Free Vascularized Fibular Grafting for Patients Receiving Postoperative Corticosteroids

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abstract

Free vascularized fibular grafting (FVFG) is an effective method to treat corticosteroid-induced osteonecrosis of the femoral head (ONFH). Some patients continued to receive maintenance doses of corticosteroids to treat the primary disease postoperatively. This study was performed to evaluate outcomes of FVFG for corticosteroid-induced ONFH in patients who continued to receive corticosteroids postoperatively. The authors retrospectively reviewed the records of 44 patients (78 hips) who had received corticosteroid treatment for their primary disease after FVFG. They were followed up for at least 2 years (mean, 5.6 years). Demographic details, Harris Hip scores, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), and radiographic data were collected and analyzed. The mean Harris Hip score for all hips was 70.9±9.9 points before surgery and increased to 84±12.1 points at the latest follow-up. There were also significant increases ($P<.05$) in physical component summary score and mental component summary score. According to the latest radiographic evaluation, 49 hips (62.8%) appeared improved, 10 hips (12.8%) appeared unchanged, and only 19 hips (24.4%) appeared worse. Seven hips (9%) underwent total hip arthroplasty during the follow-up period. Therefore, the results showed that FVFG was a viable method of treating corticosteroid-induced ONFH in patients who receive maintenance doses of corticosteroids postoperatively.

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Corticosteroid-induced osteonecrosis of the femoral head (ONFH) is a serious complication of systemic corticosteroid administration for treatment of autoimmune diseases, such as systemic lupus erythematosus (SLE), nephrotic syndrome, and rheumatoid arthritis. The prevalence of ONFH in patients receiving corticosteroids has been reported as 0.3% to 13%.1,2 The mechanisms responsible for corticosteroid-induced ONFH are highly controversial, but may include thrombus caused by a hypercoagulable state, increases in intraosseous pressure, and fat embolism.

Most patients with ONFH require surgical treatment for pain relief and improvement of hip joint function. Free vascularized fibular grafting (FVFG) is an effective method of halting the progression of osteonecrosis and promoting bone regeneration at necrotic foci. It also provides satisfactory outcomes for patients with corticosteroid-induced ONFH.3,4

Some patients with autoimmune diseases may be receiving maintenance doses of corticosteroids when ONFH is first recognized. In this case, maintaining continuous treatment of the primary disease does not permit cessation of corticosteroids after FVFG, and corticosteroids might adversely affect postsurgical outcomes. However, there are few reports of the effectiveness of FVFG in patients with postoperative corticosteroid treatment. This study was conducted to evaluate the effect of FVFG in the treatment of ONFH in patients who still take maintenance doses of corticosteroids postoperatively.

**Materials and Methods**

**Patient Selection**

The study was approved by the Regional Ethics Committee of the study hospital, and informed consent was obtained from each patient. In clinical practice, diagnoses of ONFH were based on history, clinical evaluation, and imaging modalities, including anteroposterior and frog-leg lateral radiographs as well as magnetic resonance imaging (MRI). The Steinberg classification was used to evaluate radiographs, and ONFH was classified as stages 0 to VI.5 Patients with stage II, III, and IV ONFH underwent FVFG. Before surgery, patients were evaluated by practicing physicians to ensure that the primary disease was under control and that the daily dose of corticosteroids was 10 mg or less.

The authors retrospectively reviewed the records of patients with corticosteroid-induced ONFH who received FVFG in the study hospital from 2000 to 2011. Patients included in this study received ongoing maintenance corticosteroid therapy for the primary disease for at least 6 months after FVFG. Patients with worsening primary disease and those whose corticosteroid dose had exceeded 10 mg/day during the follow-up period were excluded. Patients who were lost to follow-up were also excluded.

**Preoperative Evaluation**

Preoperative assessments, including complete blood cell count, erythrocyte sedimentation rate, C-reactive protein assay, urea monitoring, electrocardiography, and other tests were performed as appropriate to ensure patient fitness for surgery. Patient demographic characteristics and information about corticosteroid administration (route, daily dose, total cumulative dose, and duration of corticosteroid treatment) were recorded. When multiple corticosteroids were used, an equivalent dose of prednisolone was calculated as a standard for comparison. Clinical and imaging data that were recorded preoperatively included Harris Hip score (HHS), Medical Outcomes Study (MOS) 36-Item Short-Form Health Survey (SF-36), plain radiographs, and MRI.

**Operative Management**

All surgery was performed by the corresponding author (C.-Q.Z.) using previously reported methods.6,7 During surgery, histologic examination of subchondral bone was performed to confirm the diagnosis of ONFH. Postoperative prophylactic antibiotics were used twice a day for 3 days, and anticoagulants were administered for 6 weeks after the operation. Postoperative pain was managed with nonsteroidal anti-inflammatory drugs (NSAIDs). Patients were instructed to avoid bearing weight on the leg that underwent FVFG for 3 months. Weight bearing was increased gradually to full weight bearing over the next 3 months.

**Follow-up**

Regular follow-up was performed every 3 months for 1 year, every 6 months for 3 years, and annually thereafter. The end point was conversion to total hip arthroplasty (THA). During the follow-up period, clinical and radiographic results, information about postoperative steroid administration, and postoperative complications were recorded.

Clinical results were evaluated using HHS and SF-36 health surveys. Results were considered excellent for HHS of 90 points or greater, good for HHS of 80 to 89 points, fair for HHS of 70 to 79 points, and poor for HHS of less than 70 points. The physical component summary score and mental component summary score were widely adopted to provide an overall index of the SF-36 health survey. These scores were calculated using norm-based scoring methods.8,9 Higher scores represent good health-related quality of life.

Femoral heads were assigned to one of 3 categories postoperatively, based on radiographic findings. (1) The 1st category was improved (ie, necrosis was healed or was being replaced with new bone). In stage II, the crescent had disappeared or the density of the cystic lesion had increased, with trabecular formation at the tip of the vascularized fibula. In stage III, the collapsed lesion healed or became more rounded, with trabecular formation at the tip of the vascularized fibula. (2) The 2nd category was unchanged (ie, no change or no progression compared with

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the preoperative state). (3) The 3rd stage was worse (ie, based on the stage or evidence that the femoral head had collapsed by more than 3 mm). Evaluations were performed independently by 2 radiologists who were blind to the clinical results.

**Statistical Analysis**

Statistical analysis was performed with SPSS version 17.0 software (SPSS Inc, Chicago, Illinois). Paired t tests were used to compare preoperative and postoperative values. P<.05 was considered statistically significant.

**RESULTS**

Forty-four patients (78 hips) met the inclusion criteria for the study. All patients were ethnic Chinese. Of these patients, 34 had bilateral ONFH and underwent concurrent bilateral FVFG. Patient demographic characteristics and therapeutic regimens are summarized in the Table. The mean follow-up time was 5.6 years (range, 2-10 years). Primary diseases requiring corticosteroid treatment included SLE in 22 patients (41 hips), renal disease in 9 patients (15 hips), idiopathic thrombocytopenic purpura in 8 patients (13 hips), and dermatomyositis in 5 patients (9 hips). According to the Steinberg classification, 19 hips were considered stage II, 36 hips were stage III, and 23 hips were stage IV. Seven hips (9.0%) underwent THA during the follow-up period. Of them, 2 hips in stage III (5.6%) and 5 hips in stage IV (21.7%) were converted to THA. Some patients with worsening radiographs were not willing to undergo THA, and some of them took NSAIDs to relieve pain. They were advised to undergo THA when their lives were severely affected.

All patients fully complied with rehabilitation instructions. No patients had serious acute complications. Eight hips had wound hematomas. Three patients had deep venous thrombosis and were successfully treated with oral medication. Six limbs showed clawing of the big toe. These patients were treated nonsurgically and recovered gradually. No patients had pain associated with the harvest site or around the ankle.

**Harris Hip Scoring**

Clinical outcomes were evaluated with HHS. Preoperatively, the mean HHS was 70.9±9.9 points for all hips, 80.7±5.5 points for stage II hips, 72.9±5.7 points for stage III hips, and 60.1±8.7 points for stage IV hips. At the last follow-up, the mean HHS was 84±12.1 points for all hips, 92.8±7 points for stage II hips (P<.05), 84.4±11.9 points for stage III hips (P<.05), and 76.3±11.1 points for stage IV hips (P<.05) (Figure 1). The average increase in HHS was 12.1 points (range, -5 to 22 points) for stage II hips, 11.5 points (range, -13 to 23 points) for stage III hips, and 16.2 points (range, -8 to 38 points) for stage IV hips.

**SF-36 Health Survey**

All patients completed SF-36 questionnaires. The mean preoperative physical component summary score was 76±6.3 points, and the mean preoperative mental component summary score was 70.7±8.5 points. At the last follow-up examination, the mean physical component summary score was 86.6±7.8 points and the mean mental component summary score was 79.5±11.3 points. There were significant improvements (P<.05) in the physical component summary score and the mental component summary score at the last follow-up examination compared with preoperative scores (Figure 2).
Radiographic Results

Radiographic results were evaluated with the criteria described earlier. According to the latest radiographic evaluation, 49 hips (62.8%) appeared improved (Figure 3), 10 hips (12.8%) appeared unchanged, and 19 hips (24.4%) appeared worse. According to the Steinberg classification, 14 stage II hips (73.7%), 23 stage III hips (63.9%), and 12 stage IV hips (52.2%) appeared improved; 1 stage II hip (5.3%), 6 stage III hips (16.7%), and 3 stage IV hips (13%) appeared unchanged; and 4 stage II hips (21.1%), 7 stage III hips (19.4%), and 8 stage IV hips (34.8%) appeared worse.

Discussion

Corticosteroid-induced ONFH is a serious complication of corticosteroid therapy. Current treatment options for ONFH include conservative treatment, core decompression, proximal femoral osteotomy, vascularized bone grafting, and THA. The outcome of conservative treatment is usually poor with this option because of the natural history of ONFH.10 For many young patients, hip replacement cannot be expected to last the patient’s lifetime. Therefore, attempts should be made to save the femoral head before collapse. Free vascularized fibular grafting has been shown to be an effective method for treating ONFH, especially for patients with subchondral bone collapse.11,12 During the procedure, necrotic bone is excised, and this may interrupt the cycle of ischemia and intraosseous hypertension and promote local revascularization. Then the defect is filled with osteoinductive graft to support the subchondral surface. After the surgery, a period of limited weight bearing benefits the healing construct. Yoo et al13 reviewed 81 hips that received FVFG, with a mean follow-up period of 5.2 years, and found that 71% had radiologic improvement. Judet and Gilbert14 assessed 68 hips, with an average follow-up of 18 years, and found good results in 80% of patients. Berend et al15 found that patients with postcollapse osteonecrosis of the femoral head benefit from FVFG, with good overall survival of the joint.

Generally, patients with autoimmune disease receive high-dose corticosteroids early in the course of disease. Subsequently, the corticosteroid dose is gradually decreased to a maintenance dose (daily prednisolone equivalent dose is ≤10 mg) as clinical improvement is achieved. Maintenance doses of corticosteroids can be given for 3 months to several years. ONFH often develops while patients are receiving maintenance doses of corticosteroids. Once ONFH is diagnosed, patients should undergo surgery immediately because outcomes are better at earlier stages of ONFH. Postoperatively, these patients should continue to take corticosteroids to treat the primary disease.

However, corticosteroids have a harmful effect on the femoral head at many aspects. Takano-Murakami et al16 found that supraphysiologic doses of glucocorticoids suppressed osteoblast proliferation and the recruitment of osteoclast precursors. Corticosteroids also stimulate bone marrow stromal cells to develop into adipocytes while increasing the size of fat cells.17,18 Drescher et al19 reported that methylprednisolone enhances contraction of the lateral epiphyseal arteries of the femoral head and reduces femoral head blood flow. In this case, corticosteroids may have an adverse effect on the femoral head preoperatively.

It is widely accepted that high doses of corticosteroids can lead to ONFH. However, there are no reports on whether maintenance doses of corticosteroids affect postoperative outcomes of FVFG for the treatment of corticosteroid-induced ONFH. Therefore, it is necessary to evaluate the effect of FVFG in patients who still receive corticosteroids postoperatively.

This study retrospectively reviewed 44 patients (78 hips) with corticosteroid-induced ONFH who had received cortico-

Figure 3: Preoperative radiographs (anteroposterior position) of the pelvis of a 26-year-old man with lupus and stage II bilateral hip osteonecrosis. The preoperative Harris Hip scores were 77 (right) and 82 (left). The patient received corticosteroid treatment at maintenance doses until the latest follow-up (A). Preoperative magnetic resonance imaging of this patient (B). Postoperative radiographs obtained in the anteroposterior position (C) and the frog-leg position (D) 5 years after free vascularized fibular grafting showed stability of the articular cartilage and femoral head. The postoperative Harris Hip scores at the latest follow-up were 94 (right) and 95 (left).
steroid treatment for primary disease after FVFG. They were followed up for at least 2 years. The results showed significant improvement in HHS and SF-36 results at the latest follow-up. In addition, most of the radiographic results were improved and the rate of conversion to THA was very low. These data showed that FVFG in patients who received maintenance doses of corticosteroids postoperatively had good outcomes. There may be 2 potential reasons for the good outcomes. First, the postoperative steroid doses were low. Studies found that corticosteroids adversely affect the femoral head in a dose-dependent manner. Maintenance doses of corticosteroids may minimally affect recovery from ONFH. Second, FVFG has an excellent ability to promote new bone regeneration and revascularization to an extent that exceeds the harmful effects of low-dose corticosteroids.

This study did not use a matching control group of patients who did not receive postoperative corticosteroids. Therefore, it was not possible to determine whether postoperative corticosteroid administration had an adverse effect on FVFG outcomes. However, the data suggested that FVFG is an effective method to treat corticosteroid-induced ONFH in patients who still receive maintenance doses of corticosteroids postoperatively to treat the primary disease.

**REFERENCES**