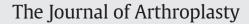
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## Treatment of Secondary Osteonecrosis of the Knee With Local Debridement and Osteoprogenitor Cell Grafting



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#### ARTICLE INFO

ABSTRACT

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Keywords: osteonecrosis avascular necrosis knee osteoprogenitor cell grafting femur Secondary osteonecrosis of the knee (SOK) affects young individuals with chronic diseases and corticosteroid use. We report a series of young patients in whom the osteonecrotic lesion was openly debrided, and concentrated bone marrow osteoprogenitor cells (OPCs) harvested from the iliac crest were placed in the defect. Twelve patients (fourteen knees) have undergone debridement and grafting of distal femoral osteonecrotic lesions. Age at surgery averaged 23 years. Follow-up averaged 5 years. None of the patients have undergone further surgery, or were taking medications for ipsilateral knee pain. Knee Society Score and Knee Function Score averaged 87 and 85 respectively. The technique of open debridement and osteoprogenitor cell grafting for SOK is relatively simple, efficacious, has low morbidity, and does not preclude future interventions.

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#### Secondary osteonecrosis of the knee (SOK) is a disorder that generally affects young individuals with chronic diseases in whom long-term corticosteroid treatment is prescribed [1–3]. SOK is associated with hematologic diseases (leukemia, sickle cell disease etc.), asthma, dermatologic, gastrointestinal, and renal disorders, juvenile idiopathic arthritis, lupus erythematosis and others [1,4–7]. SOK frequently accompanies multifocal osteonecrosis, making treatment of the young patient even more difficult. When the knee is symptomatic, the patient complains of diffuse pain, stiffness, swelling and poor function. Treatment in this younger population emphasizes joint preservation if possible, rather than joint arthroplasty. Thus, if the cartilage surface is not depressed or arthritic, treatment options include core decompression, or debridement of the osteonecrotic lesion usually with some form of bone grafting.

Five years ago, we reported a series of 3 young patients, aged 18–23 with osteonecrosis of the femoral condyles due to steroid use, in which the osteonecrotic lesion was openly debrided through a cortical "trap door(s)", and bone marrow osteoprogenitor cells (OPCs) were harvested from the iliac crest, the OPC concentrated in a selective retention device, and the cells were placed in the defect with a carrier [8]. After 2 years, all 3 patients had excellent pain relief and function, integration of the graft and no radiographic evidence of subchondral collapse. Others have reported preliminary findings using other techniques of debridement and autologous bone or cell grafting [9–13].

The purpose of this study is to report the clinical outcome of these 3 patients at intermediate follow-up; in addition, the outcome of 9 additional patients is reported.

#### **Materials and Methods**

Twelve patients (fourteen knees) have undergone the procedure in which iliac crest OPC harvesting and concentration, and open debridement and grafting of the distal femoral osteonecrotic lesion was performed.

These young patients comprised a heterogeneous series of diagnoses, but all had taken many weeks of corticosteroids for a serious lifethreatening medical condition including lupus erythematosis (4 patients, 5 knees), acute leukemia/lymphoma (3 patients, 3 knees), Crohn's disease (2 patients, 3 knees), cardiac transplantation (1 patient, 1 knee), DRESS syndrome (Drug Reaction [or Rash] with Eosinophilia and Systemic Symptoms) (1 patient, 1 knee), and pseudotumor cerebri (1 patient, 1 knee) (Table 1). Two patients had bilateral staged procedures. Age at original surgery averaged 23 years, with a range 13–37. At the time of surgery, 3 of the 4 patients with lupus were still taking oral corticosteroids (prednisone 5–10 mg per day); one of the other patients was also taking prednisone 7 mg. Six of the twelve patients were also taking systemic disease-modifying antirheumatic drugs (DMARDs) for their medical condition. Four patients were taking non-steroidal anti-inflammatory medication (NSAIDs). Three patients were diabetics.

DMARDs were discontinued peri-operatively and restarted based on the recommendations of the rheumatologist. NSAIDs were discontinued 10 days pre-operatively and restarted 6 weeks post-operatively.

Comprehensive analysis of the knee MRI with the musculoskeletal radiologist pre-operatively determined that there was no collapse or degradation of the cartilage surface (a contra-indication to this operation). The surgical procedure was similar to that previously described, except for minor changes [8]. Arthroscopy immediately prior to the

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Table 1
Patient Demographics.

Patient	Primary Diagnosis (Leading to SOK)	Age at Surgery	Time of Surgery: NSAIDs (Y or N)	Time of Surgery: DMARDs	Time of Surgery: Steroids and Dose	Follow-Up (Years)	Age at Follow-Up	Function Score at Follow-Up	Total Knee Score at Follow-Up	Other Relevant Information
1	DRESS syndrome	13	Ν	Ν	Prednisone – 7 mg	3	16	90	95	DM
2	Lupus	32	Y	Plaquenil	N	1	33	100	95	DM Bilateral THA
3	Leukemia	23	Y	Ν	Ν	7	29	90	94	Bilateral THA
4	Crohn's disease	26	Ν	Imuran	Ν	5	30	80	100	
5	Lupus	19	Ν	Cellcept Plaquenil	Prednisone 7.5 mg	3	22	100	94	Pericarditis
6	Lymphoma	37	Y	N	Ν	2	39	100	100	
7	Lupus	18	Ν	Plaquenil Cellcept	Prednisone - 10 mg	2	20	15	99	Left THA
8	Drug induced pseudotumor cerebri	25	Ν	N	Ν	9	34	100	99	Left THA Right hip – core decompression
9	Leukemia	19	Ν	Ν	Ν	2	21	70	89	Right THA
10-a	Crohn's disease	25	Y			4	29	100	94	0
10-b	Crohn's disease	21	Y	Remicade		8	29	100	94	
11	Cardiac transplant	19				11	30	100	64	
12-a	Lupus	20	Ν	Plaquenil Cellcept	Prednisone – 5 mg	4	25	70	52	DM
12-b	Lupus	19	Ν	Plaquenil Cellcept	Prednisone – 5 mg	5	25	70	52	

SOK = secondary osteonecrosis of the knee; DRESS syndrome = Drug Reaction (or Rash) with Eosinophilia and Systemic Symptoms; Lupus = lupus erythematosis; DM = diabetes mellitus; THA = total hip arthroplasty.

debridement and grafting procedure is no longer performed. Using the pre-operative radiographs and MRI as guides, the affected distal femoral condyle(s) was (were) debrided through a replaceable medial and/or lateral condyle bone window(s) using small saws, osteotomes, sharp curettes and drills. The medial and lateral cortical windows were placed longitudinally immediately anterior to the femoral insertion of the collateral ligaments and measured approximately 2-3 cm long and 1 cm wide. The bone windows were fashioned as keystones with wider external than internal dimensions. The debridement was accomplished without intra-operative radiographic imaging. No attempt was made to excise the entire osteonecrotic lesion, but simply to drill into it using multiple angles and excise easily accessible loose necrotic bone. Originally, the selective retention method using the Cellect Graft Preparation Device (DePuy, Warsaw, IN) was used for osteoprogenitor cell harvest and concentration. However, as this device became unavailable later in the series, we used other devices incorporating cell harvest and centrifugation in order to concentrate the OPC pellet aspirated from the iliac crest (MarrowStim Concentration System, Biomet Biologics Inc., Warsaw, IN). Only one iliac crest was harvested for each patient. Care was taken to constantly redirect the needle into multiple sites so as not to harvest the same area. The final pellet was then mixed with gelatinous demineralized bone matrix and the composite was directly placed within the debrided bone defect. The cortical window(s) was (were) replaced; the keystones facilitated locking of the windows within the adjacent bone. The soft tissues over the windows were closed to further stabilize these windows.

All patients in this series had both femoral condyles operated on at the time of surgery.

Patients were mobilized weight bearing as tolerated with crutches for six weeks, and underwent active assisted range of motion and strengthening exercises. Clinical examinations were performed at 6 weeks, 3 months, 1 year, and then every 1–3 years thereafter. Radiographs of the affected knee were taken at 6 weeks, 1 year, then every few years (Figs. 1–3). Follow-up MRIs were not performed.

The data were collected prospectively by the surgeon, and research associate in clinic, and included demographic and peri-operative data, and clinical outcome. Pain and function of the knee were evaluated by the Knee Society Score with a maximum of 100 points for each of the Knee Score and the Knee Function Score.

Post-operative radiographs were assessed to determine whether there was preservation or collapse of the grafted condyle, or the presence of arthritic changes in the knee (joint space narrowing, subchondral sclerosis, osteophytes).

#### Results

#### Clinical Results

Age at most recent follow-up averaged 27 years old, with a range 16–38. Mean follow-up was 5 years, with a range of 1–11. All but 1 patient had at least 2 years of follow-up. Two of the three patients with lupus were still on prednisone. Five patients were taking DMARDs. One patient was taking an NSAID and six patients were on narcotic analgesics for generalized pain not related to the operative knee. Five of the patients had undergone unilateral (3) or bilateral (2) total hip arthroplasty for osteonecrosis.

Pre-operative Knee Society Knee and Function scores were not available for the majority of the patients. The pre-operative scores from the original 3 patients in the series were between 50 and 60 for both indices. Post-operative Knee Society scores averaged 87 degrees (range 52–100) for the knee score and 85 degrees (range 15–100) for the knee function score at final follow-up. The one patient with a function score of 15 was awaiting a similar operation on the contralateral knee, and had ongoing pain and disability from systemic disease (lupus erythematosis).

None of the patients have undergone further surgery on their operated knee. None were taking pain medications for specifically for knee pain from the operative knee.

#### Radiographic Results

The classification system of Aglietti et al [14], a modification of the system of Koshino [15] was used to stage the degree of osteonecrosis using preoperative radiographs and magnetic resonance imaging scans; the preoperative stage was 3 in all the patients.

The size of the osteonecrotic lesion has important implications for subsequent prognosis. The size can be measured by either the ratio [16] or the area [17] technique. Studies have shown that there is no difference between the two methods in predicting prognosis [18,19]. We used the ratio method and classified a lesion as being large if it involved more than 0.32 of the involved condyle width. All of our patients had large lesions.

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