

THE PREVALENCE AND NATURAL HISTORY OF EARLY OSTEONECROSIS (ON) OF THE FEMORAL HEAD

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ABSTRACT

We performed limited MRI exams of the hips of renal transplant patients to determine the prevalence of osteonecrosis (ON) and the natural history of early lesions. Of 132 subjects, ten patients and 15 hips were considered positive for ON (prevalence = 7.6%, bilaterality = 50%). Eleven of the MRI-positive hips were Ficat Stage 0 (asymptomatic, pre-radiographic) and were followed with serial radiographs and MRI exams. With an average follow-up of 22 months, only one of these early lesions progressed beyond Ficat 0. The other ten hips neither developed progressive MRI changes nor progressed to radiographic stages.

Although our follow-up of 22 months is short, the results suggest that early ON may have a benign course in many cases. This supports the recent work of Kopecky et al., who found that many early lesions in renal transplant patients seemingly stabilize or disappear. While the prevalence was lower than in some previous reports, a significant number of patients did demonstrate previously unsuspected disease.

Given the recent reports of poor results and high complication rates using "prophylactic" surgery such as core decompression for early ON, we recommend further study into the natural history of these lesions to assess the need for such procedures.

In addition, we describe the use of a simple, quick and cost-effective method to screen high risk patients for early ON.

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INTRODUCTION

Osteonecrosis of the femoral head, from whatever cause, is known to have a poor prognosis once it reaches the radiographic stages (Ficat II-IV)¹. Several studies have shown inexorable progression to collapse and advanced degenerative arthritis in most cases treated non-operatively^{2,3,4,5}. The only satisfactory treatment for advanced ON is total joint arthroplasty. However, because the disease most commonly affects young adults who are not good candidates for joint replacement, many joint preserving operations such as core decompression have been recommended. All these procedures are reported to give better results if performed early in the course of ON^{2,3,6,7,8,9}. Most authors recommend "prophylactically" treating hips diagnosed prior to radiographic changes to halt progression. Thus an emphasis has been placed on early diagnosis using MRI, bone scans, or biopsy, especially in patients at high risk. This has and will continue to result in earlier diagnoses in many cases. However, the natural history of these early lesions is not known. Prophylactic surgery in effect presupposes that these hips will follow the same course as later stages, but no study has documented this assumption. The scant information available suggests the contrary; that is, many early lesions may have a benign natural history and do not require treatment¹⁰. In addition, none of the numerous investigations into core decompression and other procedures suggest completely satisfactory results^{11,12,13,14,15}. Recent literature questions whether surgery alters the natural history of any stage whatsoever.

MATERIALS AND METHODS

Our research protocol had the approval of our Institutional Review Board. To recruit subjects, we reviewed the computer records and/or charts of patients selected randomly from the list of our transplant clinic. Patients were contacted by phone and asked to participate in the study if they: 1) Were at least 18 years old, had a functioning renal transplant and were at least three months post transplant

surgery; 2) Had no previous diagnosis of ON; and 3) Were willing to undergo a brief MRI exam. Patients were not excluded for any other reason. Those with hip pain but no previous diagnosis of ON were included in an attempt to identify both Ficat Stage 0 and I.

Of the approximately 220 patients contacted, 132 underwent the initial MRI screening exam. Those patients not scanned included seven patients already diagnosed with ON while the remainder failed to show, became claustrophobic, or could not fit in the scanner. Prior to the procedure, the exam, and scope and purpose of the project were explained to each patient. Each patient signed informed consent and filled out a questionnaire regarding hip pain and limp, in order to stage positive scans. Data collected from the chart of each patient tested included: age, weight, cause of renal failure, time since transplant, serum creatinine level, current steroid dose, and estimated cumulative steroid dose.

The first 63 patients had scans in the coronal plane; the remaining scans were done in the axial plane to accommodate a related study. Images were obtained with either a Picker Vista (Picker International, Inc., Highland Heights, OH) 0.5 Tesla magnet or a General Electric Signa (General Electric Company, Milwaukee, WI) 1.5 Tesla magnet. For the Picker scanner, scan parameters included 5 mm slice thickness, no interslice gap, a spin-echo pulse sequence with TR = 600 and TE = 20, a 192 x 256 acquisition matrix, and four signal acquisitions. For the General Electric unit, scan parameters were similar with a 5 mm slice thickness, 1.5 mm interslice gap, a spin-echo pulse sequence with TR = 600 and TE = 12, a 192 x 256 acquisition matrix and two signal averages. Total examination time was approximately 15 minutes, including patient positioning. A grant was charged \$326 for each scan based upon an estimate of the resource expenditure, excluding physician fees (no patient was charged).

One of two musculoskeletal radiologists (DR and CW) interpreted the MRI examinations at the time they were performed. They interpreted the scans as either normal, indicative of ON, or equivocal. MR images were considered normal if the signal intensity of the femoral head was uniform throughout. Images were indicative of ON if they demonstrated crescentic areas of low signal intensity in the weight-bearing portion of the head, rings of low signal intensity, or collapse of the femoral head^{16,17}. After an interval of six months, the same two musculoskeletal radiologists interpreted all images in conference without knowledge of the original interpretation of the scans. We compared the original and consensus interpretations.

Anterior-posterior and Lowenstein lateral pelvis radiographs were obtained on each patient whose MRI was considered positive or equivocal. These films were also read independently and in consensus by the same two

radiologists. These patients also had a complete history and physical exam of the hips including palpation, ROM, Trendelenberg sign and assessment of gait. The hips were staged according to a modification of the Ficat staging system⁷:

- 0 - asymptomatic, normal exam and normal x-rays
- I - symptomatic and abnormal exam, normal x-rays
- II - trabecular changes on x-rays w/o collapse
- III - radiographic collapse w/o DJD
- IV - radiographic DJD

To differentiate Stage I from Stage 0, a patient had to have more or less constant hip or groin pain with a concomitant exam demonstrating limited hip motion, pain with range of motion, and limp. Those hips diagnosed in Stage II and beyond were excluded from the study and the patient offered referral to a joint reconstructive surgeon. Patients with pre-radiographic stages were followed with repeat plain films every six months, and a repeat MRI every year. All imaging studies were reviewed by the same musculoskeletal radiologists. If a patient progressed into a radiographic stage he/she was offered referral to a joint reconstructive surgeon.

Logistical regression analysis was used to determine whether or not any of the various clinical parameters predicted the occurrence of ON.

RESULTS

The MRI images in every case were similarly interpreted on the initial reading and later in conference. Two hips were initially read as equivocal by both observers but were later considered normal by consensus opinion. One other initially equivocal reading was rated equivocal by consensus six months later. The femoral head in this case had changes consistent with either necrosis or a bone cyst. This hip was followed per protocol, did not change in appearance on MRI, and no radiographic changes developed; it was not included in the group diagnosed as ON. In no case was a T-2 weighted image considered necessary to confirm or refute the diagnosis; an original exam was repeated to confirm artifact in one case and to confirm ON in another.

Of the 132 tested, ten patients and 15 hips had MR changes consistent with ON. Thus, the prevalence of ON in these patients was 7.6%, and lesions were bilateral in 50% of patients. After a thorough history, physical exam and A-P and Lowenstein lateral radiographs, the hips were staged. Eleven of the 15 were Ficat 0 (four of these eleven hips were described as painful but did not meet the criteria for Ficat 1). Two were Ficat II and two were Ficat III. There were no Ficat Stage I or IV hips. None of the four patients with radiographic lesions had previously sought medical attention for their hip, and they did not desire consideration for surgery. Because three of the four had contralateral pre-radiographic lesions, both hips were

followed in the study for progression. Therefore, all 15 hips were discovered because of the screening exam, and otherwise would have remained undiagnosed. Eleven of the 15 were radiographically normal, diagnosed solely by MRI.

The patient's age, weight, cause of renal failure, time since transplant, creatinine level, current and estimated cumulative steroid dose were not significant predictors of ON, individually or in combination.

The 11 pre-radiographic hips were followed with serial radiographs every six months and an MRI every year. Average follow-up was 22 months (range six to 29 months) and eight hips in six patients had a greater than two year follow-up. Only one hip progressed, from Ficat 0 to Ficat II. This change occurred one year into the study and he remains asymptomatic on that side. He has a Stage III lesion on the contralateral side with moderate symptoms. Every other early lesion remained essentially the same by MRI and did not progress into radiographic stages. None of these patients developed new symptoms and all remained Ficat 0 at the last follow-up.

DISCUSSION

Osteonecrosis, most commonly of the femoral head, is a well known complication of renal transplantation. Previous reports of the incidence have ranged from 3 to 41%, with most estimating around 20% based on radiographs and/or bone scans¹⁸. However, two revolutions have occurred since these studies. First, better immunosuppressants have afforded a reduction in steroid dosing, and some evidence suggests this has lowered the incidence of ON¹⁸. Second, MRI has emerged as the most sensitive exam for detecting ON, especially in the earliest stages^{17,19,20,21}. The incidence or prevalence of ON at this time using MRI is not well known. Some studies have recently used MRI as a screening exam for ON, and others have suggested screening all patients at high risk^{10,19,22,23}. A current estimate of the expected prevalence should be known prior to such wide scale screening with an expensive test.

Using an abbreviated screening MRI, we found a prevalence of ON of the femoral head of 7.6%, and lesions were bilateral 50% of the time. Of note, none of the ten patients we discovered had previously sought medical attention for the hip(s), including the four Ficat Stage II and III hips. Eleven of the 15 hips were radiographically normal, diagnosed solely by the screening MRI. Therefore, each patient could potentially benefit from being diagnosed by a screening exam, and specifically the MRI in most cases.

This prevalence of 7.6% agrees closely with that reported recently by Tervonen, et al., who discovered 6.0% of asymptomatic renal transplants had ON using a similar abbreviated MRI²³. Both of these figures are lower than

previous reports, possibly due to decreased steroid dosing or other factors. This lower estimate should be kept in mind prior to considering any wide scale screening of high risk patients.

Neither in our study nor that of Tervonen, et al., could specific risk factors for ON be identified. Therefore, selective testing of subsets of particularly high risk transplant patients does not seem feasible at this time.

We elected to use an abbreviated T-1 weighted MRI for several reasons. For one, T-2 images are less accurate for detecting ON, and frequently only confirm the diagnosis made by T-1^{10,24}. Secondly, scanning in one plane should be adequate to make the diagnosis. This reduced scan cost to \$326, approximately one-third the cost of a standard hip MRI. The exam time of 15 minutes is also one-third the standard exam time. This more cost-effective exam should be considered if screening of high risk patients is undertaken. The fact that each scan was interpreted similarly by the two radiologists and that only one scan was considered equivocal throughout the study supports the use of this limited exam. These relatively quick and inexpensive scans were believed useful to scan for and study the natural history of ON in high-risk groups.

The goal of any surgical intervention is to positively influence an otherwise adverse natural history. This implies that treatment is available to improve the prognosis. In the case of early ON, the natural history has been presumed to be the same as later stages (i.e., progression to collapse and secondary degeneration), and it has been further presumed that intervention such as core decompression with or without grafting would halt this progression. However, the natural history of early lesions is unknown and surgical procedures have had variable reports of success.

Using core decompression, Ficat reported excellent results for Stage I and II only, and stated the "prognosis depends entirely on early diagnosis and effective treatment"⁷. Hungerford and Zizic have reported similar results supporting early diagnosis and core decompression, and recommended against coring beyond Stage II as it did not prevent femoral head collapse^{2,3}. These authors advocated a functional exploration of bone on any suspicious, radiographically negative hip. If intraosseous hypertension or evidence of ON existed on venography, they recommended proceeding with core decompression, noting a high correlation of these tests with eventual biopsy results. Steinberg, et al. reported better success in earlier stages using coring with added cancellous bone grafting, with or without electrical stimulation⁹. They advocated using MRI in suspicious cases to diagnose early lesions, but noted that ON could be present even with a negative MRI. Finally, Meyers found limited success using vascularized muscle pedicle grafts for lesions already displaying

a crescent sign, compared to outstanding success in treating early lesions⁸. The initially encouraging results in treating early ON, along with other supportive studies^{6,25}, prompted enthusiasm for making the earliest diagnosis and intervening early with core decompression and other procedures.

However, most recent literature has reported higher failure and complication rates for these procedures. Camp and Colwell reported progression in 60% of Stage I and II hips treated with core decompression at a mean follow-up of 18 months and a ten percent incidence of perioperative femoral fracture¹¹. Similarly poor success was demonstrated by Hopson and Siverhus, Saito, et al., and Seiler, et al^{15,12,26}. Learmonth, et al., reported the highest rate of failure, with radiographic progression in 75% of Stage I and 86% of Stage II hips at a mean follow-up of 31 months¹³. Nelson and Clark reviewed the efficacy of structural bone grafting, and found progression in at least 82% of hips with a minimum of two year follow-up¹⁴. These studies have tempered the enthusiasm for prophylactic surgery for ON, and the efficacy of surgery to preserve the natural femoral head in any stage has to be questioned.

More importantly, the untreated natural history of these early lesions is largely unknown. The available evidence suggests a more benign course than previously presumed. Kopecky, et al., discovered 14 patients and 25 hips with MR changes consistent with ON by prospectively scanning 106 renal transplant patients serially two years after transplant¹⁰. The MR images returned to normal in six of these hips and the lesions decreased in size in seven hips in five asymptomatic patients. Only seven hips (28%) in four patients developed pain and radiographic changes over a mean follow-up of 16 months.

In the current study, only one of the eleven Ficat Stage 0 hips progressed into the radiographic stages. The other ten hips have not developed new symptoms, radiographic changes or a change in appearance by MRI. The mean follow-up of 22 months is short, and other hips may progress over time. However, previous studies documenting progression in later stages have shown progression to occur over periods less than this follow-up^{4,5}. We will continue to follow these hips for progression to determine their long-term natural history.

In conclusion, we describe a quick, simple and relatively inexpensive limited MRI to screen patients at high risk for ON of the femoral head. Using this exam, ten of 132 patients had 15 hips with ON; these cases would otherwise not have been diagnosed. However, given the rather benign natural history of these lesions, and that prophylactic surgery may not alter the natural history, this study provides additional evidence as to the questionable appropriateness of such procedures.

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