listed in Table 1. Data from 10 studies which included eight direct comparisons and 806 hips, was available for NMA. Figure 2 presented the network structure of the analyzed comparisons for the primary outcomes. The methodological quality assessment (Supplementary Table 1, Supplemental Digital Content 4, http://links.lww.com/JS9/A58) shows that there were three medium-quality studies (scored 6 or 7) and seven high-quality studies (scored 8 or 9). Comparison-adjusted funnel plots (Supplementary Fig. 1, Supplemental Digital Content 4, http://links.lww.com/JS9/A58) show that most of the studies were evenly distributed on both sides of the vertical line, suggesting the little possibility of publication bias. There is heterogeneity among comparisons of different treatments on HHS improvement, conversion to THA rates, and femoral head necrosis progressed rates (Supplementary Table 2, Supplemental Digital Content 4, http://links.lww.com/JS9/A58). Meanwhile, it showed that the inconsistency between the direct effect and indirect effect of comparisons of different treatments on three outcomes have no significant difference, which indicated that the Bayesian NMA' results are reliable (Supplementary Tables 3–5, Supplemental Digital Content 4, http://links.lww.com/JS9/A58).

**Table 1**

**Characteristics of included individual studies**

| References | Enrollment period | Country | Design | Mean age (years) | Cases (hip) | Inclusion criteria | Group comparison | Follow-up (yea) |
|---|---|---|---|---|---|---|---|---|
| Cao *et al.*[19] | 2010–2012 | China | RCT | 31 | 21/21 | ARCO I–IIIB | CD vs. FVBG | 3 |
| Feng *et al.*[20] | 2006–2012 | China | Retrospective cohort | 33.2/32.8 | 84/51 | ARCO IIIA–IIIC | FVBG vs. ABG | 6–8 |
| Sallam *et al.*[21] | 1999–2012 | Egypt | Retrospective cohort | 33.21/32.67 | 38/33 | Ficat I–IIIB | CD vs. ABG | 3–14 |
| Ma *et al.*[22] | 2009–2010 | China | RCT | 34.78/35.60 | 24/25 | Ficat I–III | ABG vs. BG + BM | 2 |
| Li *et al.*[23] | 2009–2010 | China | RCT | 38.2/34.1 | 20/21 | Ficat II–III | ABG vs. BG + BM | 10 |
| Young *et al.*[24] | 2009–2013 | China | Retrospective cohort | 35.49/37.12 | 38/46 | Steinberg I–IIIA | BBG vs. ABG | 3 |
| Zhang *et al.*[25] | 2016–2917 | China | RCT | 31.54/32.31 | 16/20 | ARCO IIA–IIIC | ABG vs. BBG | 2 |
| Wan *et al.*[8] | 2005–2015 | China | RCT | 29.64/28.83/30.56/30.48 | 45/46/45/46 | ARCO IIA–IIB | BG + BMvs. FVBG vs. ABG vs. BBG | 4 |
| Wang *et al.*[26] | 2009–2014 | China | Retrospective cohort | 39.1/38.1 | 59/66 | ARCO IIA–IIC | CD vs. BBG | 4 |
| Li *et al.*[27] | 2015–2021 | China | RCT | 35.4/39.4 | 22/29 | Ficat I–IV | BG + BM vs. BBG | 2 |

ABG, autologous bone graft;; ARCO, Association Research Circulation Osseous BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; FVBG, free vascular bone graft; RCT, randomized controlled trial.

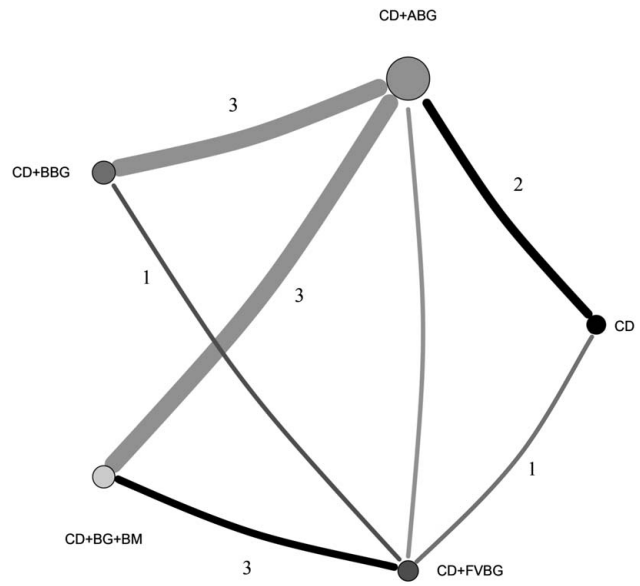


**Figure 2.** Network plot of direct evidence in network meta-analysis. Nodes represent the compared interventions. Node size represents the number of assigned participants. Edges and line thickness represent the available direct comparisons and the number of comp. ABG, autologous bone graft; BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; CD, core decompression; FVBG, free vascular bone graft.

### *Conversion to total hip arthroplasty*

All included studies report the data of conversion to THA. There are no differences in the rate of THA conversion (Table 2). In rankgrams (Fig. 3a), BG + BM was estimated to have a 73% chance of being the best intervention for preventing conversion to THA, the second is BBG (54%), and the third is ABG (50%).

### *Femoral head necrosis progress*

All included studies report the data on ONFH progress. Bayesian NMA indicates that ABG, BBG, BG + BM, and FVBG are significantly more effective than CD, and BG + BM is significantly more effective than ABG (Table 3). In rankgrams (Fig. 3b), BG + BM was estimated to have a 75% chance of being the best intervention for preventing ONFH progress, followed by the second FVBG (42%), the third BBG (43%), the fourth ABG (77%), and CD (99%) is worst.

### *HHS improve*

Eight included studies report the data of conversion to THA. There are no differences in HHS improvement (Table 4). In rankgrams (Fig. 3c), BG + BM was estimated to have a 57% chance of being the best intervention for improving HHS, followed by second BBG (38%) and third ABG (30%) and FVBG (30%) tied, and CD (86%) is worst.

**Table 2**

**Network meta-analyses result of conversion to THA**

| | | | | |
|---|---|---|---|---|
| CD | 0.68 (0.22, 1.88) | 0.42 (0.09, 1.81) | 0.25 (0.05, 1.13) | 0.92 (0.18, 3.50) |
| | ABG | 0.62 (0.22, 1.84) | 0.37 (0.11, 1.17) | 1.34 (0.38, 4.02) |
| | | BBG | 0.61 (0.14, 2.20) | 2.16 (0.44, 8.51) |
| | | | BG + BM | 3.56 (0.73, 16.84) |
| | | | | FVBG |

ABG, autologous bone graft; BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; CD, core decompression; FVBG, free vascular bone graft; THA, total hip arthroplasty.

## Discussion

When making treatment decisions, it is often necessary to consider multiple potential interventions' relative efficacy and safety. Unlike traditional pairwise meta-analysis, NMA allows for the simultaneous comparison of more than two interventions and for comparisons between interventions that have not been directly compared[28,29]. Network connectivity, homogeneity, transitivity, and consistency are four critical assumptions of NMAs. The requirement for network connectivity is unique to NMA, which means interventions must be connected to the network to conclude their direct and indirect relationships with other interventions. Similar to pairwise meta-analyses, different potential sources of heterogeneity must be considered in studies included in NMAs. The assumptions of transitivity and consistency refer to our assessment of potential clinical and methodological effect modifiers across a network of interventions. When there are imbalances across the network, subgroup analyses or meta-regression could be used to explore their influence on NMA effect estimates[30].

Whether CD can prevent ONFH progress, the collapse of the femoral head and the subsequent THA remain controversial[31–33]. Some research[34–36] suggests that the hip preservation treatment failure after CD is the lack of mechanical support intrafemoral head. The bone graft is an effective method to recover the internal biomechanics of the femoral head and accelerate the bone regeneration of the femoral head necrotic zone[37]. According to the source of the implanted bone, the bone graft can be categorized as ABG, allogeneic bone graft, and BBG. Meanwhile, bone grafting can combine with bone marrow graft (BG + BM)[38]. Besides, the bone used in grafting can contain free blood vessels (FVBG)[38].

ABG is the most commonly used bone graft, with the advantage of a stable source of bone for grafting, and the surgeon can harvest an appropriately sized bone from the patient's fibula or iliac bone for bone grafting, and no immune rejection and low infection rate[39]. Nevertheless, in the process of bone harvest, increased operative time, the amount of bleeding, and the extra-surgical incision are non-negligible factors affecting the patient's postoperative condition[8]. BBG has satisfactory biocompatibility, biodegradability, and osseointegration properties[40,41]. Compared with ABG, BBG does not need bone harvest from patients, significantly reducing procedure time and bleeding. Meanwhile, various biological modifications can be made in BBG to achieve better therapeutic effects, thus offering more significant potential in treating femoral head necrosis[42]. Evidence suggests that bone marrow contains multiple stem cells, which may contribute to bone formation and blood vessel reconstruction[43,44]. Based on this, BG + BM is applied in the clinic and achieves good effect[45]. Besides, FVBG provides blood supply to the transplanted bone by vascular anastomosis of the free vessels bone to promote the repair of bone tissue in bone defects[46]. However, because of the complexity of vascular anastomosis, the operation time and amount of bleeding of FVFG were significantly longer than that of other bone graft methods[8].

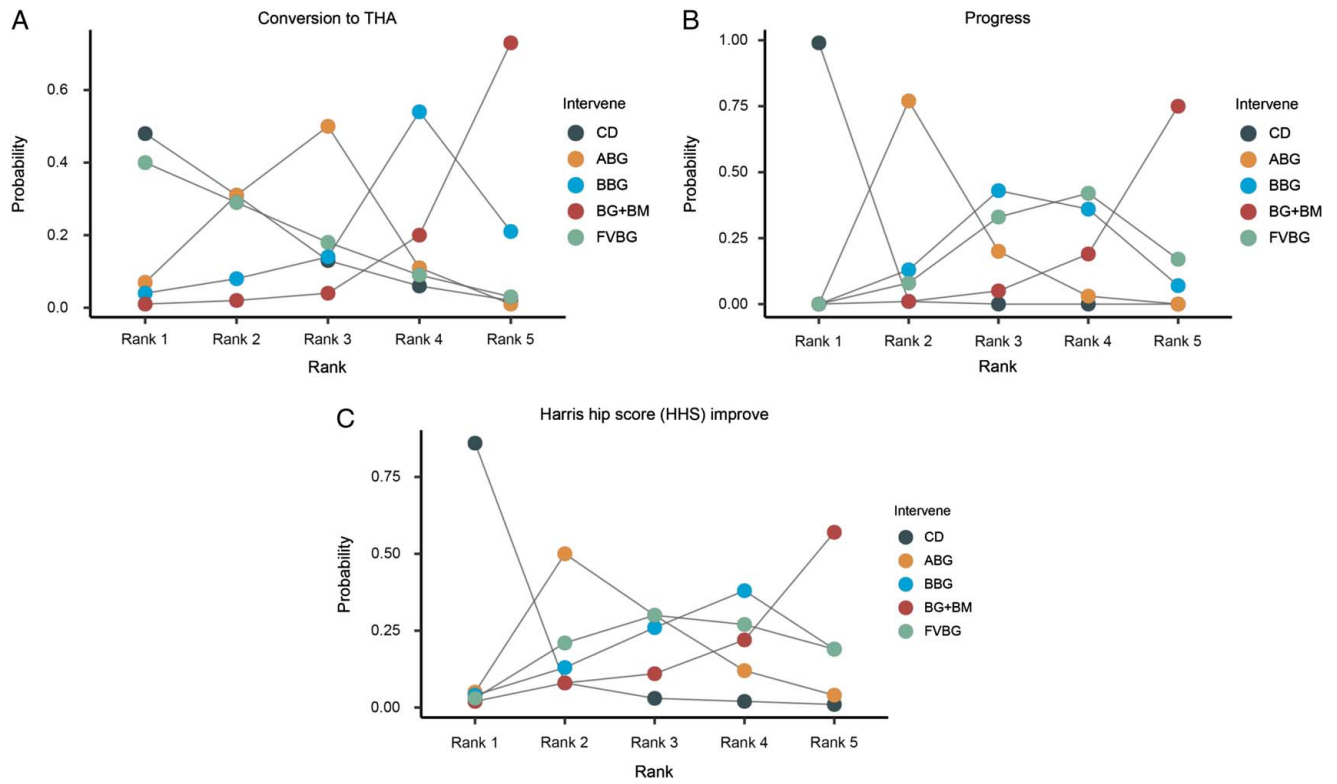


**Figure 3.** Rankings for effectiveness in (a) preventing conversion to total hip arthroplasty (THA), (b) preventing osteonecrosis of the femoral head (ONFH) progress, and (c) Harris hip score (HHS) improve. The graph displays the distribution of probabilities for each bone graft. The *x*-axis represents rank, and *y*-axis represents probabilities. Rank 1 indicates the intervention is worst, while rank 5 is best. ABG, autologous bone graft; BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; CD, core decompression; FVBG, free vascular bone graft.

The Bayesian NMA reviewed the bone graft treatments in ONFH, including the CD control group, ABG group, BBG group, BG + BM group, and FVBG group. The result shows that ABG, BBG, BG + BM, and FVBG are significantly more effective than CD, and BG + BM is significantly more effective than ABG in preventing ONFH progress, but have no significant differences in preventing conversion to THA and improving HHS. The above results may be due to the different surgical indications of the hip with ONFH included in the studies, including cases with older age, obesity, and necrosis lesion greater than 30% ARCO IIIA stage or more than[5]. However, the literature included in the Bayesian NMA did not address the relevant surgical indications.

Meanwhile, BG + BM was estimated to have the highest probability of preventing conversion to THA, the second is BBG, and the third is ABG. BG + BM also was estimated to have the highest probability of being the best intervention for preventing ONFH progress, followed by FVBG, BBG, ABG, and CD worst.

**Table 3**

**Network meta-analyses result of femoral head necrosis progress**

| | | | | |
|---|---|---|---|---|
| CD | 0.21 (0.07, 0.56) | 0.13 (0.03, 0.52) | 0.06 (0.01, 0.24) | 0.11 (0.02, 0.38) |
| | ABG | 0.60 (0.23, 1.72) | 0.29 (0.10, 0.83) | 0.53 (0.16, 1.39) |
| | | BBG | 0.47 (0.13, 1.54) | 0.87 (0.18, 3.09) |
| | | | BG + BM | 1.83 (0.40, 7.18) |
| | | | | FVBG |

ABG, autologous bone graft; BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; CD, core decompression; FVBG, free vascular bone graft.

BG + BM was estimated to have the highest chance of HHS improvement, followed by the BBG, the ABG and FVBG tied, and CD worst. Therefore, the results obtained from the NMA, the operation time, the amount of intraoperative bleeding, the damage to the patient, and the complexity of the operation were combined, we believe that BG + BM and BBG are ideal bone grafting methods for the treatment of ONFH.

Although the current study is the first Bayesian NMA comparing conventional CD with other bone graft modalities by summarizing all the available research, some limitations still exist in our Bayesian NMA study. Some research suggests that the surgical indications of implantation of bone grafts affect the final surgical outcome[5], including cases with older age, obesity, necrosis lesion greater than 30%, and ARCO IIIA stage or more. Moreover, the diversity of surgical indications makes it challenging to combine all indices[8]. Besides, only 10 related articles were included in this study, and the number of subjects in each study was small, potentially threatening the results' validity. Third, NMA includes indirect evidence, which necessitates a higher level of complexity.

## Conclusion

Our findings indicate that bone grafting after CD is necessary to prevent ONFH progression. Moreover, bone graft combined with bone marrow graft and BBG seems to be effective treatment methods in ONFH.

**Table 4**

**Network meta-analyses result of HHS improvement**

| | | | | |
|---|---|---|---|---|
| CD | 7.28 (– 3.49, 18.28) | 10.41 (– 3.30, 24.04) | 13.40 (– 2.64, 30.78) | 9.65 (– 2.82, 22.47) |
| | ABG | 3.14 (– 6.99, 12.29) | 6.07 (– 6.62, 19.80) | 2.34 (– 8.11, 12.79) |
| | | BBG | 2.94 (– 8.68, 16.11) | – 0.76 (– 12.54, 12.05) |
| | | | BG + BM | – 3.60 (– 18.72, 10.12) |
| | | | | FVBG |

ABG, autologous bone graft; BBG, biomaterial bone graft; BG + BM, bone graft combined with bone marrow graft; CD, core decompression; FVBG, free vascular bone graft; HHS, Harris hip score.

## Ethical approval

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

## Consent to participate

Not applicable.

## Consent to publish

Not applicable.


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## Authors contributions

P.-qL., G.-Z.z., and B.W. have equal contributions to the manuscript. All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. P.-qL. contributed to the study concept and design and drafted the manuscript. G.-Z.z., B.W., X.-lD. contributed to data collection. P.-qL., G.-Z.z., and B.W. contributed to preparation and data analysis. X.-lD. contributed to revision of the manuscript. All the authors contributed to the interpretation of the data and critically reviewed the manuscript for publication.

## Conflicts of interest disclosure

The authors declare that they have no competing interests.

## Research registration unique identifying number (UIN)

1. Name of the registry: Prospero.
2. Unique Identifying number or registration ID: CRD420 22357624.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=357624

## Guarantor

Decai Hou and Pengqiang Lou accept full responsibility for the work and/or the conduct of the study.

## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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