Efficacy and Safety of Icariin Capsules in Intervening Post-operative Bone Grafting for Hip Osteonecrosis in ARCO Stage II

Yuanzhuo Xu[1], Yu Zhou[1,2,3], Wei Sun[4], Fuqiang Gao[1,2,3]

Abstract

Introduction: Both hip-preserving surgery and pharmacological therapy can effectively improve symptoms in patients with early-stage osteonecrosis of the femoral head (ONFH) and are expected to delay the need for total hip arthroplasty. However, the clinical efficacy of combining hip-preserving surgery with drug therapy has not yet been widely substantiated. Therefore, we conducted a randomized clinical trial to compare the clinical outcomes of impacted bone graft (IBG) combined with Icariin (ICA) versus IBG alone.

Purposes: The aim of this study was to clinically observe and evaluate the interventional therapeutic effect of ICA in patients with corticosteroid-induced ONFH following hip-preserving surgery, by comparing the femoral head collapse rate with a placebo control group, thereby providing a reliable basis for expanding the clinical application indications of ICA.

Materials and Methods: This was a prospective randomized clinical trial. Patients with early-stage steroid-induced ONFH (ARCO stage II) who underwent hip-preserving surgery were eligible. Between September 2021 and August 2022, we randomized 46 patients to receive either IBG plus ICA or IBG alone. At the 1-year follow-up, 87% of patients (20 out of 23) in both the IBG+ICA and IBG groups were available for assessment. The observed indicators included patient-reported outcome measures ([PROMs], including Harris Hip Score [HHS], the 36-item short form health survey [SF-36], and Visual Analog Scale [VAS]) and the progression of femoral head collapse on imaging, assessed preoperatively and within 1 year postoperatively. No significant differences were noted in baseline characteristics such as age, gender, affected side, and PROMs between the two groups.

Results: We found no statistically significant difference in the improvement of the HHS (4.7 ± 3.6 vs. 4.0 ± 3.5, respectively; mean difference 0.7 [95% confidence interval [CI] −1.5–3.0]; P = 0.505) or the VAS score (0.28 ± 0.29 vs. 0.14 ± 0.25, respectively; mean difference 0.14 [95% CI −0.03–0.32]; P = 0.099) between the IBG + ICA group and the IBG group at 3 months postoperatively. However, significant differences began to emerge by 6 months postoperatively (HHS at 6 months: 8.4 ± 3.0 vs. 5.4 ± 2.8, respectively; mean difference 3.0 [95% CI 1.1–4.8]; P = 0.003; HHS at 12 months: 10.8 ± 3.3 vs. 7.7 ± 3.4, respectively; mean difference 3.1 [95% CI 1.0–5.3]; P = 0.005; VAS at 6 months: 0.48 ± 0.27 vs. 0.30 ± 0.17, respectively; mean difference 0.18 [95% CI 0.03–0.32]; P = 0.021; VAS at 12 months: 0.84 ± 0.26 vs. 0.50 ± 0.25, respectively; mean difference 0.34 [95% CI 0.18–0.51]; P < 0.001). Furthermore, the IBG+ICA group demonstrated a significantly greater improvement in the SF-36 score at 12 months postoperatively compared to the IBG group (7.9 ± 3.1 vs. 3.5 ± 3.2, respectively; mean difference 4.4 [95% CI 2.4–6.4]; P < 0.001). No significant difference in the progression of femoral head collapse was observed between the two groups. Furthermore, no drug-related adverse reactions were reported.

Conclusion: Based on the 1-year follow-up of the two groups of patients and the analysis results, IBG + ICA did not bring more significant clinical symptom improvement to the patients compared to IBG at 3 months postoperatively. However, from 6 months postoperatively, the former showed better clinical efficacy. There was no significant difference in the impact on the progression of femoral head collapse between the

[1]Department of Orthopedic Surgery, China-Japan Friendship Hospital (Institute of Clinical Medical Sciences), Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China,
[2]Center for Hip Preservation, Osteonecrosis and Developmental Dysplasia of the Hip, China-Japan, Friendship Hospital, Beijing, China,
[3]Department of Orthopedic Surgery, Capital Medical University, China-Japan Friendship School of Clinical Medicine, Beijing, China,
[4]Department of Orthopaedic Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA.

Address of Correspondence
Dr. Wei Sun,
Department of Orthopaedic Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA.
E-mail: wei.sun@pennmedicine.upenn.edu


Dr. Yuanzhuo Xu


Dr. Yu Zhou


Dr. Wei Sun


Dr. Fuqiang Gao

Submitted Date: 19 Oct 2025, Review Date: 18 Nov 2025, Accepted Date: Nov 2025 & Published: 30 Dec 2025

Journal of Regenerative Science | Available on www.jrsonweb.com | DOI:10.13107/jrs.2025.v05.i02.173

two intervention methods within the 1-year follow-up period postoperatively. The safety of ICA during the perioperative period has been confirmed. For patients with severe pain or poor quality of life due to early ONFH, IBG+ICA treatment may be a good choice to improve the patient's pain and quality of life.

Keywords: Icariin, Impacted bone graft, Hip osteonecrosis, Outcomes, Statistical Package for the Social Sciences

Introduction

Osteonecrosis of the femoral head (ONFH) is a prevalent and refractory orthopedic disorder characterized by progressive structural deterioration and eventual collapse of the femoral head. Clinical manifestations typically include pain, limping, and restricted hip joint function, often leading to disability, and predominantly affect younger patients [1, 2, 3, 4, 5, 6]. ONFH is broadly categorized into traumatic and non-traumatic types, with key risk factors for the latter including corticosteroid use, excessive alcohol consumption, hyperlipidemia, obesity, certain occupations (such as diving), smoking, and diabetes mellitus [7].

In advanced stages, total hip arthroplasty (THA) is often required. However, joint-preserving interventions can effectively slow disease progression and delay the need for THA [8, 9, 10]. Among these, impacted bone graft (IBG) serves as a core procedure that provides robust structural support to the femoral head, mitigates further collapse, and partially restores morphological contour. Its advantages include a relatively straightforward technique, low complication rate, and reduced operative time [11, 12]. The pursuit of effective hip-preserving strategies has spurred the development of several surgical variants. For instance, the "lightbulb" technique – IBG augmented with a wire coil – has shown value in selected patients with early-stage disease and limited lesion size [13]. Similarly, vascularized bone graft implantation, particularly vascularized iliac bone flap transplantation, is widely practiced and regarded as an important approach even in cases with early collapse [14, 15].

Beyond surgical options, the potential of pharmacological interventions has gained attention. Icariin (ICA), a primary active constituent of Epimedium, has demonstrated efficacy in animal models of steroid-induced ONFH. It is reported to reverse the osteonecrosis process by restoring the balance between osteogenic and adipogenic differentiation of mesenchymal stem cells, inhibiting apoptosis, and modulating osteoblast and osteoclast activity. At the vascular level, ICA enhances vascular function and protects bone marrow endothelial cells from steroid-induced injury by correcting glucocorticoid-related miRNA-335 expression imbalance [16, 17, 18]. Furthermore, ICA helps preserve bone tissue against glucocorticoid-induced structural damage, improving overall morphology and stabilizing bone microstructure [19].

Despite these surgical advances and the promising pharmacological profile of ICA, clinical studies exploring the combined use of such agents with hip-preserving procedures remain limited. In a manner analogous to the enhancement of bone repair seen with recombinant human bone morphogenetic protein-2 in IBG [10], we hypothesize that ICA may similarly improve the clinical outcomes of IBG. Therefore, this study aims to evaluate the therapeutic efficacy of ICA as an adjunct to hip-preservation surgery in steroid-induced ONFH in ARCO Stage II, thereby providing a robust foundation for its expanded clinical application.

Materials and Methods

Study design and setting

The study was conducted in the Department of Orthopedics and Joint Surgery at the China-Japan Friendship Hospital (CJFH) from September 2021 to September 2023. The ICA capsules and placebos were provided by China National Pharmaceutical Group Corp. Tongjitang (Guizhou) Pharmaceutical Co., Ltd.

Participants

We enrolled 46 patients aged 18–65 with early-stage steroid-induced ONFH. The inclusion criteria were as follows: A history of high-dose corticosteroid use; diagnosis of avascular ONFH confirmed by magnetic resonance imaging (ARCO stage II); and selection for scientifically standardized hip-preserving surgery according to the CJFH classification. Patients must have met one of the following corticosteroid exposure criteria: A cumulative dose exceeding 2000 mg (calculated as prednisone equivalent) within 3 months; initial use of prednisone ≥6 tablets (5 mg/tablet) per day for more than 1 month; or high-dose steroid pulse therapy (e.g., methylprednisolone ≥800 mg/day for 3 consecutive days).

Randomization and blind method

To ensure blinding of both investigators and participants throughout the trial, a rigorous process was implemented. Indistinguishable ICA capsules and placebos are prepackaged by the sponsor with unique randomization codes. An independent third party then generates the randomization list, linking these codes to either "Drug A" (active) or "Drug B" (placebo). This critical list is secured solely with the sponsor and the Institutional Review Board for emergency access, keeping the entire research team blinded. As subjects enroll, an independent drug dispenser, who is also unaware of treatment assignments, allocates the medications sequentially based on these codes. This ensures that the treating investigators and the subjects themselves remain blinded to the assigned treatment. Emergency unblinding is permitted only in cases of serious adverse events requiring knowledge of the treatment. Formal unblinding occurs in a two-stage process after the database is locked: First to distinguish between Group A and Group B, and finally to reveal the specific treatment identity for the conclusive statistical analysis.

Participant flow

Between September 2021 and August 2022, we randomized 46 patients to undergo IBG + ICA (n = 23) or IBG (n = 23). All subjects were administered the medication twice a day, with each dose consisting of three capsules (0.5 g/capsule, containing either ICA or placebo). At the 1-year follow-up, 87% (20 of 23) of patients in both groups were available (Fig. 1).

Descriptive data

No differences of age, gender, side, or any of the patient-reported

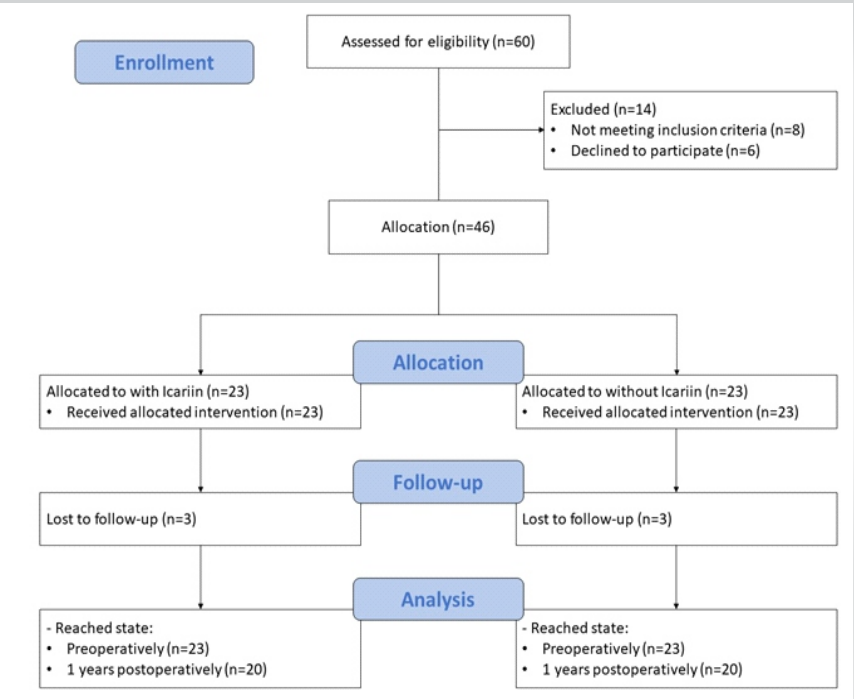

Figure 1: The consolidated standards of reporting trials flow chart for this study.

outcome measures (PROMs, including Harris Hip Score [HHS], available in http://www.ncbi.nlm.nih.gov/pubmed/5783851 [20], 36-item short form health survey [SF-36] [available in https://pubmed.ncbi.nlm.nih.gov/1285753/] [21], and Visual Analog Scale [VAS] [available in https://www.sciencedirect.com/science/article/pii/S0140673674908848] [22]) were noted between the IBG + ICA and the IBG cohort (Table 1).

Surgical technique

The surgical procedure involves femoral head and neck fenestration, necrotic lesion debridement, and IBG. Under general anesthesia, an anterolateral or posterolateral surgical approach is selected based on the necrotic focus location. The skin, subcutaneous tissues, and joint capsule are incised sequentially to adequately expose the femoral head and neck region. A fenestration is then created in the femoral head and neck, through which the necrotic bone tissue is thoroughly debrided until healthy bone surface is exposed, followed by IBG using autogenous or allogeneic bone to fill the bone defect. Finally, the joint capsule and soft tissues are closed, and the incision is sutured layer by layer. To prevent infection, all patients receive prophylactic antibiotic therapy 30 min preoperatively and continue for 24 h postoperatively.

Post-operative treatment

The post-operative care and rehabilitation protocol is as follows: Patients commence bedside bilateral quadriceps isometric contractions and ankle pump exercises on the 1st post-operative day or as soon as pain permits; within the first 3 months post-surgery, patients are required to ambulate with bilateral crutches under partial weight-bearing conditions and receive strict guidance on fall prevention; throughout the 1st year, patients must avoid excessive weight-bearing on the affected hip and refrain from any strenuous activities.

All patients were clinically and radiographically followed up at 3, 6, and 12 months postoperatively. Clinical follow-up included pre- and post-operative serial assessments of the PROMs, evaluations of hemorheology, and the incidence of adverse reactions. Radiographic follow-up consisted of serial anteroposterior and frog-leg lateral hip radiographs. When necessary, hip computed tomography scans were further performed to observe whether the necrotic lesion was partially or fully repaired and to detect the occurrence of any subchondral fractures.

Outcomes assessed

Our primary study goal was to evaluate whether IBG+ICA provides superior clinical results compared with IBG. To achieve this, we collected PROMs preoperatively and at 1 year postoperatively. The patient was asked to fill in the questionnaires at home.

The secondary research objectives of this study include: Conducting imaging evaluations through anteroposterior and lateral hip X-ray films and frog-leg lateral hip X-ray films to observe the progression of femoral head necrosis collapse; conducting hemorheological evaluations through hemorheology and coagulation/fibrinolysis tests to assess the impact of the drugs on the systemic circulation and microcirculation status. In addition, adverse reactions were recorded.

Ethical approval

Ethics committee approval was obtained from the ethical committee of CJFH, and all patients gave written informed consent (2022-KY-038). This study was registered on the Chinese Clinical Trial Registry with the registration number ChiCTR2100043127.

Table 1: Pre-operative characteristics of both the IBG+ICA and the IBG cohort

Characteristic	IBG+ICA (*n*=23)	IBG (*n*=23)
Age in years	30.9±8.0	32.9±8.8
Left hip	40 (8)	50 (10)
Women	45 (9)	45 (9)
Harris hip score	74.4±4.6	74.0±5.7
SF-36	109.2±8.9	112.2±9.6
VAS	2.14±0.59	2.40±0.59

*Data presented as mean±standard deviation or % (*n*). IBG: Impacted bone graft, ICA: Icariin, SF-36: 36-item short form health survey, VAS: Visual Analog Scale

Table 2: Pre-operative-post-operative paired *t*-test in the same patient of the IBG+ICA group

Outcome score	IBG+ICA (*n*=20)			
	Mean±standard deviation	95% confidence interval		*P*-value
		Lower limit	Upper limit	
HHS				
Post-3 m	−4.7±3.6	−6.4	−3.0	<0.001
Post-6 m	−8.4±3.0	−9.7	−7.0	<0.001
Post-12 m	−10.8±3.3	−12.4	−9.3	<0.001
SF-36				
Post-12 m	−7.9±3.1	−9.4	−6.4	<0.001
VAS				
Post-3 m	0.28±0.29	0.14	0.42	<0.001
Post-6 m	0.48±0.27	0.35	0.61	<0.001
Post-12 m	0.84±0.26	0.72	0.97	<0.001

*HHS represents the Harris hip score. IBG: Impacted bone graft, ICA: Icariin, SF-36: 36-item short form health survey, VAS: Visual Analog Scale

Statistical analysis

We used the IBM Statistical Package for the Social Sciences Statistics 27, developed by International Business Machines Corp., as the statistical analysis software. In this study, we performed an intention-to-treat analysis. Categorical data analysis was performed using the chi-square test. Homogeneity of variances was evaluated using the Levene test. Normality of continuous variables was tested with the Shapiro-Wilk test and confirmed through box plots. Parametric data were analyzed using independent t-tests, while nonparametric data were assessed using the Mann–Whitney U-test.

Results

Paired-sample t-tests (comparing pre-operative scores with post-operative scores at each time point) revealed that IBG significantly improved all clinical symptom outcomes at every follow-up time point compared to pre-operative levels, regardless of ICA administration (Table 2 and Table 3). Consequently, the absolute value of the change in each patient's indicators was calculated. Independent-sample t-tests were then used to compare whether significant differences existed in the improvement of clinical symptom outcomes between IBG+ ICA and IBG groups (Table 4). The analyses indicated no statistically significant difference in the improvement of the HHS (4.7 ± 3.6 vs. 4.0 ± 3.5, respectively; mean difference 0.7 [95% confidence interval [CI] −1.5–3.0]; P = 0.505) or the VAS score (0.28 ± 0.29 vs. 0.14 ± 0.25, respectively; mean difference 0.14 [95% CI −0.03–0.32]; P = 0.099) between the two groups at the 3-month post-operative mark. However, significant differences began to emerge by 6 months postoperatively (HHS at 6 months: 8.4 ± 3.0 vs. 5.4 ± 2.8, respectively; mean difference 3.0 [95% CI 1.1–4.8]; P = 0.003; HHS at 12 months: 10.8 ± 3.3 vs. 7.7 ± 3.4, respectively; mean difference 3.1 [95% CI 1.0–5.3]; P = 0.005) (VAS at 6 months: 0.48 ± 0.27 vs. 0.30 ± 0.17, respectively; mean difference 0.18 [95% CI 0.03–0.32]; P = 0.021; VAS at 12 months: 0.84 ± 0.26 vs. 0.50 ± 0.25, respectively; mean difference 0.34 [95% CI 0.18–0.51]; P < 0.001). Furthermore, the IBG+ ICA group demonstrated a significantly greater improvement in the SF-36 score at 12 months postoperatively compared to the IBG group (7.9 ± 3.1 vs. 3.5 ± 3.2, respectively; mean difference 4.4 [95% CI 2.4–6.4]; P < 0.001). During the follow-up period, no femoral head collapse or progression of ARCO staging was observed in either group. Both groups showed varying degrees of repair, with no occurrence of subchondral fractures or collapse of the femoral head.

Discussion

This prospective randomized controlled trial aimed to assess the efficacy and safety of IBG combined with ICA in treating early-stage steroid-induced ONFH. Our key findings revealed that while IBG+ICA did not yield significant advantages in the early post-operative phase (3 months), it brought about superior and lasting improvements in hip function (evaluated through HHS, pain relief (assessed by VAS score), and quality of life (measured using SF-36 score) from the 6-month follow-up onwards, with these positive effects persisting through the 12-month assessment. Notably, there was no significant difference between the two treatment groups in terms of radiographic progression of femoral head collapse at the 1-year mark, and the combined therapy did not lead to an increased incidence of adverse reactions.

Table 3: Pre-operative-post-operative paired *t*-test in the same patient of the IBG group

Outcome score	IBG (*n*=20)			
	Mean±standard deviation	95% confidence interval		*P*-value
		Lower limit	Upper limit	
HHS				
Post-3 m	−4.0±3.5	−5.6	−2.3	<0.001
Post-6 m	−5.4±2.8	−6.7	−4.1	<0.001
Post-12 m	−7.7±3.4	−9.3	−6.1	<0.001
SF-36				
Post-12 m	−3.5±3.2	−5.0	−2.0	<0.001
VAS				
Post-3 m	0.14±0.25	0.02	0.25	0.026
Post-6 m	0.30±0.17	0.22	0.39	<0.001
Post-12 m	0.50±0.25	0.38	0.62	<0.001

*HHS represents the Harris hip score. IBG: Impacted bone graft, ICA: Icariin, SF-36: 36-item short form health survey, VAS: Visual Analog Scale

Table 4: Independent t -test of improvement differences between the two patient groups

Outcome score improvement value	IBG+ICA (n=20)	IBG (n=20)	*P*-value
HHS			
Post-3 m	4.7±3.6	4.0±3.5	0.505
Post-6 m	8.4±3.0	5.4±2.8	0.003
Post-12 m	10.8±3.3	7.7±3.4	0.005
SF-36			
Post-12 m	7.9±3.1	3.5±3.2	<0.001
VAS			
Post-3 m	0.28±0.29	0.14±0.25	0.099
Post-6 m	0.48±0.27	0.30±0.17	0.021
Post-12 m	0.84±0.26	0.50±0.25	<0.001

***HHS represents the Harris hip score. All data in the table are improvement values, which represent the absolute value of the difference in the same metric from pre- to post-operation. IBG: Impacted bone graft, ICA: Icariin, SF-36: 36-item short form health survey, VAS: Visual Analog Scale**

Statistically significant disparities were observed between the two groups in the HHS (with a 3.1-point difference at 12 months) and the VAS (a 0.34-point difference at 12 months). These results fully illustrate the additional benefits of supplementing with ICA. The notable advantage in the SF-36 score (with an average difference of 4.4 points) further reflects the comprehensive enhancement in the overall health-related quality of life among patients in the combined treatment group. It is important to acknowledge, however, that there is currently no established minimal clinically important difference specifically for patients with early ONFH who have undergone hip preservation surgery. In addition, our interpretation of the clinical relevance of the reported results for this patient population primarily relies on statistical inference, and further validation through future studies is warranted.

Our findings offer solid clinical evidence supporting the adjunctive role of ICA in hip-preserving surgery. The absence of significant differences at the 3-month follow-up may be attributed to the predominant influence of surgical trauma recovery during this early period. In contrast, the biological effects of ICA appear to unfold gradually over time. These clinical findings are consistent with a body of preclinical research. Numerous animal studies have demonstrated that ICA can reverse the glucocorticoid-induced imbalance between osteogenic and adipogenic differentiation of mesenchymal stem cells, inhibit apoptosis, and promote angiogenesis, thereby restoring bone microcirculation [14,15,16,17,18,19,23,24]. Consequently, the superior clinical improvements seen in the IBG + ICA group during the mid- to long-term follow-up are likely rooted in ICA's ability to enhance the biological repair and regeneration of the necrotic area, going beyond the mere mechanical support provided by bone graft alone.

An interesting observation from this study is the lack of significant difference in radiographic collapse progression despite the marked clinical improvements. This suggests that while ICA's primary mechanisms of action may target the biological microenvironment – alleviating pain and inflammation, and potentially improving bone quality – its capacity to strengthen mechanical support against subchondral collapse in established necrotic lesions may be limited. In addition, the 1-year follow-up period might be insufficient to detect differences in the slow, progressive process of femoral head collapse. Therefore, a longer observation period is necessary to draw definitive conclusions regarding the impact of ICA on radiographic outcomes.

The clinical implication of this study is that for patients with early-stage ONFH experiencing significant pain and functional impairment, the adjunctive use of ICA alongside standard hip-preserving surgery constitutes a safe and effective strategy to enhance mid-term quality of life and functional outcomes. This provides high-level evidence for expanding the clinical application of this traditional Chinese medicine formulation within the field of orthopedics.

Limitation

This study has several limitations. First, the sample size was relatively small, which may limit the statistical power and generalizability of the findings, despite the significant results observed. Second, the follow-up was limited to 1 year, precluding assessment of the long-term durability of the treatment effect and its impact on the eventual rate of THA. Furthermore, the study focused exclusively on steroid-induced ONFH, and whether the results can be generalized to alcohol-induced or idiopathic ONFH remains unknown.

Future research should involve larger, multicenter studies with extended follow-up periods to validate these findings. In addition, integrating advanced imaging techniques and exploring specific biomarkers could help elucidate the precise mechanisms of ICA action at a microscopic level and identify patient subgroups most likely to benefit from this combined therapeutic approach.

Conclusion

Based on the 1-year follow-up and analysis, IBG+ICA did not bring more significant clinical symptom improvement to the patients compared to IBG at 3 months postoperatively. However, from 6 months postoperatively, the former showed better clinical efficacy. There was no significant difference in the impact on the progression of femoral head collapse between the two intervention methods within the 1-year follow-up period postoperatively. The safety of ICA during the perioperative period has been confirmed. For patients with severe pain or poor quality of life due to early ONFH, IBG+ICA treatment may be a good choice to improve the patient's pain and quality of life.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil

Source of support: China-Japan Friendship Hospital Horizontal Project/Spontaneous Research Funding (2022-HX-9, 2024-HX-6, 2022-HX-JC-7), Capital's Funds for Health Improvement and Research (CFH 2024-2-40611), Beijing Natural Science Foundation (7242127),National High Level Hospital Clinical Research Funding (2025-NHLHCRF-JBGS-B-ZH-01), National Clinical Research Center for Orthopedics and Sports Rehabilitation Innovation Fund Special Fund for Science Popularization Construction (NCRC-CXJJ-KP-2025-013), Special Project of China Association of Medicine and Education (ZXRH-MXGB-003), Key Project of Digital Medical Concept Validation Plan of Digital Medical Concept Validation Center in Chaoyang District, Beijing (2025SLQY02), and Joint Project of BRC-BC (Biomedical Translational Engineering Research Center of BUCT-CJFH) (RZ2020-02).

References

1. Li Z, Shao W, Lv X, Wang B, Han L, Gong S, et al. Advances in experimental models of osteonecrosis of the femoral head. J Orthop Translat 2023;39:88-99.

2. Zhang J, Cao J, Liu Y, Zhao H. Advances in the pathogenesis of steroid-associated osteonecrosis of the femoral head. Biomolecules 2024;14:667.

3. Quan H, Ren C, He Y, Wang F, Dong S, Jiang H. Application of biomaterials in treating early osteonecrosis of the femoral head: Research progress and future perspectives. Acta Biomater 2023;164:15-73.

4. Zhao Y, Li S, Feng M, Zhang M, Liu Z, Yao Y, et al. Effects of puerarin-loaded tetrahedral framework nucleic acids on osteonecrosis of the femoral head. Small 2023;19:e2302326.

5. Chen CY, Rao SS, Yue T, Tan YJ, Yin H, Chen LJ, et al. Glucocorticoid-induced loss of beneficial gut bacterial extracellular vesicles is associated with the pathogenesis of osteonecrosis. Sci Adv 2022;8:eabg8335.

6. Huang C, Qing L, Xiao Y, Tang J, Wu P. Insight into steroid-induced ONFH: The molecular mechanism and function of epigenetic modification in mesenchymal stem cells. Biomolecules 2023;14:4.

7. Zhao D, Zhang F, Wang B, Liu B, Li L, Kim SY, et al. Guidelines for clinical diagnosis and treatment of osteonecrosis of the femoral head in adults (2019 version). J Orthop Translat 2020;21:100-10.

8. Wu CT, Kuo FC, Yen SH, Lin PC, Wang JW, Lee MS. Impaction bone grafting augmented with a wire coil by the lightbulb technique for osteonecrosis of the femoral head. J Arthroplasty 2022;37:2063-70.

9. Rosenwasser MP, Garino JP, Kiernan HA, Michelsen CB. Long term followup of thorough debridement and cancellous bone grafting of the femoral head for avascular necrosis. Clin Orthop Relat Res 1994;306:17-27.

10. Sun W, Li Z, Gao F, Shi Z, Zhang Q, Guo W. Recombinant human bone morphogenetic protein-2 in debridement and impacted bone graft for the treatment of femoral head osteonecrosis. PLoS One 2014;9:e100424.

11. Chu K, Wang Y, Liu B, Li Z, Wang Z, Zhang J, et al. Direct anterior approach versus posterior approach in total hip arthroplasty after ONFH with failed vascularized iliac crest bone grafting for hip preservation: A retrospective comparative study. BMC Musculoskelet Disord 2025;26:686.

12. Zhao D, Huang S, Lu F, Wang B, Yang L, Qin L, et al. Vascularized bone grafting fixed by biodegradable magnesium screw for treating osteonecrosis of the femoral head. Biomaterials 2016;81:84-92.

13. Lou P, Zhou G, Wei B, Deng X, Hou D. Bone grafting for femoral head necrosis in the past decade: A systematic review and network meta-analysis. Int J Surg 2023;109:412.

14. Xu J, Deng W, Zhu X, Han D, Zheng Y, Zheng Q. Potential efficacy and mechanisms of icariin for the animal model of osteonecrosis of the femoral head. Front Pharmacol 2025;16:1508971.

15. Sun ZB, Wang JW, Xiao H, Zhang QS, Kan WS, Mo FB, et al. Icariin may benefit the mesenchymal stem cells of patients with steroid-associated osteonecrosis by ABCB1-promoter demethylation: A preliminary study. Osteoporos Int 2015;26:187-97.

16. Yue J, Yu H, Liu P, Wen P, Zhang H, Guo W, et al. Preliminary study of icariin indicating prevention of steroid-induced osteonecrosis of femoral head by regulating abnormal expression of miRNA-335 and protecting the functions of bone microvascular endothelial cells in rats. Gene 2021;766:145128.

17. Huang Z, Cheng C, Cao B, Wang J, Wei H, Liu X, et al. Icariin protects against glucocorticoid-induced osteonecrosis of the femoral head in rats. Cell Physiol Biochem 2018;47:694-706.

18. Yu H, Yue J, Wang W, Liu P, Zuo W, Guo W, et al. Icariin promotes angiogenesis in glucocorticoid-induced osteonecrosis of femoral heads: In vitro and in vivo studies. J Cell Mol Med 2019;23:7320-30.

19. Yang X, Shi L, Li A, Gao F, Sun W, Li Z. Phase-contrast imaging with synchrotron hard X-ray reveals the effect of icariin on bone tissue morphology and microstructure in rabbits with

early glucocorticoid-induced osteonecrosis of the femoral head. Front Cell Dev Biol 2023;11:1155532.

20. Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: Treatment by mold arthroplasty. An end-result study using a new method of result evaluation. J Bone Joint Surg Am 1969;51:737-55.

21. Ware JE Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.

22. Huskisson EC. Measurement of pain. The Lancet 1974;304:1127-31.

23. Xie X, Pei F, Wang H, Tan Z, Yang Z, Kang P. Icariin: A promising osteoinductive compound for repairing bone defect and osteonecrosis. J Biomater Appl 2015;30:290-9.

24. Zhang X, Li H, Chen F, Chen Y, Chai Y, Liao J, et al. Icariin regulates miR-23a-3p-mediated osteogenic differentiation of BMSCs via BMP-2/Smad5/Runx2 and WNT/β-catenin pathways in osteonecrosis of the femoral head. Saudi Pharm J 2021;29:1405-15.

Acknowledgement: Dr. Yuanzhuo Xu and Dr. Yu Zhou contributed equally to this work.

Conflict of Interest: NIL

How to Cite this Article

Xu Y, Zhou Y, Sun W, Gao F | Efficacy and safety of Icariin capsules in intervening post-operative bone grafting for hip osteonecrosis in ARCO stage II | Journal of Regenerative Science | Jul-Dec 2025; 5(2): 13-19.