

Original Article

Core decompression combined with superselective arterial infusion in treating early nontraumatic osteonecrosis of femoral head

Qian Chen, Li Qian, Liang Zhang, Da-Shou Wang, Qi Pan, Qian-Ming Wu, Meng He, Yong Jin, Yan Chen, Rui-Hong Huang, Yue Zhai, Jin-Yu Luo, Dan Liao, Yang Xiao, Yang-Ming Sunwen

Department of Pain Medicine, Orthopedics Hospital of Guizhou Province, Guiyang 550002, China

Received December 18, 2015; Accepted March 5, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: The aim of this study was to investigate the early- and mid-term therapeutic effects of core decompression (CD) combined with superselective arterial infusion (SAI) in treating the osteonecrosis of femoral head (ONFH). 71 patients with Ficat stage I-III avascular necrosis of femoral head and accepted the CD treatment were randomly divided into: group A: simply performed the CD surgery, group B: CD+SAI. The pain rating index (PRI) and the Harris score were measured before the surgery, as well as 1 and 6 months after the surgery, the bi-hip MRI examination was performed before and 6 months after the surgery. PRI of Ficat stage I-II patients in group B at all postoperative time points were lower than group A, while the Harris scores were higher than group A ($P<0.05$). The Ficat stage III patients in group A showed no significant changes 1- and 6-month after the PRI surgery, while the postoperative Harris scores were increased first (1 month after the surgery), then fell to the preoperative level; the group B PRI was reduced 1- and 6-month after the surgery, while the Harris scores were increased. The reduction rate of MRI necrotic area of group B 6-month after the surgery was significantly higher than group A ($P<0.05$). The post-CD SAI could be more effective in relieving the avascular necrosis of femoral head.

Keywords: Osteonecrosis, core decompression, arterial infusion, pain

Introduction

The osteonecrosis of femoral head (ONFH) could be divided into traumatic and nontraumatic according to the pathogenic factors [1], among which the main pathophysiological characteristics of the noninvasive ONFH (long-term application of corticosteroids, alcoholism, radiotherapy, chemotherapy and idiopathic osteonecrosis) were the occurrence of femoral head ischemic events, secondary cartilage fracture and collapse, etc. [2]. Therefore, the treatment of noninvasive ONFH was mainly focused on promoting the angiogenesis, blood flow and structural support towards the necrotic region, slowing the progress of ONFH and improving the patients' life qualities [3-5].

The CD surgery was currently the most widely used surgical treatment in treating the ischemic ONFH, with the effective rate as 63.5% (33%-95%) towards the early ONFH patients (Ficat I, II) [6]. While the effects of simple CD

surgery towards the patients with subchondral fracture even collapse were not obvious, the patients still needed to be combined with the structure or cell support to improve the efficacies [7-9], especially the treatment towards the Ficat stage III patients still remained controversial. The uncertain indications and difficulties in selecting the treatment programs (CD+structural support or total hip replacement) were the main difficulties during the treatment [10].

In view of this, based on the treatment principles of ischemic ONFH, our department selected CD combined with superselective arterial infusion to treat the ischemic ONFH patients (Ficat stage I-III) and achieved better clinical efficacies.

Methods

General information

71 non-traumatic ONFH patients (71 hips), treated in our hospital from May 2010 to

Table 1. Clinical characteristics of the 2 groups

Clinical features	Group A (n=42)	Group B (n=29)	P
Age (years)			
The median age	38	41	>0.05
Range	18-62	20-59	
Gender (No, %)			
Male	26/42 (61.90%)	18/29 (62.03%)	>0.05
Ficat stage (%)			
I-II (n=51)	33/42 (78.57%)	18/29 (62.07%)	>0.05
III (n=20)	9/42 (21.43%)	11/29 (37.93%)	
Cause of disease			
Corticosteroids application	21/42 (50.00%)	16/29 (55.17%)	>0.05
Excessive alcohol abuse	13/42 (30.95%)	7/29 (24.14%)	
Without apparent reason	8/42 (19.05%)	6/29 (20.69%)	

December 2013, were selected, the diagnostic criteria were as follows: joint pain mainly at thigh, groin and buttock, the hip's mobility was limited, with the history of trauma, corticosteroid application or alcohol abuse, etc., the X-ray examination exhibited cystic degeneration, hardening or "crescent sign", MRI showed the necrotic femoral head. Among the patients, 51 cases were in Ficat stage I-II and 20 cases were in stage III. The patients included 44 males and 27 females, aged 20 to 59 years old. Causative factors: 37 cases of corticosteroids application, 20 cases of excessive alcohol abuse, and 14 cases had no apparent reason. Depending on different treatment programs, the patients were randomly divided into two groups, group A (n=42) was performed CD; group B (n=29) was performed the ipsilateral SAI 7 to 10 days after the CD surgery. All patients were informed about the experiments, and this experiment met the relevant requirements of the Declaration of Helsinki on Ethics. It could be known from **Table 1** that: age distribution, gender, stage proportion and etiology proportion of the two groups had no significant difference ($P>0.05$) (non-parametric Chi-Square test and Kruskal-Wallis H test), the two groups were comparable. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Orthopedics Hospital of Guizhou Province. Written informed consent was obtained from all participants.

Treatment methods

Method of CD surgery: The patient was preoperatively applied the continuous epidural block,

and placed in the lateral position, with the diseased limb placed upwards, the contralateral leg straightened and the ipsilateral leg flexed. The patient was performed the surface positioning to determine the drilling location, then one puncture point was selected 1 cm below the greater trochanter of diseased femur for one 4 mm incision. under the guidance of C-arm X-ray machine, one 4.0 mm bone puncturing needle was used to puncture to the bone cortex, then one 3.5 mm solid core drill was

used to break the cortical bone to determine the needling direction and point under the guidance of C-arm X-ray machine, which set the center of necrotic area as the needling end point. When puncturing into the necrotic area, it should be careful not to break through the subchondral bone, after entered the necrotic area, pull out the needle core, used the cannulated reamer to drill through the necrotic region along the guide needle and removed partial bone tissues, then pull out the cannulated reamer; then drilled again with the solid drill a little until the necrotic lesions, then used the bone cement injector to inject the calcium sulfate bone substitute alternatively, with the needle withdrawn during the injection, when the needle was withdrawn to the base of femoral neck, the gel hemostatic sponge was then injected to fill the channel. The second decompression channel was completed with the same method while towards different direction. The sterile elastic bandage was then used to fix and pressure-dress the puncture site **Figure 1**.

Method of SAI surgery: The patients was placed in the supine position, then under the guidance of C-type X-ray machine, the puncture point was selected at the artery pulse site, which was 1 cm below the midpoint of contralateral groin against the necrotic femoral head, after routinely disinfected and paved the surgical towels, the patient was given 3 ml of 2% lidocaine for the topical anesthesia, and performed 0.2 cm incision, the arterial puncture needle was used to puncture the femoral artery, then pulled out the needle core, placed into the soft guide-wire and 5F arterial sheath, the C2 or C3 catheter was then introduced into the obturator

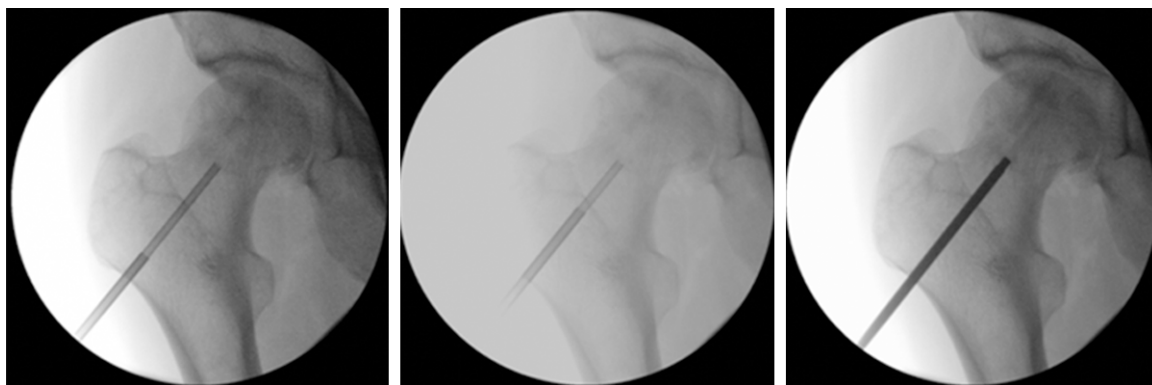


Figure 1. Images of CD surgery.

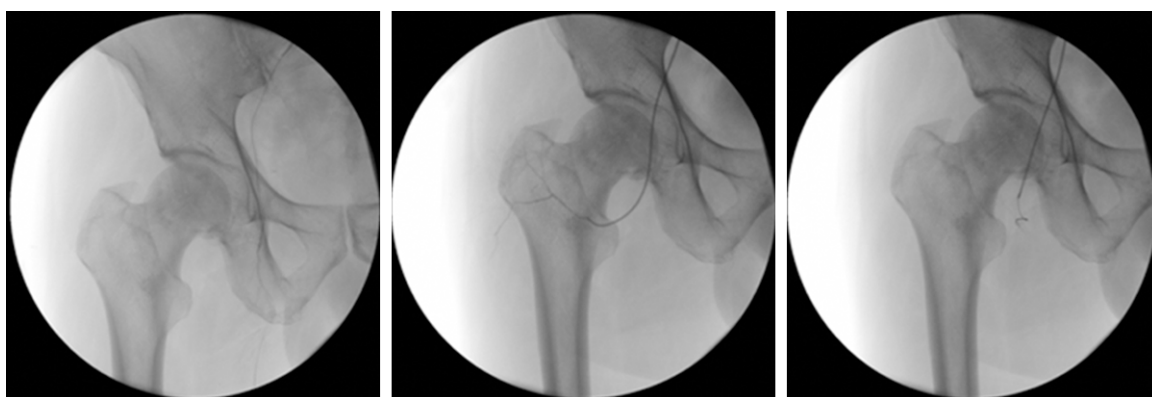


Figure 2. Images of SAI surgery. Note: circumflex femoral lateral artery (left) circumflex femoral internal artery (middle) obturator artery (right).

artery, as well as the openings of circumflex femoral internal and external arteries, and alternatively infused papaverine (30 mg+NS100 ml), urokinase (300,000 u+NS100 ml), Aogezhalei (80 mg+NS100 ml) and alprostadil (30 mg+NS100 ml), the catheter and arterial sheath were pulled out after the surgery, and incision was bond with gauze and the puncture point was fixed, the external site was pressured with salt bag and the diseased limb was stretched for more than 12 h **Figure 2**.

Evaluation indexes

The simplified McGill pain questionnaire was used preoperatively, as well as 1- and 6-month after the surgery, to evaluate the patient's pain assessment index (PRI) and Harris hip score. The PRI values and the Harris scores obtained at the above time points were then compared. MRI was re-performed 6 months after the surgery to understand the osteonecrotic changes and compare with the preoperative.

Statistical processing

SPSS 17.0 statistical software was used for the analysis, the measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$). The repeatedly measured analysis of variance and factorial analysis, as well as the trends and changes of measurement data at different time points and among different groups, were then analyzed. The main effects and the interactions among different time points and different groups (staging) were analyzed. If there existed the interactions between time and group (stage), the One-Way ANOVA should be performed with time, grouping (staging) fixed, respectively. The intragroup comparison selected the LSD method or the Game-Howell method based on the homogeneity of variance or not. The counting data were compared with the non-parametric Chi-Square test and the Kruskal-Wallis H-test, with $P < 0.05$ considered as the statistical significance, the statistical software was SPSS13.0.

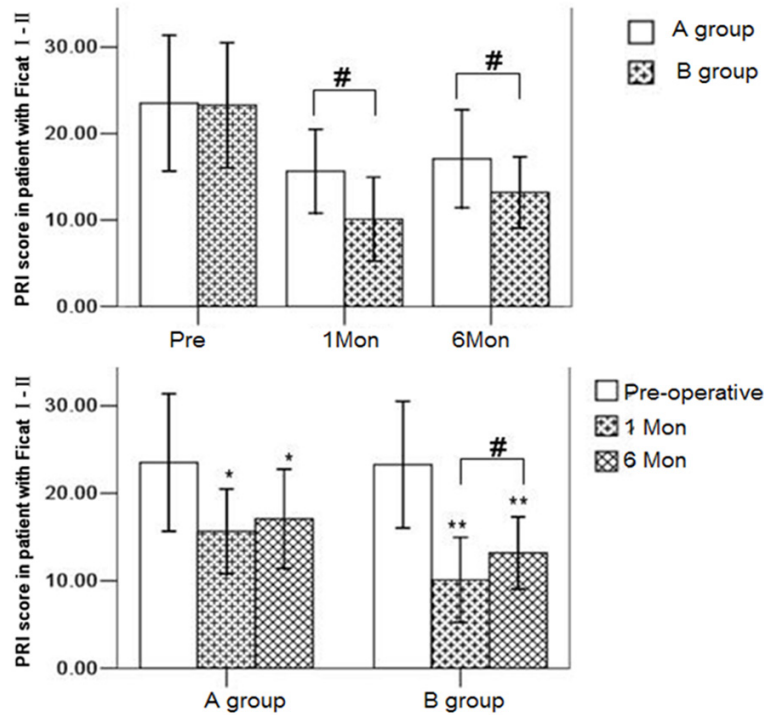


Figure 3. PRI changing trends of Ficat I-II patients at different time points and different groups. Different bars represented different groups (time points), the error bars represented the standard deviation. *: Compared with the pre-operative $P < 0.05$, **: $P < 0.01$, #: Intergroup pairwise comparison $P < 0.05$, ##: $P < 0.01$.

Results

PRI changing trends of the two Ficat I-II groups

The impacts of time and grouping on PRI had the significant differences, the main effects of time and grouping were < 0.05 , and these two factors existed the interactions ($P < 0.05$) (Figure 3). When fixed the time factor, the results showed that: the preoperative PRI values of group A (23.51 ± 7.84) and group B (22.89 ± 7.26) had no significant difference; 1 month after the surgery, PRI of group A (15.64 ± 4.87) was significantly higher than group B (10.08 ± 5.51); 6 months after the surgery, PRI of group A (17.07 ± 5.67) was significantly higher than group B (13.19 ± 4.11). When fixed the grouping factor, the results showed that: the PRI values of group A and B at 1- and 6-month after the surgery were significantly reduced than those before the surgery, there was no significant difference between the 1-month PRI value and 6-month PRI value in group A; while that in group B at 6 months after the surgery was slightly higher than that at 1 month after the surgery.

Changing trends of Harris hip scores between the Ficat I-II groups

Time and grouping exhibited statistical difference towards the Harris scores, the main effects of time and grouping were < 0.05 , and these two factors existed the interactions ($P < 0.05$) (Figure 4). When fixed the time factor, the results showed that: the preoperative Harris hip scores of group A (40.93 ± 3.79) and group B (42.76 ± 7.25) had no significant difference; 1 month after the surgery, the Harris hip scores of group A (68.02 ± 4.84) and group B (76.38 ± 6.41) had no significant difference; 6 months after the surgery, the Harris hip score of group A (58.93 ± 3.27) was significantly lower than group B (67.88 ± 8.05). When fixed the grouping factor, the results showed that: the Harris hip scores of group A and B at 1- and 6-month

after the surgery were significantly higher than those before the surgery, there was no significant difference between the 1-month and 6-month Harris hip scores in group A; while that in group B at 6 months after the surgery was slightly reduced than that at 1 month after the surgery.

PRI changing trends of two Ficat II-III groups

Time and grouping had statistical difference in affecting the PRI values of the Ficat II-III patients, the main effect of time was < 0.05 , while that of grouping was > 0.05 , and these two factors existed no interactions ($P < 0.05$) (Figure 5). When fixed the time factor, the results showed that: the preoperative PRI values of group A (32.80 ± 6.23) and group B (31.93 ± 6.45) had no significant difference; 1 month after the surgery, PRI of group A (31.99 ± 8.00) was significantly higher than group B (26.57 ± 4.54); 6 months after the surgery, PRI of group A (33.08 ± 4.99) was significantly higher than group B (28.42 ± 4.06). When fixed the grouping factor, the results showed that: the PRI values of group A at different time points

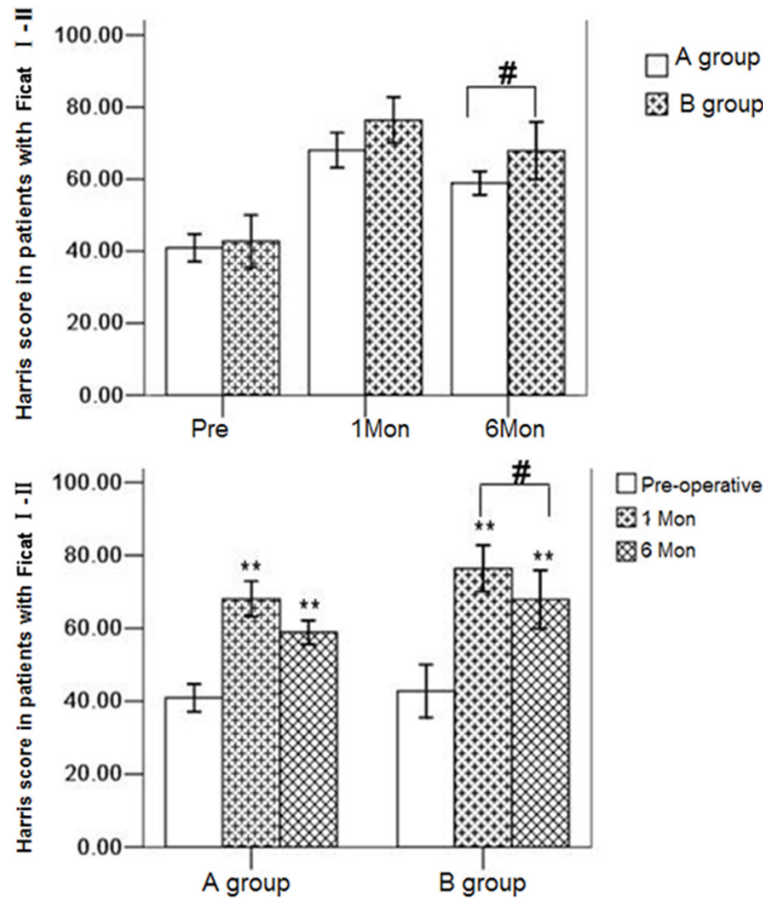


Figure 4. Changing trends of Harris hip scores of Ficat I-II patients at different time points and different groups. Different bars represented different groups (time points), the error bars represented the standard deviation. *: Compared with the preoperative $P < 0.05$, **: $P < 0.01$, #: Intergroup pairwise comparison $P < 0.05$, ##: $P < 0.01$.

had no significant difference, while those of group B were significantly reduced at 1- and 6-month than the preoperative; while the PRI values of group B between the postoperative 1- and 6-month had no significant difference.

Changing trends of Harris hip scores between the Ficat II-III groups

Time and grouping exhibited statistical difference towards the Harris scores, the main effects of time and grouping were < 0.05 , and these two factors existed the interactions ($P < 0.05$) (Figure 6). When fixed the time factor, the results showed that: the preoperative Harris hip scores of group A (36.68 ± 3.50) and group B (32.98 ± 4.36) had no significant difference; 1 month after the surgery, the Harris hip score of group A (53.73 ± 4.13) was signifi-

cantly lower than group B (60.46 ± 1.89); 6 months after the surgery, the Harris hip score of group A (45.93 ± 5.47) was significantly lower than group B (54.05 ± 2.99). When fixed the grouping factor, the results showed that: the Harris hip score of group A at 1-month after the surgery was significantly higher than that before the surgery, while decreased to the preoperative level at the postoperative 6-month (comparison of the Harris hip scores before and 6-month after the surgery, $P > 0.05$); the Harris hip scores of group B at 1- and 6-month after the surgery were significantly higher than those before the surgery, while the comparison between the 2 postoperative time points showed no significant difference.

Changes of osteonecrotic region 6 months after the surgery

6 months after the surgery, the patients were reviewed MRI, 5 cases of group A exhibited the osteonecrotic region was narrowed, with the reduction rate as 11.90%, group B had 11 cases that showed the narrowed osteonecrotic region, and the reduction rate was 37.93%. Compared with group A, the reduction rate of group B was increased ($P < 0.05$) (Table 2).

Discussion

CD was still one of the most widely used clinical surgical treatments towards the ischemic ONFH, with the advantages as simple operations, little injuries, shorter postoperative bed time and would not increase the complexity of subsequent surgery, etc. [11, 12]. Its main mechanism was to mitigate the edema of femoral medullary cavity, and delay the progression of osteonecrosis. However, simple CD was only effective to early ischemic ONFH patients (Ficat stage I-II), while the efficacies were poor

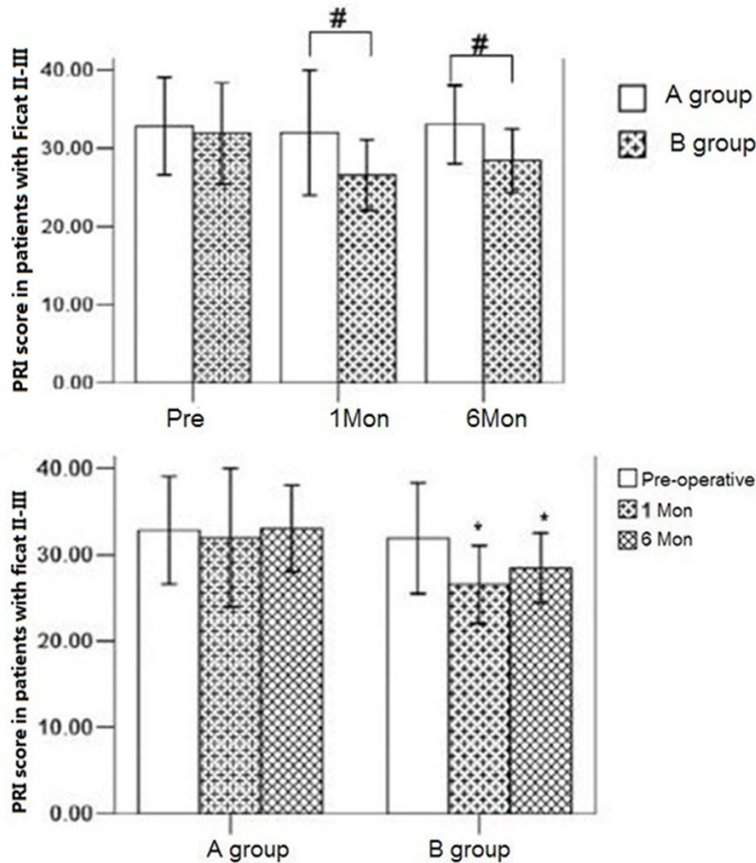


Figure 5. PRI changing trends of Ficat II-III patients at different time points and different groups. Different bars represented different groups (time points), the error bars represented the standard deviation. *: Compared with the preoperative $P < 0.05$, **: $P < 0.01$, #: Intergroup pairwise comparison $P < 0.05$, ##: $P < 0.01$.

towards the stage III patients. Therefore, it was more inclined that on the basis of CD, the structural support or stem cell transplantation support was combined to improve the efficacies of treatment [10, 13]. However, the structural support (such as Ti rod) was expensive, thus it would be difficultly carried out in the primary hospitals, especially in the economically underdeveloped regions, the high price had hindered its wide applications. In addition, although the efficacies of stem cell transplantation had been confirmed, limited to the laboratory qualification and technical requirements towards the collection, sorting and culture system of stem cells, its clinical operability and usability was even worse than the structural support treatment. The effects of CD combined with the concentrated autologous bone marrow transplantation were not clear [14]. Therefore, whether could a simple, easy, cheap, workable

method be found to strengthen the efficacies of CD?

In this study, SAI was selected as the supportive therapy to enhance the efficacies of CD, this method was simple and convenient, thus suitable for the primary hospitals, meanwhile, the price and the technical requirements were lower. Given the big pathophysiological changes among the patients with different Ficat stages (mainly stage II and III), this study combined the two methods in treating the ischemic ONFH and performed the stratification assessment towards the treatment efficacies. The assessment results showed that: as for the patients with Ficat stage I-II, simple CD and combined therapy could significantly reduce the PRI pain scores and improve the Harris hip scores, but the efficacies of simple CD was significantly lower than the combined therapy. In addition, we also found that although the Harris hip scores of patients with Ficat stage I-II showed no significant

difference between the simple CD group and the combined therapy group at the postoperative 1 month, the recovery degree of the combined therapy group at the postoperative 6 months was better than the simple CD treatment group. The results confirmed that the efficacies and persistence of the combined therapy group were significantly better than the simple CD treatment.

There had always existed considerable controversy about the treatment of patients with Ficat stage III [15-18]. Because the femoral head in Ficat stage III still had some functions, the method of total hip replacement was still premature. But the simple CD, CD+stem cell therapy or Ti rod support also exhibited poor effects towards the Ficat stage III in which the cartilages had already collapsed. This study also confirmed that the simple CD therapy had little

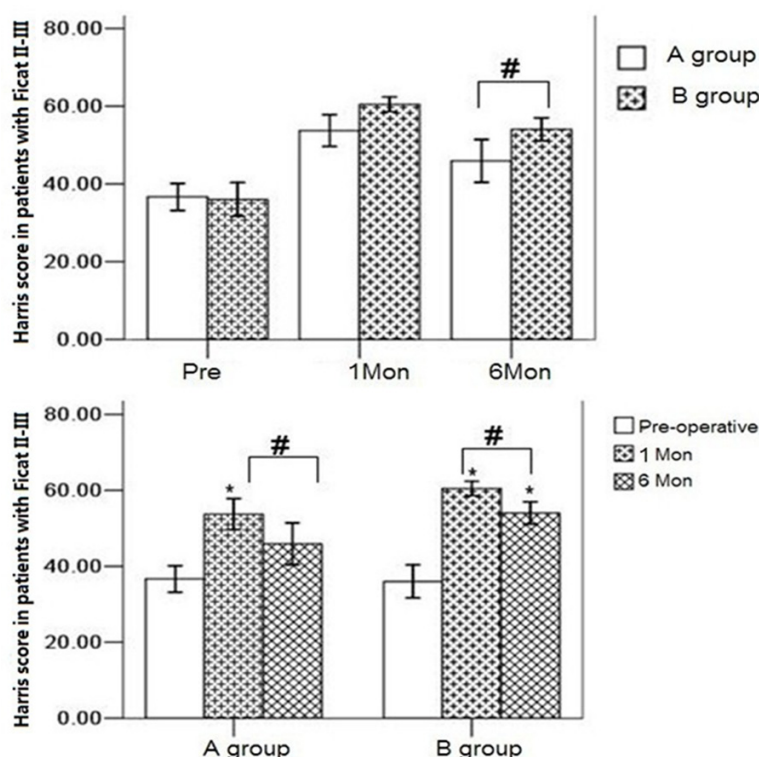


Figure 6. Changing trends of Harris hip scores of Ficat II-III patients at different time points and different groups. Different bars represented different groups (time points), the error bars represented the standard deviation. *: Compared with the preoperative $P < 0.05$, **: $P < 0.01$, #: Intergroup pairwise comparison $P < 0.05$, ##: $P < 0.01$.

Table 2. Changes of osteonecrotic regions of the 2 groups 6 months after the surgery (cases)

Time point	Cases with narrowed osteonecrotic region	Cases without change or dilation in the osteonecrotic region	reduction rate (%)
Group A	5	37	11.90
Group B	11	18	37.93 ^a

Note: Compared with group A, ^a $P < 0.05$.

effects towards the patients with Ficat stage III, the PRI scores 1 and 6 months after the surgery did not change significantly, although the Harris hip scores were slightly increased 1 month after the surgery, they returned to the preoperative levels 5 months later, similar to previous literature [19]. The patients with CD+SAI exhibited significantly decreased PRI scores 1 and 6 months after the surgery, and the Harris scores were significantly increased. The results confirmed that CD+SAI could effectively relieve pain and improve the hip score.

According to the pathophysiological mechanisms of the occurrence and development of

ischemic ONFH, the principles of treating the ischemic ONFH were to promote the circulation in the necrotic areas and delay the occurrence of non-vascular events. In this study, the SAI drugs were selected to dilate the blood vessels, anticoagulate, improve the local circulation and release the pain. The previous studies had confirmed that these drugs were all the commonly used non-surgical treatment drugs towards the ischemic ONFH, but these drugs were mostly administrated intravenously, and showed poor efficacies towards the patients with already-collapsed cartilages [20]. However, this study confirmed that by changing the administration route, namely injected the above drugs directly into the femoral artery through the intervention way, not only could the effects of CD towards the patients with Ficat stage I-II be further enhanced, but also effective towards the patients with Ficat stage III. The postoperative MRI scanning also confirmed the efficiency rate towards the osteonecrotic range obtained by the combined therapy was significantly higher than the simple CD

treatment. But the exact mechanism still needed to be further explored.

This study did not focus on comparing the efficacies of CD combined with SAI against other treatment methods (such as osteotomy, hip resurfacing, total hip replacement, Ti rod support, stem cell transplantation, etc.) in treating ONFH, while focused on providing an effective, simple, inexpensive, feasible clinical alternative method. Although the long-term effects still needed to be assessed, the early- and mid-term results showed that the effectiveness and efficacy's persistence had been demonstrated. Based on the actual situations of our country,

as well as the actual distribution ratio of clinical resources, CD combined with SAI was applicable to the most patients, could be undertaken in the primary hospitals, and should be popularized.

Disclosure of conflict of interest

None.

Address correspondence to: Qian Chen, Department of Pain Medicine, Orthopedics Hospital of Guizhou Province, 25 South Shachong Road, Guiyang 550002, China. Tel: +86 851 5793204; E-mail: qianchendoc@163.com

References

- [1] Wang XS, Zhuang QY, Weng XS, Lin J, Jin J and Qian WW. Etiological and clinical analysis of osteonecrosis of the femoral head in Chinese patients. *Chin Med J (Engl)* 2013; 126: 290-295.
- [2] Mao Q, Wang W, Xu T, Zhang S, Xiao L, Chen D, Jin H and Tong P. Combination Treatment of Biomechanical Support and Targeted Intra-arterial Infusion of Peripheral Blood Stem Cells mobilized by granulocyte-colony stimulating factor for the Osteonecrosis of the Femoral Head: A Randomised Controlled Clinical Trial. *J Bone Miner Res* 2015; 30: 647-656.
- [3] van der Jagt D, Mokete L, Pietrzak J, Zalavras CG and Lieberman JR. Osteonecrosis of the femoral head: evaluation and treatment. *J Am Acad Orthop Surg* 2015; 23: 69-70.
- [4] Tripathy SK, Goyal T and Sen RK. Management of femoral head osteonecrosis: Current concepts. *Indian J Orthop* 2015; 49: 28-45.
- [5] Chen CH, Chang JK, Lai KA, Hou SM, Chang CH and Wang GJ. Alendronate in the prevention of collapse of the femoral head in nontraumatic osteonecrosis: A two-year multicenter, prospective, randomized, double-blind, placebo-controlled study. *Arthritis Rheum* 2012; 64: 1572-1578.
- [6] Bozic KJ, Zurakowski D and Thornhill TS. Survivorship analysis of hips treated with core decompression for nontraumatic osteonecrosis of the femoral head. *J Bone Joint Surg Am* 1999; 81: 200-209.
- [7] Grayson WL, Bunnell BA, Martin E, Frazier T, Hung BP and Gimble JM. Stromal cells and stem cells in clinical bone regeneration. *Nat Rev Endocrinol* 2015; 11: 140-150.
- [8] Rackwitz L, Eden L, Reppenhagen S, Reichert JC, Jakob F, Walles H, Pullig O, Tuan RS, Rudert M and Nöth U. Stem cell- and growth factor-based regenerative therapies for avascular necrosis of the femoral head. *Stem Cell Res Ther* 2012; 3: 7.
- [9] Zhao D, Wang B, Guo L, Yang L and Tian F. Will a vascularized greater trochanter graft preserve the necrotic femoral head? *Clin Orthop Relat Res* 2010; 468: 1316-1324.
- [10] Floerkemeier T, Lutz A, Nackenhorst U, Thorey F, Waizy H, Windhagen H and von Lewinski G. Core decompression and osteonecrosis intervention rod in osteonecrosis of the femoral head: clinical outcome and finite element analysis. *Int Orthop* 2011; 35: 1461-1466.
- [11] Wei BF and Ge XH. Treatment of aosteofecrosis of the femoral head with core decompression and bone grafting. *Hip Int* 2011; 21: 206-210.
- [12] Lieberman JR. Core decompression for osteonecrosis of the hip. *Clin Orthop Relat Res* 2004; 29-33.
- [13] Zeng YR, He S, Feng WJ, Li FL, Li J, Jian LY, Zeng JC and Fan YG. Vascularised greater trochanter bone graft, combined free iliac flap and impaction bone grafting for osteonecrosis of the femoral head. *Int Orthop* 2013; 37: 391-398.
- [14] Chotivichit A, Korwutthikulrangsri E, Auewarakul C and Sarirasirid S. Core decompression and concentrated autologous bone marrow injection for treatment of osteonecrosis of the femoral head. *J Med Assoc Thai* 2012; 95: S14-20.
- [15] Baksi DP, Pal AK and Baksi DD. Long-term results of decompression and muscle-pedicle bone grafting for osteonecrosis of the femoral head. *Int Orthop* 2009; 33: 41-47.
- [16] Hungerford DS. Osteonecrosis:avoiding total hip arthroplast. *J Arthroplasty* 2002; 17: 121-124.
- [17] Koc ON and Lazarus HM. Mesenchymal stem cells:heading into the clinic. *Bone Marrow Transplant* 2001; 27: 235-239.
- [18] Yoo MC, Kim KI, Hahn CS and Parvizi J. Long-term followup of vascularized fibular grafting for femoral head necrosis. *Clin Orthop Relat Res* 2008; 466: 1133-1140.
- [19] Pierannunzii L. Endoscopic and arthroscopic in femoral head core decompression. *Arthrosc Tech* 2012; 1: e225-230.
- [20] Maruotti N, Corrado A, Neve A and Cantatore FP. Bisphosphonates: effects on osteoblast. *Eur J Clin Pharmacol* 2012; 68: 1013-1018.