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ORIGINAL PAPER

Minimally invasive treatment for osteonecrosis of the femoral head with angioconductive bioceramic rod

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Abstract

Purpose To describe the rationale, the surgical technique, and the short-term follow-up results of a new minimally invasive treatment of osteonecrosis of the femoral head (ONFH) with an angioconductive bioceramic rod (ABR) implant.

Methods Sixty-two patients (72 hips) with ARCO stage IIA-IIIC ONFH treated with the minimally invasive ABR from January 2012 to December 2016 were reviewed (17 females, 45 males, mean age 44.49). This technique used the angioconductive properties of the porous implant to repair the necrosis by driving vascularization from the trochanter to the necrotic area. Patients had a mean follow-up period of 26.74 months. The outcomes were evaluated by hip joint survival, radiograph, and the Harris Hip Score (HHS). The complications occurred during the treatment period were recorded.

Results No serious post-operative complications occurred during the treatment. The overall joint survival rate was 90.27%, with seven conversions to THA. Improvements were observed in 23 (31.95%) hips, 24 (33.33%) hips remained stable, and 25 (34.72%) hips had worse results according to the radiographic evaluation. The mean HHS at the end follow-up significantly improved compared to the pre-operative mean HHS (82.27 vs 58.14, $p < 0.001$). In both radiographic evaluation and HHS, the treatment was more effective on patients beneath 44 years old ($p < 0.05$); ARCO stage II compared to stage III ($p < 0.05$); and China-Japan Friendship Hospital (CJFH) type C compared to CJFH type L ($p < 0.05$).

Conclusions The minimally invasive treatment of ONFH with ABR showed promising results in delaying or even terminating the progression of the necrosis and improving hip function, especially in younger patients and in the early stages of the disease.

Keywords Osteonecrosis · Femoral head · Hip-preserving · Bioceramics · Angioconduction

Introduction

Osteonecrosis of the femoral head (ONFH) is a common refractory orthopaedic disease, which has become an increasing global health problem with over twenty million patients worldwide among whom seven million are in China [1, 2]. The morbidity of ONFH is increasing every year, with most of the patients aged from 20 to 50 years old [3, 4]. In the absence

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of intervention, most patients will have severe dysfunction within one to four years and will need to undergo arthroplasty. Although many new therapeutic methods have been invented in the past few decades, ONFH remains an extremely challenging disease because of its ill-defined aetiopathogenesis. There are many hypotheses about the latter, but the ultimate common pathway of ONFH is the damage to the vascular system of the femoral head [5]. The blood supply of the normal femoral head is mainly derived from epiphyseal arterial network and retinacular arterial system [6]. The superior, inferior and anterior retinacular arteries, branching off the C-shaped artery ring around the fondus of the neck, constitute the unidirectional blood flow to the femoral head, which, once damaged, is difficult to restore [7]. A large number of studies revealed the microcirculatory disturbance in ONFH: necrotic tissue healing through angiogenesis is limited by the unidirectional vascular characteristic of the femoral head and the osteosclerotic zone, meaning that the necrotic zone cannot be completely repaired and finally progresses to collapse [8].

The angioconductive capacity of porous bioceramics was presented in our previous studies, showing a correlation between the internal structure and vascularization [9, 10]. Porous bioceramics with macropore diameter of 500–600 μm and interconnection diameter of 120 μm were identified as a good compromise between angioconductivity and mechanical property. In this study, an angioconductive bioceramic rod (ABR) with the above-described porous structure was used to treat ONFH. The rod acts as a bridge, bringing the rich blood flow from the great trochanter to the necrotic zone of the femoral head. With the degradation of the material and the growth of the new blood vessels, the necrotic areas were naturally repaired and the femoral head regained biomechanical support. Up to date, this technology has been used in multiple hospitals in China and a multicentre prospective clinical study has been registered. In this report, the reliability of the treatment was confirmed by a multicentre retrospective study, and the clinical evaluation of the therapeutic effect was carried out.

Materials and methods

β-TCP porous bioceramics

The β-tricalcium phosphate (β-TCP) porous bioceramics made of high-purity β-TCP powder were designed and produced by Shanghai Bio-lu Biomaterials Co, Ltd., China. An organic scaffold was formed by surface chemical dissolution of polymethyl methacrylate (PMMA) spherical granules. Pore and interconnection diameters were respectively controlled by sieving and reaction time. β-TCP slurry was poured inside the scaffold, dried, debinded, and sintered to obtain the bioceramics. The ABR technique for the treatment of ONFH includes three elements (Fig. 1): (1) White irregular porous granules of controlled microstructure (pore and interconnection diameters 500–600 μm and 120 μm, porosity 70%) with a diameter of 1.0–3.0 mm. (2) White irregular dense granules (porosity 7%) with a diameter of 1.0–3.0 mm. (3) White cylindrical porous bioceramic rod (diameter 10 mm, length 80 mm) with a similar macrostructure to porous granules.

Patients

A total of 72 hips in 62 ONFH patients (17 females, 45 males) treated with the minimally invasive ABR technique from January 2012 to December 2016 were analyzed retrospectively. The average age of the patients was 44.49 years (ranging from 17 to 76 years). The etiologies of osteonecrosis were alcohol abuse in 30 patients (48.39%), corticosteroid application in 15 patients (24.19%), post-traumatic in six patients (9.68%), and idiopathic in 11 patients (16.13%). The diagnosis of ONFH was based on the symptoms and imaging data of the hip joints. MRI was chosen as the gold standard for the diagnosis of ONFH when the X-ray radiograph was negative. According to the Association Research Circulation Osseous (ARCO) classification, the imaging data showed 43 (59.72%) hips in stage II and 29 (40.28%) hips in stage III. According to the classification standard of China-Japan Friendship Hospital (CJFH) [11], 14 (19.44%) hips were classed as type C and 58 (23.61%) as type L (Table 1). The Harris hip score (HHS) was used as an assessment of hip function in patients. Informed consent was obtained from all individual participants included in the study.

Surgical technique

Ancillary instruments were designed to simplify the removal of necrotic tissue, including expendable reamers (Chinese Patent CN102038544 B) and a graft delivery system. All the surgeons were trained beforehand and all operations were carried according to a standardized procedure. Surgery was performed with the patient in supine position, with a hip elevation of 10 cm and under either general or combined spinal anesthesia. A 3-mm-diameter K-Wire was inserted from 2 cm below the trochanter major, through the centre of the femur neck, to 5 mm below the cartilage of the femoral head (Fig. 2a). Insertion axis was confirmed by anteroposterior and lateral X-rays. With the K-Wire as centre, an approximately 1.5- to 3-cm skin incision was made; subcutaneous fascia and muscles were carefully cut layer by layer until reaching the bone. A 12-mm bone channel was made with the cannulated drill over the K-Wire to achieve core decompression (Fig. 2b). During drilling, bone sludge containing mesenchymal stem cells, stromal cells, and blood cells was collected then immediately mixed with the implants to increase their bioactivity. Necrosis debridement was carried out with the reamer through progressive expansion of the blades (Fig. 2c). Using the graft delivery system, porous (3 g) and dense (5 g) granules

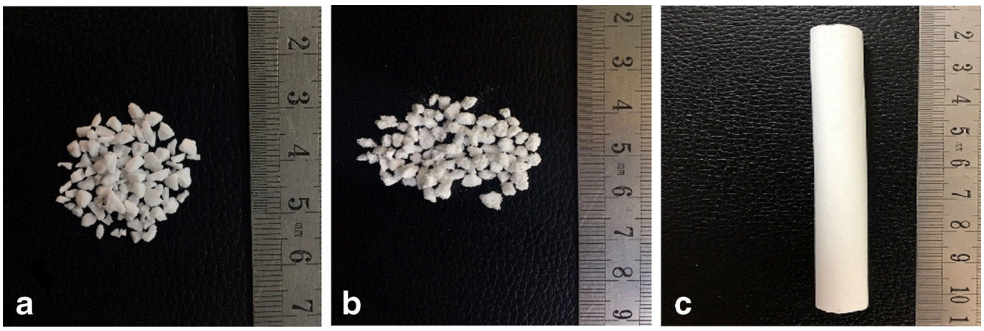

Fig. 1 The bioceramics used for the treatment of ONFH. **a** Dense β-TCP granules (diameter1.0–3.0 mm, no macroporosity). **b** Porous β-TCP granules (diameter 1.0–3.5 mm, macropore 500–600 μm, interconnection 120 μm). **c** Porous bioceramic rod (diameter 10 mm, length 80 mm, macropore 500–600 μm, interconnection 120 μm)

previously mixed with bone sludge were grafted and impacted (Fig. 2d). The ABR is then inserted without impaction (Fig. 2e) and must extend at least to the two third of the femoral head to facilitate new tissue formation. After fluoroscopic confirmation of implant positioning, the incision was cleaned and sutured. The average time of the surgery was 40 minutes.

Rehabilitation

All patients followed a rehabilitation and training program post-operatively. They walked with two crutches and non-weight-bearing on the affected limb for three months, plus exercise in bed to prevent thrombosis, muscle atrophy, and osteoporosis. The patients were then allowed to walk with a single crutch for three to six months depending on radiographic evidence of bone healing.

Table 1 Main characteristics of the patients and hips

	Patients	Hips
Gender		
Male	45	/
Female	17	/
Age		
Patients younger than 20 years old	4	/
Patients between 21 to 40 years old	14	/
Patients between 41 to 60 years old	33	/
Patients older than 60 years old	11	/
Risk factors		
Alcohol abuse	30	39
Corticosteroid application	15	15
Post-traumatic	6	6
Idiopathic	11	12
Pre-operative ARCO classification		
ARCO stage II	/	43
ARCO stage III	/	29
CJFH classification		
CJFH type C	/	14
CJFH type L	/	58
Total	62	72

Assessment

Follow-up examinations were scheduled at three and six months, then once half a year. Anteroposterior and frog-lateral X-rays were used as the main clinical assessment method. CT or MRI were used to evaluate biodegradation of the bioceramic implants, bone healing, and state of articular surface. The imaging results were divided into three grades: improved, when the necrotic lesions were replaced by new bone, crescent disappeared, and bioceramic materials biodegraded; stable, when cystic region, crescent, sequestrum, and the shape of the femoral head remained unchanged compared with that in the pre-operative stage; and worse, when the necrosis progressed or the collapse of the femoral head was aggravated. The function of the hip joints was assessed using the HHS and was divided into four grades: excellent (HHS > 90), good (HHS = 80–90), average (HHS = 70–80) and poor (HHS < 70). Complications during treatment were all recorded. All of the above assessments were carried out by more than two researchers in order to reduce personal bias.

Statistical analysis

All statistical analyses were conducted using SPSS software (version 18.0, Inc., Chicago, Illinois). Age and HHS were described as the mean and standard deviation (SD). Pre-operative and final post-operative HHS were compared using a paired *t* test, while a two-sample *t* test was used when comparing HHS increases between ARCO stage II and III. The difference of HHS between multiple groups was evaluated by variance analysis and comparison between count data was carried out by chi-square test. Significance was set at $p < 0.05$.

Results

The mean final follow-up period was 26.74 ± 10.38 months (ranging from 14 to 67 months) and no serious post-operative complications occurred during the treatment. Due to excessively fast bone grafting thus air entering damaged blood vessels in the bone channel, one patient developed gas embolism during surgery. After resuscitation, surgery was performed without

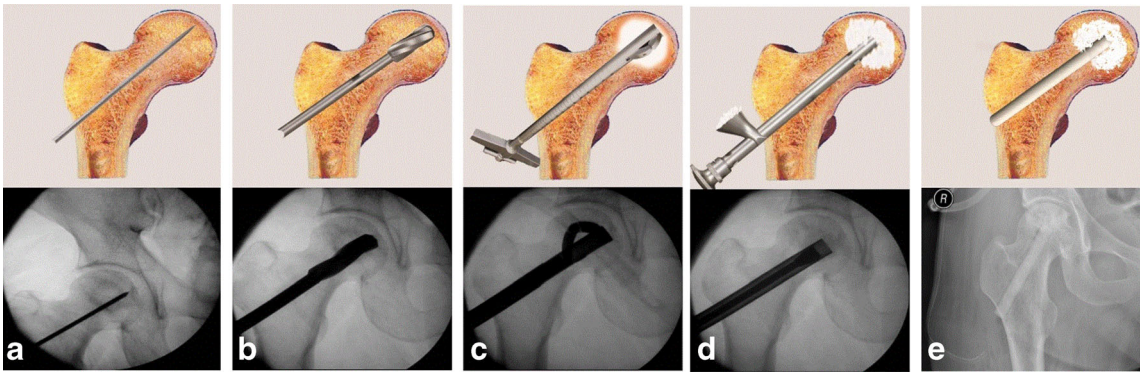

Fig. 2 Standard operation protocol. **a** Insertion of K-wire. **b** Core decompression. **c** Necrosis debridement. **d** Bioceramic granule grafting. **e** Insertion of the ABR

further complication and no sequelae were observed post-operatively. The results of ABR treatment were assessed according to the survival rate of femoral heads, radiography, and HHS.

Survival rate of the femoral head

Three (4.2%) hips in ARCO stage II and four (5.56%) hips in ARCO III were converted to THA at an average of 28.00 ± 6.68 months after surgery. Among them, imaging showed the collapse of four femoral heads combined with a severe restriction of mobility; the two operated hips of one patient, who felt pain after surgery and had to remain permanently in bed due to lumbar disease, were replaced respectively 18 and 24 months post-operatively. The joint survival rate of the whole group was 90.27% at the last follow-up, with 92.86% for ARCO stage II and 86.67% for ARCO stage III, but no significant difference in survival rate was found between the two groups ($p > 0.05$). According to the aetiological classification, five of the hips which had THA were alcoholic necrosis and two were idiopathic necrosis. All THA were performed on patients over 44 years old (16.67%), which was significantly different compared to younger patients ($p < 0.05$).

Radiographic evaluation

On post-operative radiographies, a gap was observed between ABR and the bone channel; the edges of granules were sharp (Fig. 3c). Six months post-operatively, the bone tissue partly grew into the ABR, and the edge of the granules began to blur (Fig. 3d). One year after the operation, the gap disappeared, and granules were integrated into the surrounding bone (Fig. 3e). Most of the implanted materials were replaced by the new bone and the necrosis was repaired at two years (Fig. 3f). According to the radiographic evaluation, improvement was observed in 23 (31.95%) hips, 24 (33.33%) hips remained stable, and 25 (34.72%) hips had worse results. During the follow-up period, 11 hips progressed to the collapse of the femoral head, of which two underwent hip replacement. The rest of the nine hips had no joint replacement because of their mild symptoms and improved function. Among ARCO stage II and ARCO stage III cases, respectively, 18 of 43 hips (41.86%) and five of 29 hips (17.24%) showed improvement ($p < 0.05$). Improved results were also observed in 8 (57.14%) hips with CJFH type C and 15 (25.86%) hips with CJFH type L ($p < 0.05$). Results of patients under 44 years old were better than those older ($p < 0.05$), but no difference was observed between different aetiologies ($p > 0.05$). The details are listed in Table 2.

Harris Hip Score

The mean HHS were 58.14 and 82.27, respectively, pre-operatively and at the last follow-up. HHS increased by an average of 23.99 points overall. The mean HHS was improved from 60 to 87 in ARCO stage II ($p < 0.05$), and from 55 to 75 in ARCO stage III ($p < 0.05$). According to HSS grading, 33 (45.83%) hips had excellent results, 18 (25.00%) were graded as good, 5 (6.94%) as average, and 16 (22.22%) as poor. Of 43 ARCO stage II hips, 35 (81.40%) had good to excellent results, whereas 16 (55.17%) in stage III had good to excellent results, which indicated a significant difference between these two stages ($p < 0.05$). No significant difference at the last follow-up was observed between steroid, alcoholic, traumatic, and idiopathic necrosis ($p > 0.05$). HSS at the last follow-up was patients under 44 years old, significantly higher than those older ($p < 0.05$). HHS for CJFH type C osteonecrosis was significantly higher than those type L ($p < 0.05$). The details are listed in Table 3.

Discussion

ONFH is recognized as a refractory disease which often results in dysfunction and deterioration of the hip joint. Hip-preserving surgeries such as core decompression, tantalum rod, femoral osteotomy, and non-vascularized bone-grafting are common treatments, but none of these techniques is fully satisfactory as they cannot restore blood supply in the femoral head [12].

Fig. 3 A 42-year-old man with ARCO stage IIIA osteonecrosis of the left hip (pre-operative HHS 65.74; post-operative HHS100.00). **a** Pre-operative radiography with visible crescent sign (arrow). **b** Pre-operative MRI. **c** Post-operative radiography. **d**–**f** 6, 12, and 24 months post-operative radiography

Tricalcium phosphate bioceramics combine good biocompatibility, bone conductivity, and biodegradability. The main degradation products are Ca^{2+} and PO_4^{3-}, which participate in the mineralization of bone and also promote its formation. In addition, our previous studies revealed a correlation between the angioconductive properties and the macrostructure of porous β-TCP bioceramics [9, 10], which was used here to treat ONFH. Four major principles guide this operation: (1) The ABR conducts the rich blood flow of the greater trochanter to the femoral head, carrying the necessary nutrients and stem cells to repair the necrosis; (2) The necrotic tissue inside the head is debrided by the expandable reamer, followed by grafting of bioceramics mixed with autogenous bone sludge and bone marrow, enhancing bioactivity of the implants; (3) Through core decompression, the intraosseous hypertension is released, achieving pain relieve and providing the basic environment for tissue repair; (4) Impaction grafting of dense and porous granules provides early post-operative mechanical

Table 2 Outcome of the radiographic evaluation

	Improved (*n*, %)	Stable (*n*, %)	Worse (*n*, %)
Age			
Patients ≤ 44 years old	15 (50.00%)*	7(23.33%)	8 (26.67%)
Patients > 44 years old	8 (19.05%)	17(40.48%)	17 (40.48%)
p value between the two groups: $p = 0.005$			
ARCO stage			
ARCO stage II	18(41.86%)*	14(32.56%)	11(25.58%)
ARCO stage III	5(17.24%)	10(34.48%)	14(48.28%)
p value between stage II and stage III: $p = 0.028$			
CJFH type			
Type C	8(57.14%)*	4(28.57%)	2(14.29%)
Type L	15(25.86%)	20(34.48%)	23(39.66%)
p value between type C and type L: $p = 0.024$			
Etiology classification			
Alcohol abuse	11(28.21%)	13(33.33%)	15(38.46%)
Corticosteroid application	5(33.33%)	4(26.67%)	6(40.00%)
Post-traumatic	3(50.00%)	2(33.33%)	1(16.67%)
Idiopathic	4(33.33%)	5(41.67%)	3(25.00%)
p value between the four groups: $p = 0.759$			
Total	23(31.95%)	24(33.33%)	25(34.72%)

*$p < 0.05$

Table 3 Outcome of the HHS

	Pre-operative (SD)	The last follow-up (SD)	Improved score (SD)	*p* value
Age(years)				
Patients ≤ 44 years old	59.58(14.02)	88.08(16.32)	28.50(18.33)	$p < 0.001$
Patients > 44 years old	57.11(14.67)	77.87(20.12)	20.77(23.91)	$p < 0.001$
p value	$p = 0.472$	$p = 0.021$	$p = 0.125$	
ARCO stage				
ARCO stage II	59.93(14.65)	86.80(16.46)	26.87(20.50)	$p < 0.001$
ARCO stage III	55.48(13.72)	75.20(21.08)	19.72(23.68)	$p < 0.001$
p value	$p = 0.194$	$p = 0.014$	$p = 0.191$	
CJFH type				
Type C	64.12(14.86)	92.14(9.75)	28.02(13.81)	$p < 0.001$
Type L	59.32(13.48)	79.51(20.14)	23.01(23.49)	$p < 0.001$
p value	$p = 0.297$	$p = 0.003$	$p = 0.448$	
Aetiology classification				
Alcohol abuse	56.67(15.66)	80.71(20.80)	24.03(25.37)	$p < 0.001$
Corticosteroid application	56.76(14.92)	83.70(18.86)	26.92(17.60)	$p < 0.001$
Post-traumatic	59.55(13.19)	86.18(17.44)	26.63(19.41)	$p = 0.02$
Idiopathic	63.89(8.59)	82.76(16.47)	18.86(16.69)	$p = 0.002$
p value	$p = 0.478$	$p = 0.902$	$p = 0.806$	
Total	58.14(14.36)	82.27(19.26)	23.99(21.95)	$p < 0.001$

support for subchondral bone without destroying the structure of porous particles. With the degradation of bioceramics and the formation of new bone, the mechanical strength of both femoral neck and head is gradually restored, until full restoration of biomechanical support.

In our study, the total hip survival rate was 90.27% at the mean time of 26.74 months follow-up. Clinically, the success rate, defined as no significant progress of the disease in imaging and HSS ≥ 80, was 70.83%. In other studies, non-vascularized grafting procedures through a core track or a window at the base of the femoral neck, had a hip survival rate ranging from 55 to 87% [12–14], whereas some experts emitted doubts regarding reported survival rates with tantalum rod (60 to 80%) [15–17]; Only vascularized fibula transplantation was reported with a success rate over 90% [18–21]. Compared with the above methods, the success rate of ABR in the treatment of ONFH is close to vascularized fibula transplantation. In addition, it has the following advantages: (1) Blood vessels of the large trochanter are conducted to the femoral head, which fundamentally solve the problem of blood supply for ONFH. (2) The implants are biodegradable β-TCP ceramics, which do not affect MRI examination or joint replacement. (3) The processes of biodegradation and osteogenesis happen simultaneously, with an increase of the mechanical strength correlated to the formation of new bone, until permanent biomechanical support. (4) Minimally invasive surgery, together with dedicated instruments, reduces both difficulty and time of the procedure. In our study, the effect of the treatment on hips in ARCO stage II was better than for ARCO stage III in both imaging assessment and HHS, and success rate was significantly higher for younger patients, which is consistent with other reported results [22–24]. We also noticed that the treatment worked better on CJFH type C necrosis, probably due to their location, in the central part of the femoral head, reducing the effects on subchondral bone. Success of the treatment strongly depends on compliance with the indications: (1) pain or functional limitation; (2) strong desire of the patient for hip-preserving surgery; (3) ARCO stage II or III; (4) no apparent detachment of the subchondral bone. Exclusion criteria: (1) unable to undergo surgery because of cancer or other serious diseases; (2) fracture of the femur neck; (3) ARCO stage IV; (4) ARCO stage I (possibility of spontaneous remission). Compliance with the standard operation protocol and respect of post-operative instructions by the patients are crucial for the success of the surgery.

In conclusion, the treatment for ONFH with ABR can delay or even terminate the natural progress of osteonecrosis. The resulting hip joint preservation is a significant improvement for the patients compared to THA, especially for young ones. It provides a new minimally invasive option for early and middle stages of the disease. Nevertheless, the study is limited by the lack of a control group using other hip-preserving procedures and long-term follow-ups will be needed to confirm the efficacy of the treatment. This is the reason why we have started a multicentre prospective study of the ABR technique.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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