Injectable Synthetic Bone Graft Substitute Combined with Core Decompression in the Treatment of Advanced Osteonecrosis of the Femoral Head: A 5-Year Follow-Up

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Background: Osteonecrosis of the femoral head can lead to destruction of the hip joint and disabling arthritis in young adults, if left untreated. Among the salvage procedures, core decompression combined with bone graft substitutes is a viable option for joint preservation. The purpose of this study was to review the outcomes of using synthetic bone graft substitute (calcium sulfate and calcium phosphate) for the treatment of late-stage osteonecrosis of the femoral head.

Methods: From November 2008 to May 2009, 19 hips in 18 patients with osteonecrosis of the femoral head [6 hips in Association Research Circulation Osseous (ARCO) stage IIC and 13 hips in stage IIIA] were treated with core decompression combined with PRO-DENSE™ (Injectable Regenerative Graft). The average age of the patients at the time of surgery was 48 years (range 25-67 years). Twelve patients (13 hips) overused alcohol, four patients (4 hips) were idiopathic, one patient (1 hip) used corticosteroids, and one patient (1 hip) was post-traumatic. The clinical failure was defined as conversion to total hip arthroplasty or progression in head collapse.

Results: At the conclusion of the study, 3 in the 6 stage IIC hips and 8 in the 13 stage IIIA hips were converted to total hip arthroplasty in an average of 8.5 months (range 4-30 months) postoperatively. Advanced collapse of the femoral head awaiting for total hip arthroplasty was observed in the other six hips. Of the 19 hips, only 2 hips (10.5%) survived without further collapse in the 5-year follow-up. This resulted in 89.5% failure rate with early resorption of the grafting in an average of 5.3 months.

Conclusions: Core decompression combined with an injectable calcium sulfate and calcium phosphate composite graft (PRO-DENSE) were associated high failure rates in the early postoperative period. It is not recommended for the treatment of ARCO stage IIC and IIIA osteonecrosis of the femoral head.

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Key words: bone graft substitute, core decompression, osteonecrosis of the femoral head

At a Glance Commentary

Scientific background of the subject

Osteonecrosis of the femoral head would result in destruction of hip joints and disabling arthritis. Core decompression is a salvage procedure for joint preservation. Additionally, This study added injectable calcium sulfate and calcium phosphate bone graft substitute to refill the defect after reaming. The purpose is to improve initial mechanical support and prevent further collapse.

What this study adds to the field

Core decompression combined with injectable calcium sulfate and calcium phosphate composite graft were associated high failure rate with early resorption. It is possible that the osteonecrotic environment of the femoral head is lack of adequate blood supply to supply sufficient osteoinductive material and unfit for the synthetic graft to repair the lesion.

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Osteonecrosis of the femoral head is a debilitating disease and affects younger active population. It leads to destruction of the hip joint and disabling arthritis. The prognosis is influenced by the stage, size, and location of the lesion.[1,2] Steinberg *et al*. reported that 92% of 48 hips managed with nonoperative treatment progressed to collapse.[3] Since total hip arthroplasty (THA) is not a favorable treatment for this young population due to their long life expectancy, the salvage procedures for joint preservation, including core decompression with or without bone grafting, osteotomy, and vascularized or nonvascularized bone grafting, are therefore suggested for precollapsed or early collapsed hips.[4-11] Regarding the post-collapsed stage, most of the femoral head preserving procedures are not effective. Additionally, some of these procedures are technically demanding or have donor side morbidity.[12-14]

To improve the initial mechanical support to the femoral head and to prevent further collapse, a large amount of allografts or synthetic bone substitutes are needed[15,16] for impaction after cord decompression. Calcium sulfate ($CaSO_4$) and calcium phosphate ($CaPO_4$) are the commonly used bone substitutes in fracture and benign bone lesions.[17-20] They can be made injectable to refill the bone defect, and also increase initial compressive strength and stiffness property.[21] We hypothesized that core decompression combined with synthetic injectable bone substitutes for the treatment of osteonecrosis of the femoral heads can provide initial structural support, prevent further collapse, and allow bone incorporation over time. In this study, we report the treatment results of patients with precollapse or early collapsed osteonecrosis of the femoral head.

METHODS

From November 2008 to May 2009, 18 consecutive patients (19 hips) with osteonecrosis of the femoral head were enrolled retrospectively in this study. All these patients were treated with core decompression combined with $CaSO_4$ and $CaPO_4$ composite bone substitute (PRODENSE™ Injectable Regenerative Graft; Wright Medical Technology, Arlington, TN, USA) in our institution. There were a total of 4 females (4 hips) and 14 males (15 hips), with a mean age of 48 years (range 25-67 years) at the time of surgery. The risk factors included excessive intake of alcohol (consuming >400 ml per week) in 13 patients (13 hips), corticosteroids in 1 patient, and post-traumatic in 1 patient. The remaining three patients (4 hips) were idiopathic [Table 1].

The diagnosis of femoral head osteonecrosis was made using anteroposterior (AP) and frog lateral radiographs, bone scan, or magnetic resonance imaging (MRI) scan. All osteonecrotic lesions of the femoral heads were graded according to the system of the Association Research Circulation Osseous (ARCO)[22] and estimated by the modified index of necrosis.[23] Six hips were of stage IIC and the other 13 hips were of stage IIIA. Following institutional review board approval (IRB No. 99-0466B), the results of the patients were reviewed for functional and radiographic outcomes.

Surgical technique

The procedure was performed with the patient lying supine position on the fracture table. AP and lateral fluoroscopic views were used to confirm the position of instruments throughout the procedure. A 1.5-cm stab incision was made over the lateral aspect of the proximal femur. A 2-mm Kirschner wire was advanced under intensifier fluoroscopic guidance from the entry point just distal to the greater trochanter into the center of necrotic lesion of the femoral head within 5 mm of the subchondral bone. A 9-mm cannulated drill bit was used to decompress the necrotic region. The Kirschner wire and drill bit were then removed and replaced by a working cannula. A curette was used to remove necrotic tissue from the femoral head, and then a specialized reamer with an expanding tip (X-REAM™ Percutaneous Expandable Reamer; Wright Medical Technology) was inserted to remove a greater volume of the necrotic lesion. The reamer was rotated and expanded gradually until maximum expansion at 2.1 cm. During the process, the reamer was checked by fluoroscopy to avoid violation of the subchondral plate. After completing the reaming and removing debrided materials, the cavity and the core tract were cleared through repeated irrigation and suction. The cavity and the core tract was then backfilled with an injectable composite $CaSO_4$–$CaPO_4$ bone graft substitute (PRO-DENSE Injectable Regenerative Graft; Wright Medical Technology). Beginning at the most proximal portion of the defect, intraoperative fluoroscopy was used to monitor if there was adequate placement and complete filling of the bone graft substitute into the defect. After surgery, partial weight-bearing with double crutches for at least 6 weeks followed by single crutch until the healing of the femoral head was instructed.

Evaluation and end points

Clinical function of hips was evaluated using Harris hip score.[24] Clinical failure was defined as Harris hip score

Table 1: Demographic data

Total patient number	19 hips (18 patients)
Mean age	48 years (25-67 years)
Sex ratio	Male:Female=15:4
Risk factors	
Alcohol consumption	13 hips
Corticosteroid	1 hip
Trauma	1 hip
Idiopathic	4 hips

less than 70 points or conversion to a THA for any reason. Radiographic failure was defined as a more than 2-mm collapse of the femoral head or secondary osteoarthritis of the involved hip. The time-to-failure was calculated as the time between the date of core decompression and the date of total hip conversion or radiography revealing advanced head collapse. The onset time of head collapse was defined as the earliest time between the date of core decompression and the date of follow-up evaluation discovering collapse progression.

RESULTS

The mean follow-up was 17.7 months (range 4-60 months) for all 19 hips. Preoperative Harris hip score was 57 points (range 45-70 points) and it was 64 points at the final follow-up (range 51-82 points) in all hips.

The treated hips consisted of 6 ARCO stage IIC and 13 stage IIIA hips, 11 of which were converted to THAs in an average of 8.5 months (range 4-30 months) postoperatively [Table 2]. Advanced collapse of the femoral head was observed in the other six hips. Only two hips (10.5%) survived without further collapse during 5-year follow-up. The remaining 17 hips (89.5%) had either converted to THAs or advanced to head collapse in an average time-to-failure of 5.3 months. Gradual resorption of the $CaSO_4$/$CaPO_4$ bone substitute without new bone formation was noted in the early postoperative period [Figure 1]. The average onset time of head collapse was 2.2 months (range 2 weeks to 4 months) after the index surgery.

Among the 11 hips that were converted to THAs, no complication occurred due to minimally invasive and simple procedure of the index surgery. The femoral heads were sent for pathological examination. Gross examination showed the bone substitute was muddy in consistency and microscopic examination showed only fibrotic and necrotic tissue in the femoral head without evidence of new bone formation [Figure 2].

DISCUSSION

The procedure reported in this study was a simple procedure that involved augmenting the femoral head with injectable synthetic bone substitute (composite of $CaSO_4$/$CaPO_4$) after core decompression. It was an appealing approach because it could fill up the necrotic lesion, be hardened after cure, be absorbed gradually by creeping substitution, and act as an osteoconductive scaffold for the repair of the osteonecrotic femoral head. Urbna *et al*. had reported that the $CaSO_4$/$CaPO_4$ bone substitute would be gradually absorbed and replaced by new bone.[20] But in the pilot study of Rijnen *et al*. that compared incorporation and remodeling with or without the addition of $CaPO_4$ cement to morsellized cancellous bone using a femoral head critically sized defect model in the goat, inferior results were obtained in the group in which $CaPO_4$ cement was added.[25]

After core decompression, the grafting materials should provide adequate mechanical strength to prevent further collapse of the osteonecrotic femoral head. In this study, the synthetic graft substitutes had early resorption after

Table 2: Clinical outcomes in patients treated with synthetic calcium sulfate/calcium phosphate grafting

Hip	Bilaterality	Preoperative			Follow-up			Outcome
		ARCO stage	Index of necrosis*	HHS†	ARCO stage	HHS†	Survival (months)	
1	Unilateral	IIC	0.481	65	IIIA	60	6	THA
2	Bilateral	IIIA	0.521	55	IIIB	65	4	THA
3	Bilateral	IIIA	0.522	45	IIIB	57	10	THA
4	Unilateral	IIC	0.373	53	IIIB	70	30	THA
5	Unilateral	IIIA	0.426	57	IIIB	62	4	THA
6	Unilateral	IIIA	0.540	46	IIIC	56	5	THA
7	Bilateral	IIC	0.593	51	IIIB	58	8	Advanced collapse
8	Bilateral	IIIA	0.373	48	IIIC	56	6	Advanced collapse
9	Unilateral	IIIA	0.481	70	IIIA	82	60	No progression
10	Unilateral	IIIA	0.323	68	IIIB	54	9	THA
11	Bilateral	IIIA	0.563	67	IIIB	80	35	Advanced collapse
12	Bilateral	IIIA	0.562	51	IIIA	54	6	THA
13	Unilateral	IIC	0.236	64	IIIB	70	8	Advanced collapse
14	Unilateral	IIIA	0.522	54	IIIC	55	8	THA
15	Unilateral	IIIA	0.390	63	IIIB	82	32	Advanced collapse
16	Bilateral	IIIA	0.522	50	IIIB	51	4	THA
17	Unilateral	IIC	0.543	54	IIIA	56	34	Advanced collapse
18	Unilateral	IIIA	0.250	62	IIIA	84	60	No progression
19	Unilateral	IIC	0.236	53	IIIB	55	7	THA

Abbreviations: *: Index of necrosis[23]; †: Harris hip score[24]; ARCO: Association Research Cirulation Osseous

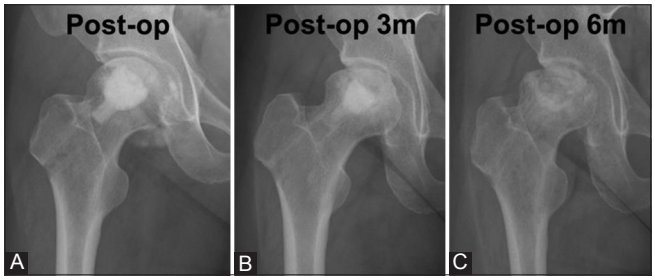

Figure 1: A 35-year-old female patient: (A) ARCO stage IIC osteonecrosis of the right femoral head; (B) postoperative radiograph at 1 month showed adequate filling of the osteonecrotic lesion by the synthetic bone substitutes; (C) At 6 months, the femoral head collapsed and the grafting materials appeared radiolucent.

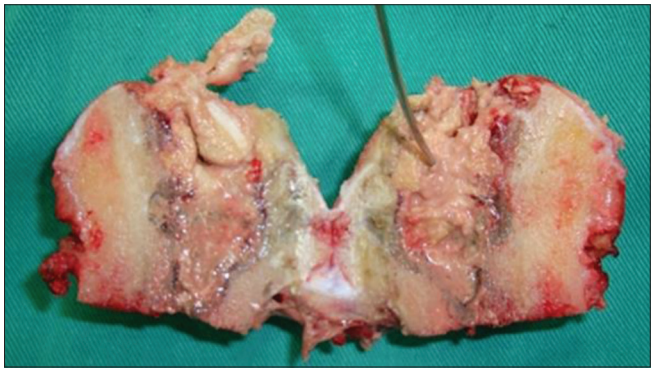

Figure 2: Conversion THA was performed 4 months after the index surgery. Only fibrous tissue and necrotic tissue in the core decompression area. Liquefaction of the synthetic grafts was pointed by probe head.

implantation. In the current study, there was a high failure rate (89.5%) on using $CaSO_4$/$CaPO_4$ bone substitute with early graft resorption and disease progression. Only two hips survived without further collapse of the femoral head. The onset of head collapse was only 2.2 months postoperatively on average. The grafts looked softened and muddy in consistency without new bone formation, with the specimens obtained during THA. The PRO-DENSE graft may have enough strength initially, but seemed to lose its structural integrity in the very early postoperative period. It is possible that the osteonecrotic environment in the femoral head is unfit for the synthetic graft to repair the lesion and the percutaneous expandable reamer did not remove adequate necrotic lesion to establish adequate blood supply and supply sufficient osteoinductive materials.

Joint preservation is the treatment goal for pre-collapse osteonecrosis of the femoral head. However, joint-sparing therapeutic techniques are associated with variable outcomes depending on the staging and complexity of the procedures.[2,4-6,8,11-13] Core decompression for Steinberg stage I disease was successful as a definitive procedure in more than 80% of patients. Steinberg stage II and III osteonecrosis were treated with decompression without requiring further surgical reconstructive intervention in 63% and 29%, respectively.[26,27] Vascularized fibular graft supplementation can delay the development of end-stage osteonecrosis after mild collapse (Steinberg stage β through δ) has occurred. Mont also reported core decompression of the femoral head for osteonecrosis using percutaneous multiple small-diameter drilling.[28] Twenty-four of 30 stage I hips (80%) had successful outcomes compared with 8 of 15 stage II hips (57%), with no surgical complications occurring with this technique. Several osteotomies including flexion, extension, varus, valgus, rotation, and subtrochanteric and intertrochanteric osteotomies have been used for the treatment of pre-collapse and early post-collapse (Steinberg stage β to δ) osteonecrosis.

Mont *et al*. impacted a large amount of allograft material, which is a combination of demineralized bone matrix, processed allograft bone, and a thermoplastic carrier, through a trapdoor to the femoral head and achieved a success rate of 86% in 21 hips.[8] On the other hand, Helbig reported 13 out of 18 Ficat stage I–IIB hips (72%) receiving core decompression combined with implantation of demineralized bone matrix requiring further surgery by THR in 9 years.[29] The allograft enriched with demineralized bone matrix has osteoconductive and osteoinductive properties. As a contrast, the PRO-DENSE graft contains only osteoconductive materials without any osteoinductive components. In this study, it failed to maintain the mechanical strength and enhance healing during the reparative process in the weakened femoral head. Immediately postoperatively, the injectable graft used in this study could be hardened during the application; yet it would be hydrolyzed gradually and lose its mechanical strength subsequently.

The limitation of this study includes a small number of patients studied and its non-randomized study design. In addition, most of the patients had a risk factor of alcohol overuse and only one patient was associated with steroid use. Whether the use of the PRO-DENSE grafts or other synthetic materials could be effective in other cases of osteonecrosis could not be answered by this study. However, this study is the first to report the poor results and early failure of using synthetic $CaSO_4$ and $CaPO_4$ composite grafts for the treatment of osteonecrosis of the femoral head. Because of the poor results, we discontinued to recommend our patients on using core decompression combined with injectable $CaSO_4$ and $CaPO_4$ composite bone graft substitute (PRO-DENSE) in the treatment of osteonecrosis of the femoral head.

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