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Review

Core decompression combined with autologous bone marrow stem cells versus core decompression alone for patients with osteonecrosis of the femoral head: A meta-analysis

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ABSTRACT

Background: The efficacy of core decompression plus autologous bone mesenchymal stem cells (BMSCs) for the treatment of osteonecrosis of the femoral head (ONFH) remains controversial. We conducted a systematic review and meta-analysis to explore the efficacy of core decompression combined with BMSCs for OFNH patients.

Methods: We searched PubMed, Embase, Web of Science, and the Cochrane library databases through October 2018 for randomized controlled trials (RCTs) assessing the effect of core decompression combined with BMSCs for OFNH patients. The primary outcome was the visual analog scale (VAS) score at 6 months, 12 months and 24 months. The pooled data were analyzed using Stata 12.0 software.

Results: Fourteen studies with 540 patients (core decompression + BMSCs = 275, core decompression alone = 265) were included in our meta-analysis. Compared with the core decompression alone group, the core decompression + BMSCs group showed a significant decrease in the VAS score at 6 months, 12 months and 24 months, and a decrease in the number of hips undergoing total hip arthroplasty (THA), the Western Ontario and McMaster Universities (WOMAC) score and the volume of the postoperative necrotic zone. Core decompression + autologous BMSCs was associated with an increase in HHS postoperatively. No significant difference existed in adverse events.

Conclusions: Compared with core decompression alone in the treatment of ONFH, the combined utilization of core decompression and autologous BMSCs has better pain relief and clinical outcomes and can delay the collapse of the femoral head more effectively.

1. Background

Osteonecrosis of the femoral head (ONFH) is a painful disorder that leads to total hip arthroplasty (THA) in 80% of cases [1]. ONFH is caused by a critical reduction in the blood supply to the femoral head and elevation of intraosseous pressure [2,3]. The first presentation of ONFH may be painless, but ultimately severe pain and loss of movement occur [4]. The pathogenesis and etiology of ONFH are not completely understood. There are a number of treatment options proposed for ONFH that include the administration of bisphosphonates [5], anticoagulants [6], vasodilators [7], and bone mesenchymal stem cells (BMSCs) [8]. Autologous BMSCs have been used for tissue regeneration in recent years because of their ability to differentiate into multiple cell lineages, including osteoprogenitor cells [9]. In addition, surgical treatment options such as core decompression, vascularized cortical bone graft implantation, and femoral osteotomies have been described.

Implanting BMSCs combined with core decompression for ONFH was proposed by Hernigou et al., in 2006 [10]. Subsequently, some other scholars have reported on their experience with stem cell therapy for ONFH [11,12]. The clinical efficacy of core decompression combined with autologous BMSCs in OFNH patients has been explored recently, but the results are inconsistent [13,14].

To make full use of the available evidence, we performed this meta-analysis, which makes a direct comparison to determine whether core decompression combined with autologous BMSCs is superior to core decompression alone.

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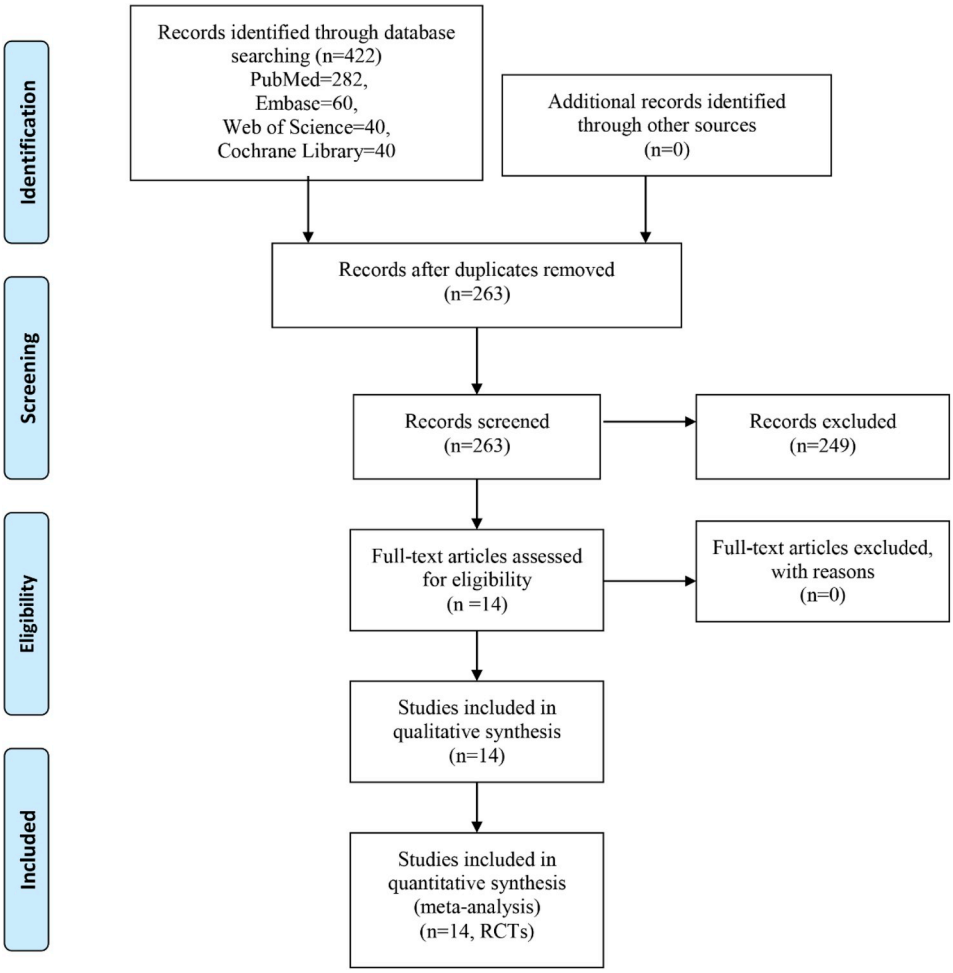

Fig. 1. Flow diagram of the review process.

2. Materials and methods

This work has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines.

2.1. Search strategy

Databases (PubMed, Embase, Web of Science and the Cochrane Library) were searched through October 2018. Searches strategies were used with medical keywords and are listed in the **Supplement S1**. We conducted manual searching techniques to identify appropriate studies and applied no language restrictions. In addition, further relevant reviews and references were manually checked for any omitted studies.

2.2. Inclusion criteria

Randomized controlled trials were included if they met the PICOS criteria as follows: Population: patients diagnosed with ONFH; Intervention: combined application of core decompression and autologous BMSCs; Comparator: core decompression treated alone; Outcomes: VAS at 6 months, 12 months and 24 months; Number of hips undergoing THA; Harris Hip Score (HHS) at 12 months and 24 months; Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) postoperatively; Volume of the necrotic zone at final follow-up and adverse events (AEs); and Study design: RCTs.

2.3. Data extraction

Two reviewers independently retrieved the relevant data from articles using a standard data extraction form. The extracted data included publication date, authors, study design, inclusion and exclusion criteria, number and demographics of participants, number of included hips, surgical procedure, duration of follow-up, and outcomes. For missing data, such as standard deviations, we first tried to contact the original author. If that did not work, we calculated missing standard deviations from other available data, such as standard errors, or the formulas in the Cochrane Handbook for Systematic Reviews of Interventions. Two reviewers extracted the data independently, and any disagreement was discussed until a consensus was reached. Pain scores evaluated by the 0–100 mm visual analog scale (VAS) were converted to the 0–10 cm (0: no pain, 10: worst imaginable pain) scale. The numerical rating scale was regarded as equivalent to the visual analog scale.

2.4. Risk of bias and quality assessment

The methodological bias and quality of the included studies were assessed by the Cochrane Collaboration's tool for assessing the risk of bias according to the Cochrane Handbook for Systematic Reviews of Interventions. It is a two-part tool with seven specific domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective outcome reporting and other sources of bias.

2.5. Statistical analysis

Stata 12.0 (Stata Corp., College Station, TX) software was used to perform the meta-analysis. We used weighted mean difference (WMD) and 95% confidence interval (CI) to assess continuous variable outcomes. For dichotomous outcomes, the risk ratio (RR) with a 95% CI was presented. Heterogeneity between studies was assessed by the I^2 test. For $I^2 < 50\%$, we used a fixed-effects model for the evaluation; otherwise, a random-effects model was used. In addition, sensitivity analysis was performed to explore the source of heterogeneity when heterogeneity existed. Publication bias, if any, was also identified.

3. Results

3.1. Search results

The process of study selection is presented as a flow diagram in Fig. 1. Four hundred and twenty-two studies were identified initially, not including additional studies from the reference lists of relevant studies, and 159 duplicates were removed. From the 263 records left, 249 were excluded by screening titles and abstracts, leaving 14 potentially relevant studies for full-text review. Finally, 14 studies [13,15–27] with 540 patients (CD + BMSCs = 275, CD alone = 265) were included in our meta-analysis (published between 2004 and 2017).

3.2. General characteristics of the included studies

The included studies were published from 2004 to 2018. In addition, these studies were mainly from Belgium and China. The mean age of the ONFH patients ranged from 32.7 to 49.7 years. The sample size of the patients ranged from 8 to 50. The general characteristics of the included studies are shown in Table 1. Detailed management of BMSCs is listed in **Supplement S2.**

3.3. Risk of bias of included studies

The risk of bias summary and risk of bias graph are presented in Figs. 2 and 3, respectively. For the random sequence generation assessment, the risk of bias was unclear in 5 out of 14 studies and was high in 1 out of 14 studies. For the allocation concealment assessment, the risk of bias was unclear and high in 4 and 2 out of 14 studies, respectively. For the blinding of participants and personnel assessment, the risk of bias of four trials was unclear, and 4 out of 14 trials had a high risk of bias in 1 out of 14 trials. For the blinding of outcomes assessment, the risk of bias was unclear in 3 out of 14 studies. For incomplete outcome data, the risk of bias in 1 out of 14 trials was unclear. For the selective reporting assessment, the risk of bias was unclear in 1 out of 14 studies. There was 1 study with an unclear risk of bias in other items.

4. Results of meta-analysis

4.1. VAS at 6 months, 12 months and 24 months

Five studies enrolling 145 hips reported VAS scores at 6 months postoperatively. Slight heterogeneity existed between the three studies (I^2 = 0%; P = 0.950, Fig. 4). Thus, a fixed-effects model was used. There was a significant difference between the two groups (MD = −7.08, 95% CI: [-10.68, −3.49], P = 0.000; Fig. 4).

Seven studies enrolling 198 hips reported VAS scores at 12 months postoperatively. No heterogeneity existed between the three studies (I^2 = 0%; P = 0.492, Fig. 4). Thus, a fixed-effects model was used. There was a significant difference between the two groups (MD = −7.28, 95% CI: [-10.16, −4.39], P = 0.000; Fig. 4).

Eight studies enrolling 136 hips reported a VAS score at 24 months postoperatively. No heterogeneity existed between the three studies (I^2 = 0%; P = 0.492, Fig. 4). Thus, a random-effects model was used. There was a significant difference between the two groups (WMD = −7.93, 95% CI: [-14.99, −0.87], P = 0.028; Fig. 4).

4.2. Number of hips undergoing THA

The number of hips undergoing THA was reported in two studies enrolling 399 hips. There was mild heterogeneity between the two studies (I^2 = 57.9%; P = 0.011, Fig. 5). A random-effects model was used. There was a significant difference between the two groups (RR = 0.39, 95% CI: [0.19, 0.78], P = 0.007; Fig. 5).

Table 1
General characteristic of the included studies.

Author	Country	Age (y, I/C)	Cases (n, I/C)	Diagnostic	Disease stage	Cell counts	Follow-up	Intervention	Control (drill diameter)
Gangji 2011	Belgium	42.2/45.7	13/11	ARCO	I/II	22.4 × 107	60 months	CD + BMSCs	CD (3.0 mm)
Gangji 2004	Belgium	40.9/48.8	10/8	NS	NS	92 × 107	24 months	CD + BMSCs	CD (3.0 mm)
Hauzeur 2018	Belgium	48.0/49.7	19/19	ARCO	NS	19.45 × 106	24 months	CD + BMSCs	CD (4.0 mm)
Pepke 2016	Germany	44.3/44.5	11/14	ARCO	I/II	118 × 106	24 months	CD + BMSCs	CD (2.0 mm)
Sen 2012	India	NA	26/25	ARCO	I/II/III	5 × 108	60 weeks	CD + BMSCs	CD (4.0 mm)
Tabatabaee 2015	Iran	31/26.8	14/14	ARCO	I/II/III	2 × 106	24 months	CD + BMSCs	CD (2.7 mm)
Zhao 2012	China	32.7/33.8	50/50	ARCO	I/II/III	2 × 106	60 months	CD + BMSCs	CD (1.0 mm)
Chang 2010	China	35.7/32.4	8/8	ARCO	II/III	2.9 × 106	12 months	CD + BMSCs	CD (3.0 mm)
Sun 2008	China	36/36	15/13	ARCO	I/II	5 × 108	18 months	CD + BMSCs	CD (2.0 mm)
Yang 2015	China	35.3/37.6	30/26	ARCO	I/II	2.9 × 106	18 months	CD + BMSCs	CD (2.0 mm)
Zhao 2016	China	30.5/35.3	18/18	Steinberg	NS	5 × 108	24 months	CD + BMSCs	CD (2.0 mm)
Guo 2008	China	42/42	10/10	ARCO	III	5 × 108	12 months	CD + BMSCs	CD (2.0 mm)
Ma 2014	China	35.6/34.8	21/18	FICAT	I/II/III	2 × 106	24 months	CD + BMSCs	CD (4.0 mm)
Rastogi 2012	India	34.7/33	30/30	ARCO	I/II/III	2.9 × 106	24 months	CD + BMSCs	CD (3.0 mm)

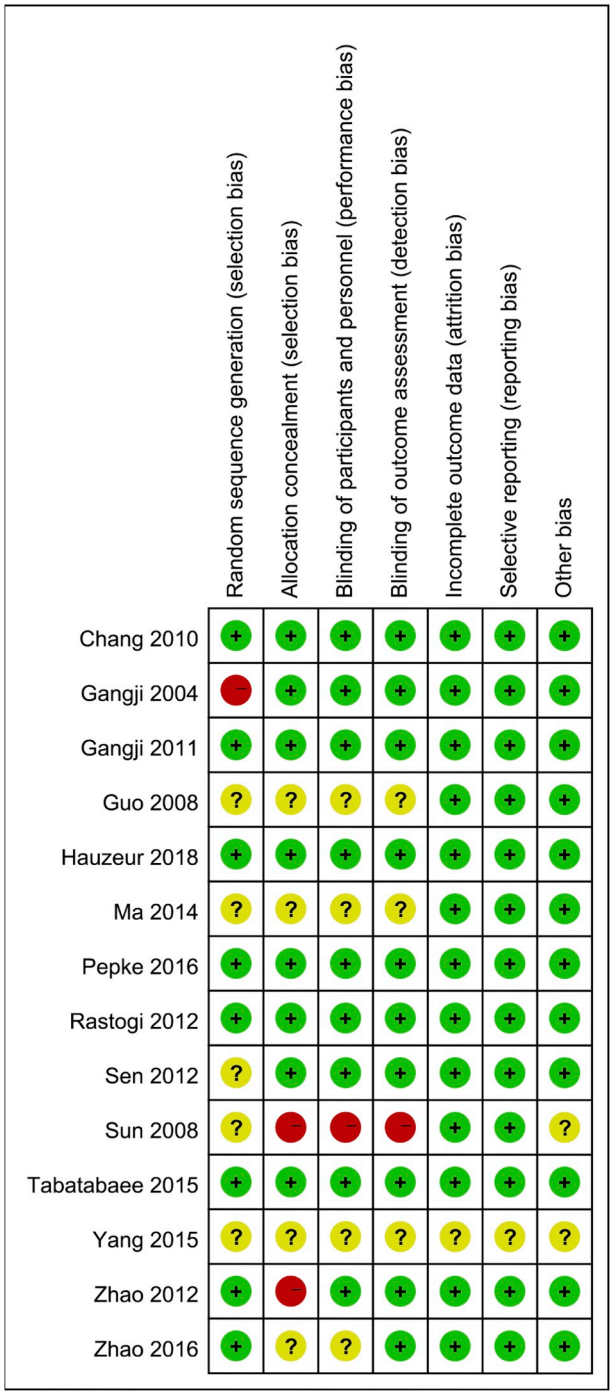

Fig. 2. Risk of bias graph.

4.3. HHS at 12 months and 24 months

Three studies including 308 hips reported HHS at 12 months postoperatively. Large heterogeneity existed between the three studies (I^2 = 56.6%; P = 0.042, Fig. 6). Therefore, we used a random-effects model. A meta-analysis showed a significant difference between the two groups (WMD = 4.80, 95% CI: [2.22, 7.39], P = 0.000; Fig. 6).

HHS at 24 months postoperatively was also reported in the three studies enrolling 280 hips. There was slight heterogeneity between the two studies (I^2 = 0.0%; Fig. 6). A fixed-effects model was used. There was a significant difference between the two groups (WMD = 4.90, 95% CI: [3.06, 6.74], P = 0.000; Fig. 6).

4.4. WOMAC score postoperatively

Five studies including 154 hips reported WOMAC scores postoperatively. There was large heterogeneity between the five studies (I^2 = 90.9%, P = 0.000, Fig. 7). We used a random-effects model, and the meta-analysis showed that autologous bone marrow stem cell combined core decompression was associated with a reduction of the WOMAC score compared with core decompression alone (WMD = −10.56, 95% CI: [-15.84, −5.28], P = 0.000; Fig. 7).

4.5. The volume of the necrotic zone at final follow-up

The volume of the necrotic zone at final follow-up was reported in five studies involving 208 hips. Significant heterogeneity existed between the three studies (I^2 = 71.2%; P = 0.008, Fig. 8). Then, a random-effects model was evaluated. The meta-analysis showed that autologous bone marrow stem cells combined with core decompression was associated with a reduction of the volume of the necrotic zone at final follow-up compared with core decompression alone (WMD = −0.05, 95% CI: [-0.08, −0.02], P = 0.000; Fig. 8).

4.6. AEs

Nine studies including 296 hips reported adverse events postoperatively. We used a fixed-effects model in view of the slight heterogeneity (I^2 = 0.0%; P = 0.956, Fig. 9). The meta-analysis showed no significant difference between the two groups (RR = 1.04, 95% CI: [0.63, 1.72], P = 0.879; Fig. 9).

4.7. Sensitivity analysis and publication bias

Sensitivity analysis for VAS at 6 months, 12 months and 24 months can be seen in **Supplement S3**. After omitting each study in turn, the overall estimate had not changed. Publication bias is presented in **Supplement S4**, and the results showed that there was no publication bias for VAS at 6 months, 12 months and 24 months.

5. Discussion

This meta-analysis indicates that the addition of autologous BMSCs in core decompression can result in decreased intensity of postoperative pain at rest at 6, 12, and 24 months for the ONFH patients. The number of patients who needed THA and the volume of the necrotic zone was reduced in the autologous BMSC combined core decompression group. Moreover, autologous BMSCs combined with core decompression could significantly increase HHS at 12 months and 24 months. In addition, autologous BMSCs combined with core decompression could decrease WOMAC scores compared with core decompression alone. There was no significant difference between the two groups in terms of adverse events.

Only two relevant meta-analyses were published on this topic [28,29]. However, differences between ours and the previous one should be noted. First, we included 14 RCTs and 540 patients. Furthermore, we performed sensitivity analysis to further increase the robustness of our meta-analysis. Li et al. [29] published a relevant meta-analysis of BMSCs combined with core decompression for ONFH patients. However, this meta-analysis included both RCTs and non-RCTs for analyses.

We identified VAS at 6, 12, and 24 months as the primary outcome. The results showed that autologous BMSCs combined with core decompression have a beneficial role in reducing pain intensity at 6, 12 and 24 months. Core decompression is an easily performed and popular procedure that has been used for the treatment of ONFH for approximately three decades [30]. Previous meta-analyses did not compare the pain intensity between these two groups. This meta-analysis first identified VAS at different follow-ups as primary outcomes. The results

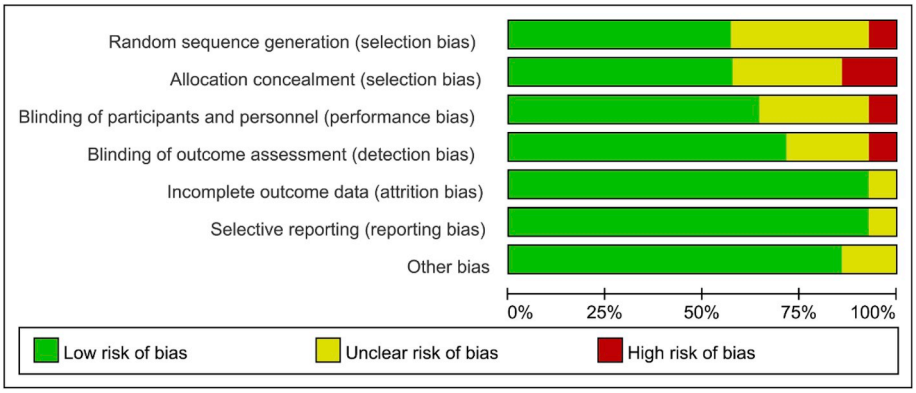

Fig. 3. Risk of bias summary.

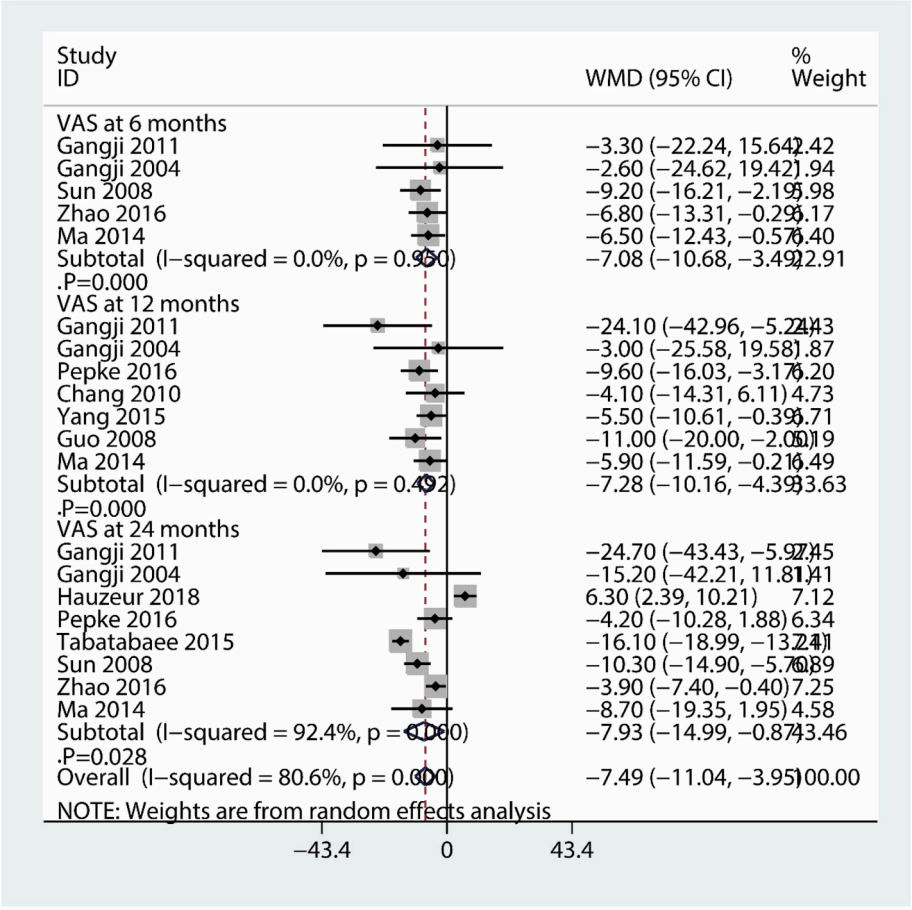

Fig. 4. Mean difference of VAS scores at 6-, 12-, 24-month postoperatively for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

confirmed that autologous BMSCs combined with core decompression were superior to core decompression alone. BMSCs have the potential to differentiate into osteoblasts, endothelial progenitor cells, and hemangioblasts, all of which function to repair the necrotic region [31]. Many studies have identified that the BMSC implantation technique is effective for early-stage ONFH [32,33].

We then compared the number of patients who needed THA between the two groups. The results showed that autologous BMSCs combined with core decompression could significantly decrease the number that needed THA. For hip function, we used HHS and WOMAC as the index. The results showed that autologous BMSCs combined with core decompression could increase HHS scores at 12 months and 24 months. Moreover, autologous BMSCs combined with core decompression could decrease WOMAC scores at the final follow-up. However, the mechanism of autologous BMSCs combined with core decompression for ONFH treatment is unknown. Additional research is needed to identify optimal culture conditions and to determine the mechanisms involved in regulating BMMSC differentiation into osteoblasts.

There were several limitations in this meta-analysis. First, only

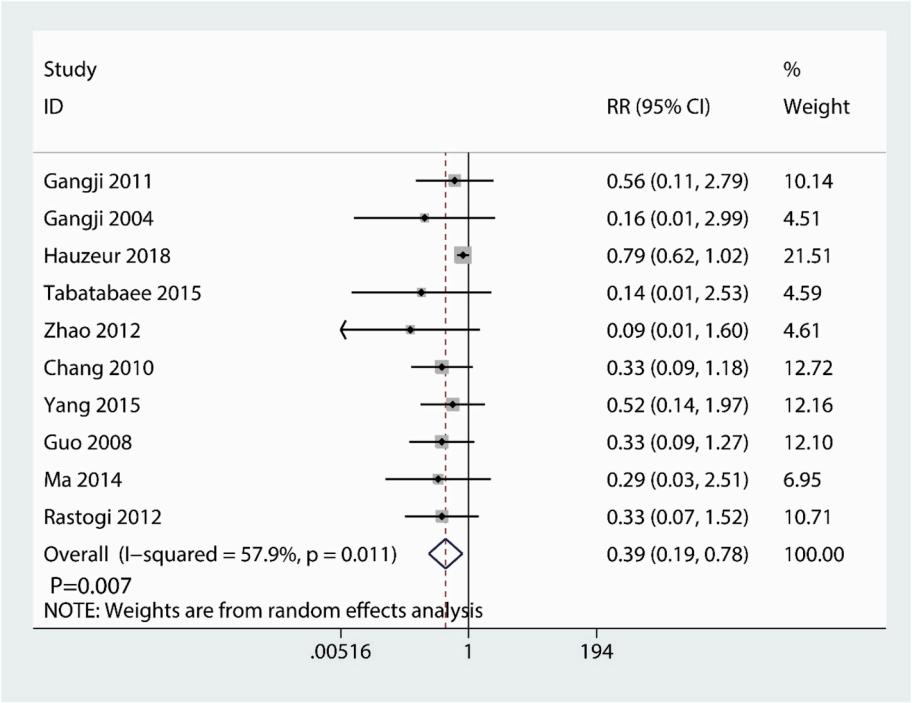

Fig. 5. Relative risk of hips undergoing THA for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

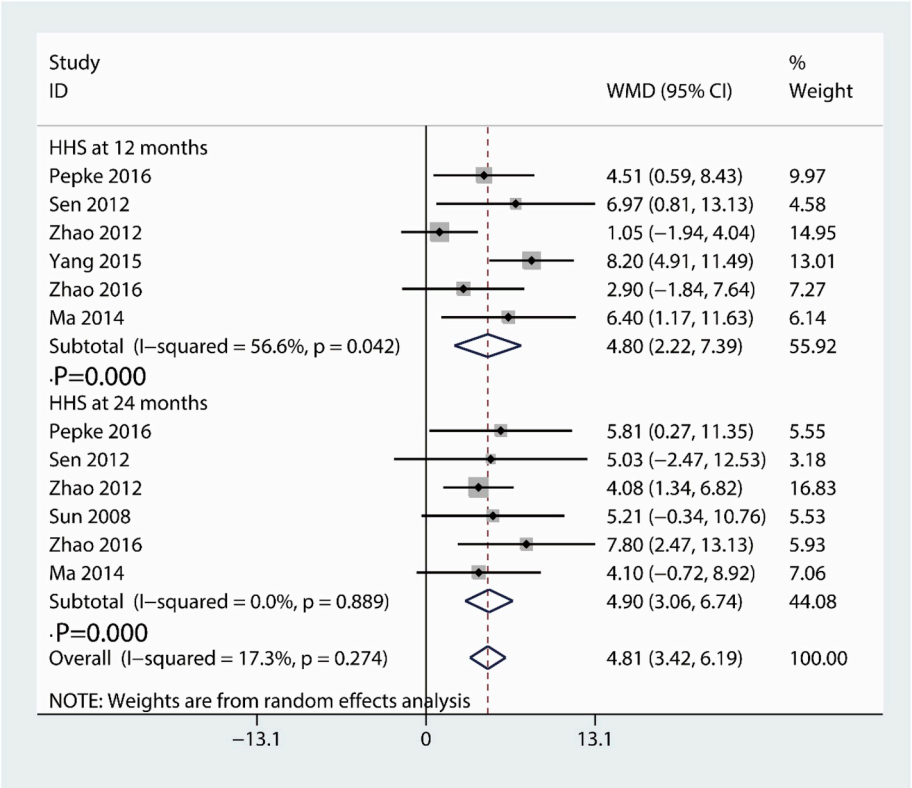

Fig. 6. Mean difference of HHS at 12- and 24-month for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

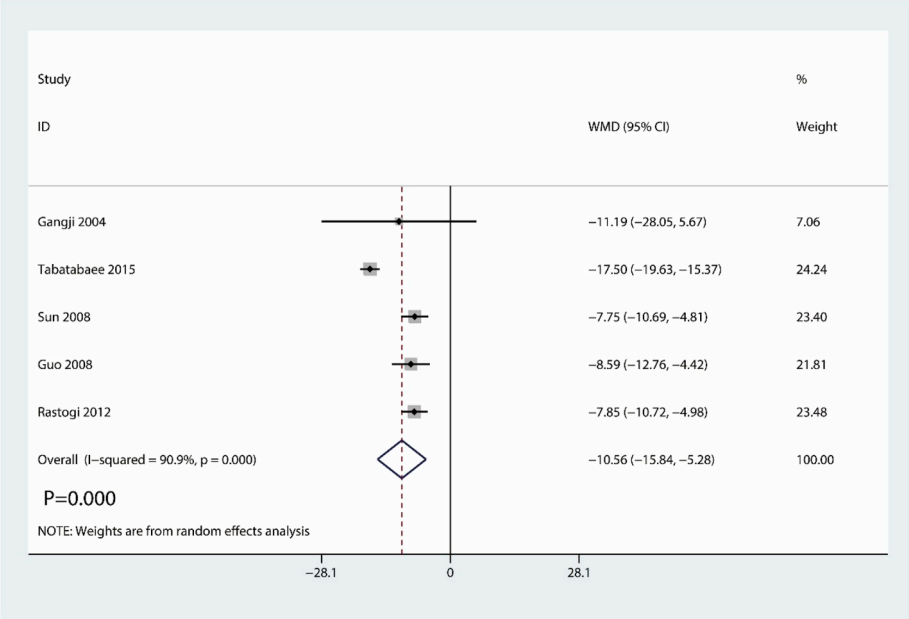

Fig. 7. Mean difference of WOMAC score postoperatively for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

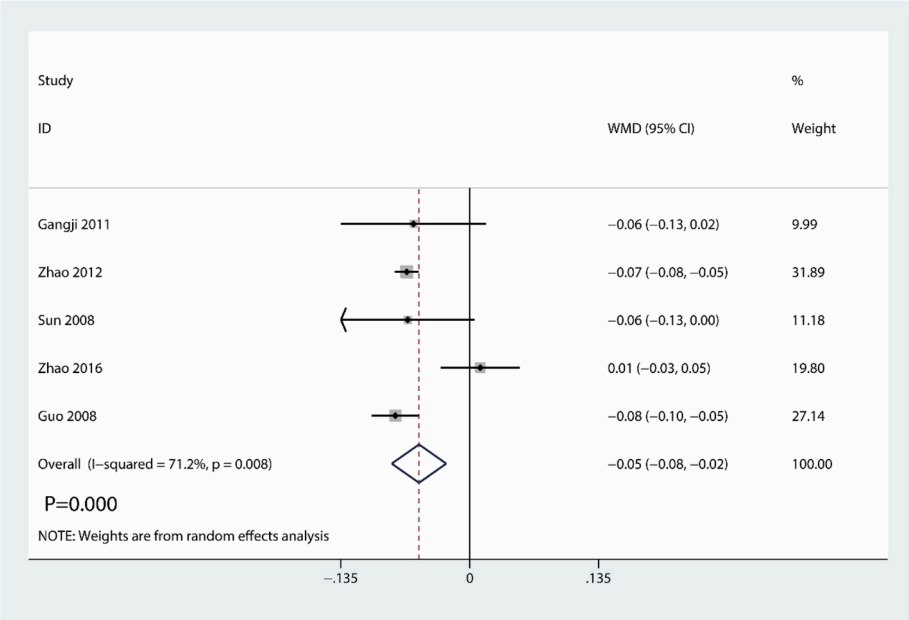

Fig. 8. Mean difference of volume of the necrotic zone at final follow-up for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

published studies were included in the present meta-analysis. Thus, publication bias may have occurred, although we followed the inclusion and exclusion criteria strictly to reduce selection bias and the results of a statistical test did not indicate otherwise. Second, there was large heterogeneity between the included studies, and the large heterogeneity may influence the final decision for orthopedic surgeons. Third, the sample size was small in the included studies ($n < 50$), which may affect the final results. Overestimation of the treatment effect was more likely in smaller trials compared with larger samples.

6. Conclusion

Compared with core decompression alone in the treatment of ONFH, the combined utilization of core decompression and autologous BMSC implantation has better pain relief and clinical outcomes and can delay the collapse of the femoral head more effectively. Considering the clinical effects, we suggest the administration of combined core decompression and autologous BMSC implantation for patients with ONFH.

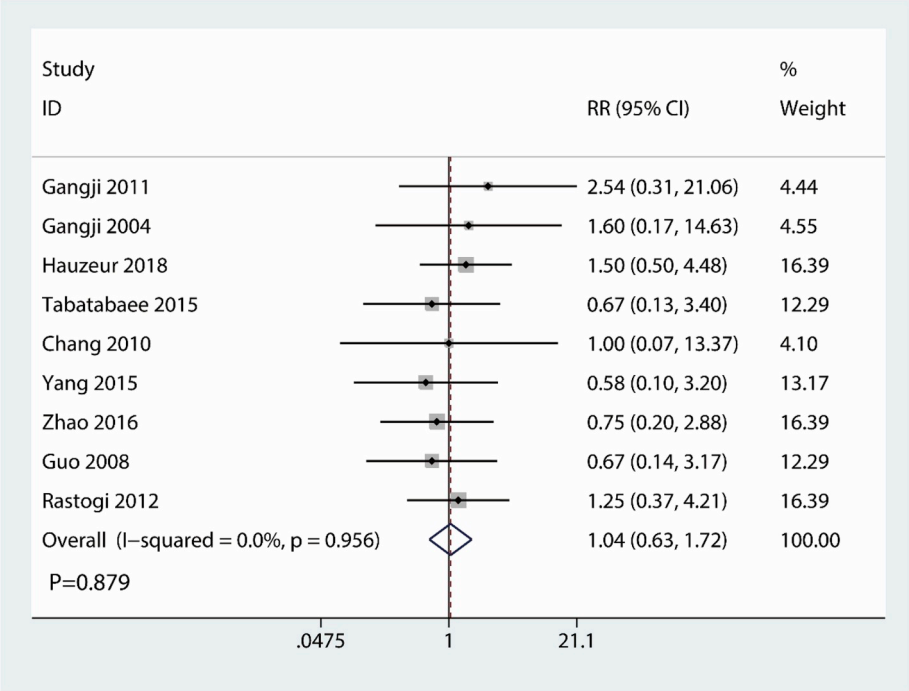

Fig. 9. Relative risk of AEs for the combined core decompression and autologous BMSCs group versus the core decompression alone group.

Ethics approval and consent to participate

This is a meta-analysis; no related problems exist.

Sources of funding

Not applicable.

Author contribution

Zhan Wang and **Qi-meng Sun**: data collections, data analysis and writing.

Fu-qiang Zhang and **Qun-li Zhang**: data collections and data analysis.

Li-guo Wang and Wen-ji Wang: data analysis and writing.

Wen-ji Wang: study design, data collections.

Consent for publication

Not applicable.

Guarantor

Wen-ji Wang.

Unique identifying number (UIN)

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https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/5c57dc55fb4f1e08b25cefa5

Trial registry number – ISRCTN

None.

Availability of supporting data

Supporting data are available.

Competing interests

The authors declare that they have no competing interests.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

None.

Acknowledgments

Not applicable.

Abbreviations

BMSCs	bone mesenchymal stem cells
ONFH	osteonecrosis of the femoral head
RCTs	randomized controlled trials
VAS	visual analog scale
THA	total hip arthroplasty
HHS	Harris Hip Score
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
AEs	adverse events
WMD	weighted mean difference
CI	Confidence intervals
MeSH	Medical Subject Headings

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://

doi.org/10.1016/j.ijsu.2019.06.016.

References

[1] M.A. Mont, J.J. Carbone, A.C. Fairbank, Core decompression versus nonoperative management for osteonecrosis of the hip, Clin. Orthop. Relat. Res. (324) (1996) 169–178.

[2] C. Papakostidis, T.H. Tosounidis, E. Jones, P.V. Giannoudis, The role of "cell therapy" in osteonecrosis of the femoral head. A systematic review of the literature and meta-analysis of 7 studies, Acta Orthop. 87 (1) (2016) 72–78.

[3] S. Saito, K. Ohzono, K. Ono, Joint-preserving operations for idiopathic avascular necrosis of the femoral head. Results of core decompression, grafting and osteotomy, J. Bone Joint Surg. Br. 70 (1) (1988) 78–84.

[4] T. Yamasaki, Y. Yasunaga, M. Ishikawa, T. Hamaki, M. Ochi, Bone-marrow-derived mononuclear cells with a porous hydroxyapatite scaffold for the treatment of osteonecrosis of the femoral head: a preliminary study, J. Bone Joint Surg. Br. 92 (3) (2010) 337–341.

[5] D. Li, Z. Yang, Z. Wei, P. Kang, Efficacy of bisphosphonates in the treatment of femoral head osteonecrosis: a PRISMA-compliant meta-analysis of animal studies and clinical trials, Sci. Rep. 8 (1) (2018) 1450.

[6] P. Guo, F. Gao, Y. Wang, Z. Zhang, W. Sun, B. Jiang, B. Wang, Z. Li, The use of anticoagulants for prevention and treatment of osteonecrosis of the femoral head: a systematic review, Medicine 96 (16) (2017) e6646.

[7] A. Roth, J. Beckmann, K. Bohndorf, A. Fischer, C. Heiss, W. Kenn, M. Jager, U. Maus, U. Noth, K.M. Peters, et al., S3-Guideline non-traumatic adult femoral head necrosis, Arch. Orthop. Trauma Surg. 136 (2) (2016) 165–174.

[8] M.T. Houdek, C.C. Wyles, M.S. Collins, B.M. Howe, A. Terzic, A. Behfar, R.J. Sierra, Stem cells combined with platelet-rich plasma effectively treat corticosteroid-induced osteonecrosis of the hip: a prospective study, Clin. Orthop. Relat. Res. 476 (2) (2018) 388–397.

[9] A. Oryan, A. Kamali, A. Moshiri, M. Baghaban Eslaminejad, Role of mesenchymal stem cells in bone regenerative medicine: what is the evidence? Cells Tissues Organs 204 (2) (2017) 59–83.

[10] P. Hernigou, A. Habibi, D. Bachir, F. Galacteros, The natural history of asymptomatic osteonecrosis of the femoral head in adults with sickle cell disease, J. Bone Joint Surg. Am. 88 (12) (2006) 2565–2572.

[11] S. Xu, L. Zhang, H. Jin, Autologous Stem Cells Combined Core Decompression for Treatment of Avascular Necrosis of the Femoral Head: A Systematic Meta-Analysis vol 2017, (2017), p. 6136205.

[12] L. Zhao, A.D. Kaye, A.J. Kaye, A. Abd-Elsayed, Stem cell therapy for osteonecrosis of the femoral head: current trends and comprehensive review, Curr. Pain Headache Rep. 22 (6) (2018) 41.

[13] J.P. Hauzeur, V. De Maertelaer, E. Baudoux, M. Malaise, Y. Beguin, V. Gangji, Inefficacy of autologous bone marrow concentrate in stage three osteonecrosis: a randomized controlled double-blind trial, Int. Orthop. 42 (7) (2018) 1429–1435.

[14] J.S. Kang, Y.J. Suh, K.H. Moon, J.S. Park, T.H. Roh, M.H. Park, D.J. Ryu, Clinical Efficiency of Bone Marrow Mesenchymal Stem Cell Implantation for Osteonecrosis of the Femoral Head: a Matched Pair Control Study with Simple Core Decompression vol 9, (2018), p. 274 1.

[15] V. Gangji, V. De Maertelaer, J.P. Hauzeur, Autologous bone marrow cell implantation in the treatment of non-traumatic osteonecrosis of the femoral head: five year follow-up of a prospective controlled study, Bone 49 (5) (2011) 1005–1009.

[16] V. Gangji, J.P. Hauzeur, C. Matos, V. De Maertelaer, M. Toungouz, M. Lambermont, Treatment of osteonecrosis of the femoral head with implantation of autologous bone-marrow cells. A pilot study, J. Bone Joint Surg. Am. 86-a (6) (2004) 1153–1160.

[17] W. Pepke, P. Kasten, N.A. Beckmann, P. Janicki, M. Egermann, Core decompression and autologous bone marrow concentrate for treatment of femoral head osteonecrosis: a randomized prospective study, Orthop. Rev. 8 (1) (2016) 6162.

[18] R.K. Sen, S.K. Tripathy, S. Aggarwal, N. Marwaha, R.R. Sharma, N. Khandelwal, Early results of core decompression and autologous bone marrow mononuclear cells instillation in femoral head osteonecrosis: a randomized control study, J. Arthroplast. 27 (5) (2012) 679–686.

[19] R.M. Tabatabaee, S. Saberi, J. Parvizi, S.M. Mortazavi, M. Farzan, Combining concentrated autologous bone marrow stem cells injection with core decompression improves outcome for patients with early-stage osteonecrosis of the femoral head: a comparative study, J. Arthroplast. 30 (9 Suppl) (2015) 11–15.

[20] D. Zhao, D. Cui, B. Wang, F. Tian, L. Guo, L. Yang, B. Liu, X. Yu, Treatment of early stage osteonecrosis of the femoral head with autologous implantation of bone marrow-derived and cultured mesenchymal stem cells, Bone 50 (1) (2012) 325–330.

[21] S. Rastogi, S.R. Sankineani, H.L. Nag, S. Mohanty, G. Shivanand, K. Marimuthu, R. Kumar, L. Rijal, Intralesional autologous mesenchymal stem cells in management of osteonecrosis of femur: a preliminary study, Musculoskel. Surg. 97 (3) (2013) 223–228.

[22] Y. Ma, T. Wang, J. Liao, H. Gu, X. Lin, Q. Jiang, M.K. Bulsara, M. Zheng, Q. Zheng, Efficacy of autologous bone marrow buffy coat grafting combined with core decompression in patients with avascular necrosis of femoral head: a prospective, double-blinded, randomized, controlled study, Stem Cell Res. Ther. 5 (5) (2014) 115.

[23] X.-W. Guo W-XW, Y.-F. Hong, Study of core decompression and transplant of autologous bone marrow stem cells for treatment of avascular necrosis of femoral head, J. Bone Joint Surg. Br. 29 (5) (2008) 19–21.

[24] L. Yang YY, L.-X. Cai, et al., Core decompression combined with autologous concentrated bone marrow cell transplantation for treatment of early osteonecrosis of femoral head, Clin. Orthop. Relat. Res. 44 (3) (2004) 343–344 1976-2007.

[25] R.-G. Zhao, H. BL, B. Han, et al., Efcacy of core decompression and transplant of autologous bone marrow stem cells for treatment of early stage avascular necrosis of femoral head, Peoples Militar. Surg. 59 (4) (2004) 372–373.

[26] T. Chang KT, X. Tao, et al., Treatment of early avascular necrosis of femoral head by core decompression combined with autologous bone marrow mesenchymal stem cells transplantation, Chin. J. Reparative Reconstr. Surg. 24 (6) (2010) 739–743.

[27] Y. Sun W-HZ, Y.-M. Yao, Treatment of osteonecrosis of femoral head by combination of center decompression and implantation of autogenous bone and mesenchymal stem cells, Med. J. Natl. Defend. Forces Southwest China 18 (6) (2005) 800–802.

[28] S.Z.L. Xu, H. Jin, L. Shan, L. Zhou, L. Xiao, P. Tong, Autologous stem cells combined core decompression for treatment of avascular necrosis of the femoral head: a systematic meta-analysis, BioMed Res. Int. 2017 (2017).

[29] X. Li, X. Xu, W. Wu, Comparison of bone marrow mesenchymal stem cells and core decompression in treatment of osteonecrosis of the femoral head: a meta-analysis, Int. J. Clin. Exp. Pathol. 7 (8) (2014) 5024–5030.

[30] F.P. Castro Jr., R.L. Barrack, Core decompression and conservative treatment for avascular necrosis of the femoral head: a meta-analysis, Am. J. Orthoped. 29 (3) (2000) 187–194.

[31] Z. Zhao, X. Ma, J. Ma, X. Sun, F. Li, J. Lv, Naringin enhances endothelial progenitor cell (EPC) proliferation and tube formation capacity through the CXCL12/CXCR4/PI3K/Akt signaling pathway, Chem. Biol. Interact. 286 (2018) 45–51.

[32] N.S. Piuzzi, J. Chahla, J.B. Schrock, R.F. LaPrade, C. Pascual-Garrido, M.A. Mont, G.F. Muschler, Evidence for the use of cell-based therapy for the treatment of osteonecrosis of the femoral head: a systematic review of the literature, J. Arthroplast. 32 (5) (2017) 1698–1708.

[33] H.F. Yuan, J. Zhang, C.A. Guo, Z.Q. Yan, Clinical outcomes of osteonecrosis of the femoral head after autologous bone marrow stem cell implantation: a meta-analysis of seven case-control studies, Clinics 71 (2) (2016) 110–113.