
Bone SPECT Is More Sensitive Than MRI in the Detection of Early Osteonecrosis of the Femoral Head After Renal Transplantation

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We compared the diagnostic sensitivity of ^{99m}Tc-methylene diphosphonate bone SPECT and MRI in the early detection of femoral head osteonecrosis after renal transplantation. **Methods:** The patients were 24 renal allograft recipients who underwent both bone SPECT and MRI within 1 mo of each other because of hip pain but normal findings on plain radiography. SPECT was considered positive for osteonecrosis when a cold defect was detected in the femoral head, and the defect was further classified according to the presence of adjacent increased uptake: type 1 = a cold defect with no adjacent increased uptake; type 2 = a cold defect with adjacent increased uptake. MRI was considered positive for osteonecrosis when a focal region with low signal intensity on T1 images was detected in the femoral head. Final diagnoses were made by surgical pathology or clinical and radiologic follow-up of >1 y. **Results:** A total of 32 femoral heads, including 24 of 29 painful hips and 8 of 19 asymptomatic contralateral hips, were confirmed as having osteonecrosis. SPECT detected osteonecrosis in all 32 of the femoral heads, resulting in a sensitivity of 100% (32/32), whereas MRI detected osteonecrosis in 21 femoral heads, for a sensitivity of 66% (21/32, $P < 0.005$). SPECT showed the type 1 pattern in 13 and the type 2 in 19. Ten of the 13 femoral heads with the type 1 pattern were false-negative on MRI, whereas only 1 of 19 with the type 2 pattern was normal on MRI ($P < 0.001$). There were 6 femoral heads with normal MRI findings and abnormal SPECT findings (type 1 pattern) in 3 patients, for whom hip pain decreased and radiographic findings were normal during follow-up. Follow-up bone SPECT showed a decreasing area of cold defect in 4 femoral heads. **Conclusion:** ^{99m}Tc-methylene diphosphonate SPECT is more sensitive than MRI for the detection of femoral head osteonecrosis in renal transplant recipients. Bone scintigraphy with SPECT is needed to diagnose osteonecrosis in patients with hip pain despite normal radiography results after renal transplantation. The sig-

nificance of a transient SPECT abnormality needs to be clarified by further natural history studies.

Key Words: bone SPECT; MRI; femoral head osteonecrosis; renal transplantation

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Osteonecrosis affects between 5% and 29% of renal transplant recipients and is a significant cause of disability after transplantation surgery (1). The femoral head is the most commonly involved site. Early detection is crucial because early surgical core decompression of the femoral head may arrest progress of the disease and prevent collapse of the femoral head. According to some investigators, early diagnosis is the single most important factor in effective treatment and prevention of disease progression (2).

For diagnosing osteonecrosis, MRI is sensitive and specific and has become the tool of choice for early and accurate detection (3). Several studies reported that the sensitivity of MRI is 10%–20% higher than that of bone scintigraphy (4–7). Recently, SPECT has been applied to bone scintigraphy, especially in the hip region, and improved diagnostic ability in the detection of osteonecrosis of the femoral head has been reported (8,9). On planar scintigraphic images, a photon-deficient defect in the femoral head, the earliest and most evident scintigraphic finding of osteonecrosis (8,10), may be obscured by the acetabular and other surrounding bone activity. Using SPECT, it is possible to separate the femoral head from other overlying bony structures. However, no previous studies have compared the diagnostic accuracy of bone SPECT and MRI in the diagnosis of femoral head osteonecrosis.

The purpose of this study was to compare the diagnostic sensitivity of bone SPECT and MRI for the detection of early osteonecrosis of the femoral head in renal transplant recipients.

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MATERIALS AND METHODS

Subjects

From January 1995 to December 1999, 85 of 706 patients who received a renal allograft at our institution underwent plain radiography of both hips because of unilateral or bilateral hip pain or discomfort. Among these, 30 patients showed grossly abnormal findings of one or both femoral heads suggesting advanced osteonecrosis (Ficat stage II or III) (11). The remaining 55 patients, who had normal plain radiographic findings, underwent bone SPECT ($n = 52$) or MRI ($n = 30$). Twenty-seven of 35 patients with abnormal bone SPECT findings, and none of the 17 patients with normal bone SPECT findings, underwent MRI. After excluding 3 patients for whom the interval between the 2 studies was longer than 1 mo, we finally selected as the study subjects 24 patients (14 men, 10 women; age range, 26–65 y; mean age, 39.5 ± 9.6 y) whose 48 femoral heads were normal on plain radiography. Twenty-nine hips were painful, and 19 were asymptomatic. The mean interval between bone SPECT and MRI was 9.8 ± 7.1 d (range, 0–22 d). For all patients, bone SPECT was performed before MRI. The median period from renal transplantation to bone SPECT was 144 d (range, 6 wk to 3 y). Patients were treated with low-dose steroids, azathioprine, or cyclosporin after transplantation. Seven patients had a history of short-term high-dose steroid treatment because of acute rejection.

Core decompression in 13 femoral heads and total hip replacement arthroplasty in 14 confirmed the diagnosis of osteonecrosis within 14 mo after bone SPECT. In the remaining 21 femoral heads, clinical follow-up of more than 1 y, with follow-up imaging studies that included plain radiography, bone SPECT, or MRI, ultimately resulted in a diagnosis of osteonecrosis in 5 and stress fracture in 1. The femoral heads were found to be normal in the other 15.

Bone SPECT

Whole-body planar bone scintigraphy was performed 4 h after injection of 1,110 MBq ^{99m}Tc -methylene diphosphonate using a dual-head gamma camera (Bodyscan; Siemens, Hoffman Estates, IL, or BiadXLT; Trionix, Twinsburg, OH) equipped with high-resolution or ultra-high-resolution collimators. Immediately after whole-body imaging, SPECT images of the hip were obtained using a triple-head gamma camera (TriadXLT; Trionix) equipped with a low-energy ultra-high-resolution parallel-hole collimator. Before the start of the SPECT acquisition, patients were asked to empty their bladder. The acquisition parameters included step-and-shoot mode, a noncircular rotation, 30 s per projection over 360° , a total of 120 projections, and a 128×128 matrix. The SPECT images were reconstructed using filtered backprojection with a Hamming filter (cutoff frequency, 1.2 cycle per minute).

MRI

MRI was performed using 1.5-T scanners (Magnetom Vision; Siemens, Erlangen, Germany, or Sigma; General Electric Medical Systems, Milwaukee, WI). T1-weighted, T2-weighted, and short- τ inversion recovery coronal images were obtained, and T1-weighted axial and sagittal images of both hips were also obtained. The field of view was 340×340 mm, and the matrix size was varied according to image plane ($128\text{--}256 \times 256\text{--}512$). The slice thickness and interslice gap were 4.0 and 0.8 mm, respectively.

Image Interpretation

Two nuclear medicine physicians, unaware of the MRI findings and clinical information, independently reviewed the bone SPECT

images. They reviewed both the whole-body planar bone scans and the hip SPECT images for the presence or absence of osteonecrosis. The positive criterion for osteonecrosis of the femoral heads was a cold defect in the femoral heads. The scintigraphic uptake patterns of femoral head osteonecrosis were classified into 2 categories: type 1, a cold defect without surrounding increased uptake, and type 2, a cold defect with surrounding increased uptake. Increased uptake without a cold defect was not considered osteonecrosis. Two experienced musculoskeletal radiologists, unaware of the SPECT findings and clinical information, independently interpreted the MR images. The positive criterion for osteonecrosis of the femoral heads was the presence of a reactive interface with low signal intensity on T1-weighted MR images surrounding the femoral head. A third observer, who was not informed of the clinical information and the specifics of the discrepancy, solved any discrepancies between the 2 interpreters.

The sensitivities of bone SPECT and MRI for the diagnosis of early osteonecrosis were compared by the McNemar test. The significance of the difference between MRI sensitivity in patients with type 1 and 2 SPECT findings was assessed by the Fisher exact test. $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 32 femoral heads, including 24 of 29 painful hips and 8 of 19 asymptomatic hips, were confirmed as having osteonecrosis. Sixteen femoral heads did not have evidence of osteonecrosis. One hip was considered to have a stress fracture. Bone SPECT detected all 32 femoral heads with osteonecrosis, resulting in a sensitivity of 100% (32/32), whereas MRI detected osteonecrosis in 21 of the 32 femoral heads (sensitivity, 66%; $P < 0.005$). Eleven femoral heads had false-negative MRI findings, even though all MR images had been obtained later than the bone SPECT images (Figs. 1 and 2). Of the 24 femoral heads that were painful and showed positive findings on bone SPECT, 10 had false-negative MRI findings. The patients who had normal MRI findings and abnormal bone SPECT findings are summarized in Table 1. Of the 32 femoral heads with osteonecrosis, bone SPECT showed the type 1 pattern in 13 and the type 2 pattern in 19. Ten of the 13 femoral heads with osteonecrosis and the type 1 scintigraphic pattern had false-negative MRI findings, whereas only 1 of 19 with osteonecrosis and the type 2 pattern had normal MRI findings ($P < 0.001$).

Among 7 patients with a history of high-dose steroid treatment, 3 showed the type 2 pattern of osteonecrosis on SPECT and had positive MRI findings for one or both femoral heads, whereas 4 showed the type 1 pattern of osteonecrosis on SPECT but had normal MRI findings for both femoral heads. Surgery confirmed that all had osteonecrosis.

MRI had no false-positive results. In contrast, the findings for the 6 femoral heads of 3 patients were categorized as false-positive on bone SPECT because hip pain improved during follow-up and MRI during follow-up persistently showed a normal appearance. Pathologic specimens were not obtained from these patients. The uptake pattern on bone

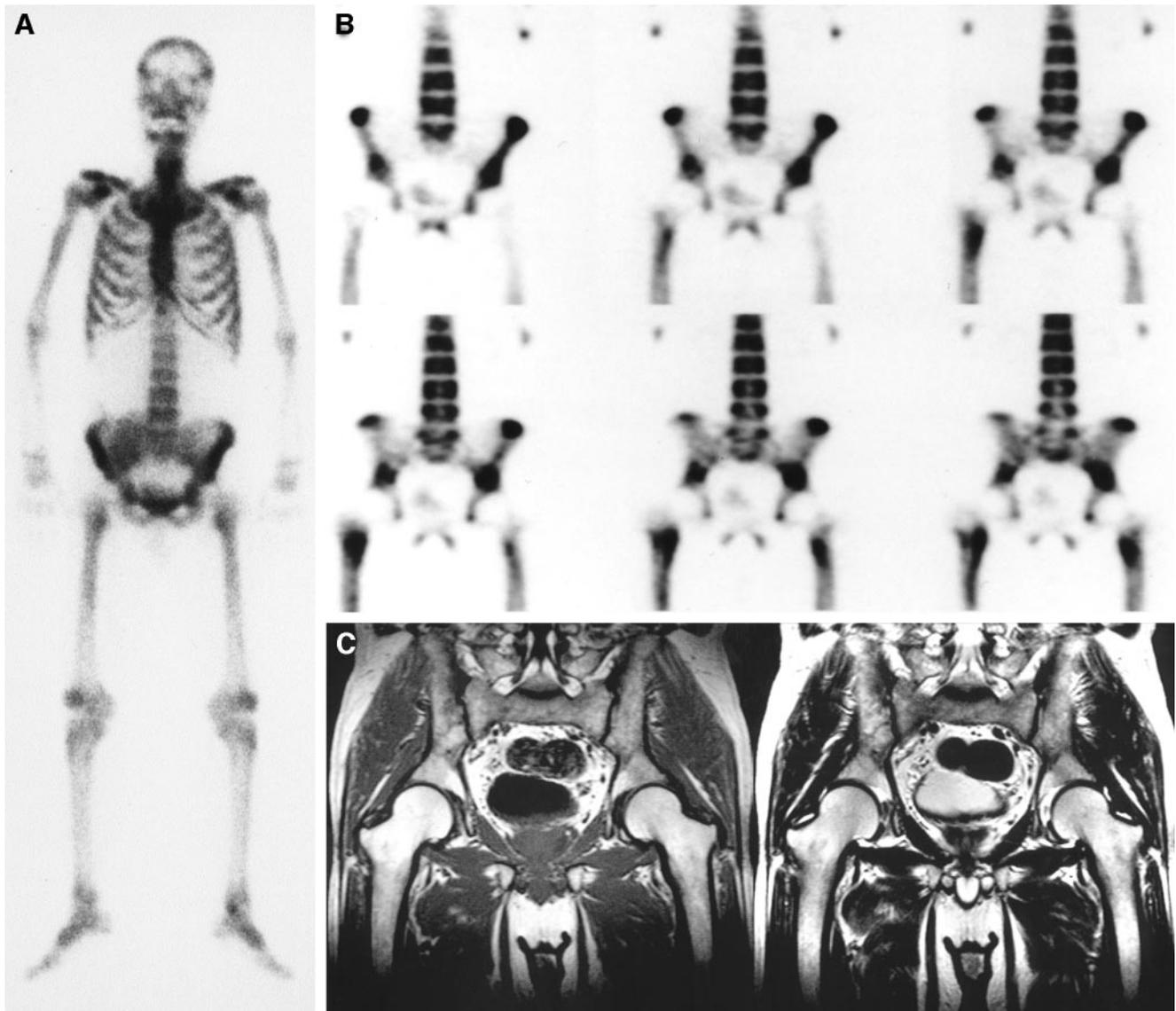


FIGURE 1. A 53-y-old male renal transplant recipient complained of bilateral hip pain. Initial whole-body bone scintigraphy (A) and bone SPECT (B) show cold areas in both femoral heads, whereas MRI of both hips shows normal findings (C).

SPECT was type 1 in all 3 patients. In 2 of these patients, hip pain decreased and follow-up bone SPECT showed decreasing areas of cold defect in the femoral heads. One patient also showed multiple areas of increased uptake in the distal femoral condyles and proximal tibiae on the initial whole-body scan (Fig. 3).

One femoral head with a stress fracture showed focal increased uptake without a cold defect on bone SPECT and abnormal signal intensity on MRI of the femoral neck. The bone SPECT and MRI findings for the patient were categorized as true-negative for osteonecrosis.

DISCUSSION

Our study revealed that bone SPECT is more sensitive than MRI for early detection of femoral head osteonecrosis in renal transplant recipients. Eleven femoral heads had

abnormal bone SPECT findings and normal MRI findings, and all of these femoral heads were confirmed as having osteonecrosis by core decompression or total hip replacement arthroplasty. No femoral heads had false-negative bone SPECT findings and true-positive MRI findings. MRI was especially less sensitive when the femoral heads showed the type 1 pattern on bone SPECT. Siddiqui et al. (12), in studying asymptomatic renal allograft recipients, reported 13 hips with normal MRI findings and abnormal bone SPECT findings consistent with avascular necrosis and 10 hips with abnormal MRI findings and normal bone SPECT findings. Siddiqui et al. suggested that both MRI and bone SPECT are needed to detect subclinical avascular necrosis. However, in those patients with discordant imaging studies, abnormal findings were transient, and the presence of osteonecrosis was not confirmed by pathology. To

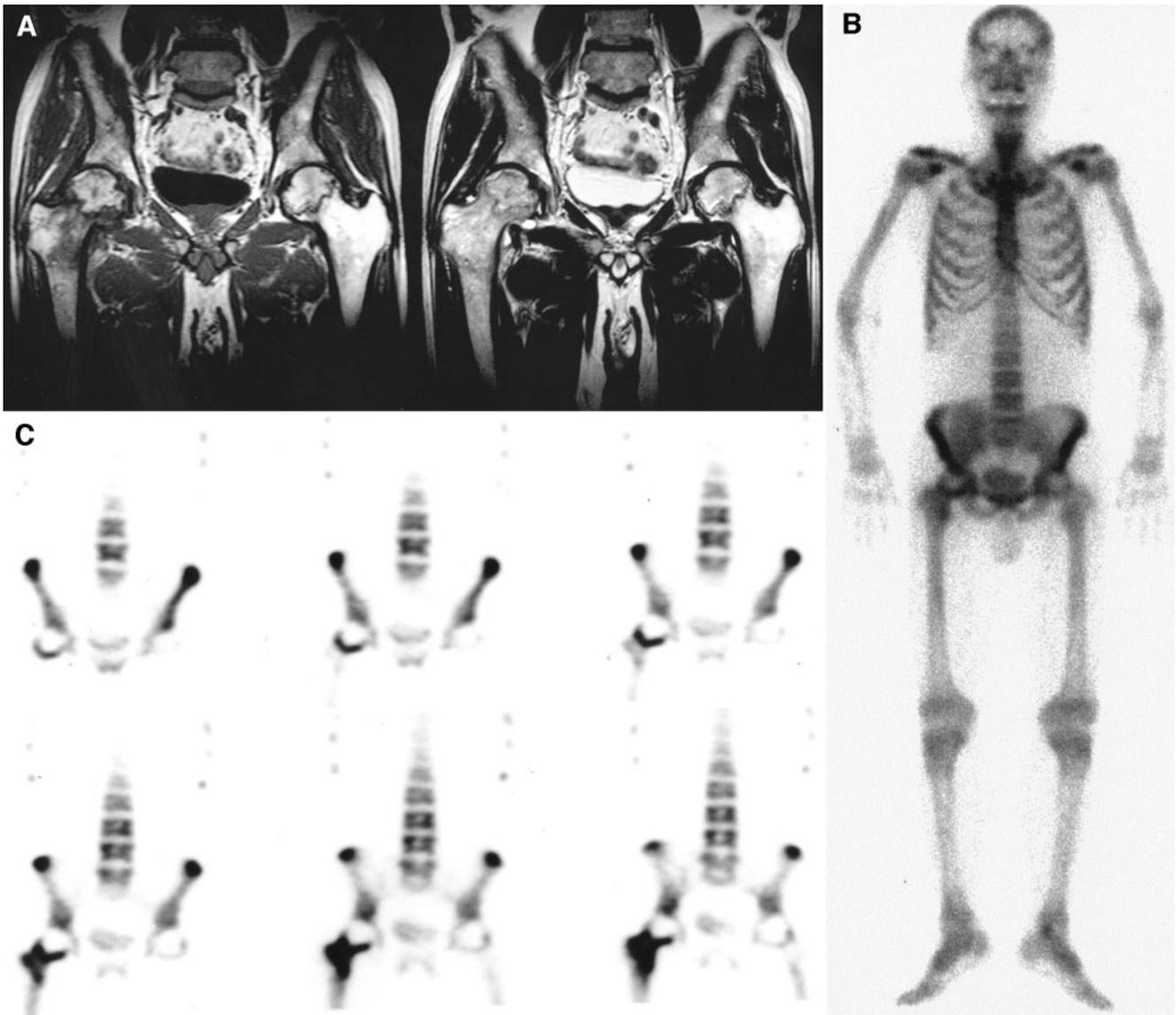


FIGURE 2. Patient of Figure 1 underwent follow-up MRI, bone scintigraphy, and SPECT. T1- and T2-weighted MR images (A) show geographic areas of low signal intensity in both femoral heads, and bone scintigraphy (B) and SPECT (C) show increased uptake surrounding cold central areas in both femoral heads. Osteonecrosis of both femoral heads was pathologically confirmed after total hip replacement.

our knowledge, ours is the first study showing bone SPECT to be significantly more sensitive than MRI for detecting osteonecrosis in renal allograft recipients.

Previous studies have shown that MRI changes may not be evident despite histologic evidence of osteonecrosis (13–15). Brody et al. (13) showed that changes in signal intensity on T1- and T2-weighted images caused by the death of marrow cells from ischemia may not occur until 5 d after arterial interruption. In a study of high-risk patients presenting with hip pain (14), MRI findings were normal but histologic results revealed osteonecrosis in 6 hips, resulting in a sensitivity of only 46%. During this early period, when osteonecrosis may not be indicated by any distinctive abnormalities on MRI, bone SPECT may show a cold defect in the femoral head, as was shown in our results. Probably,

this is the reason that the femoral heads showing false-negative results on MRI were showing mainly the type 1 pattern on bone SPECT in our study. After a certain time, as the bone marrow cells, osteocytes, and fat cells die, the signal intensity of MR images will change distinctively. Concurrently, bone SPECT will show a cold area with a surrounding increased reactive uptake reflecting increased bone remodeling (type 2 pattern) (9). To improve the sensitivity of MRI, some investigators have suggested the use of gadolinium contrast material. However, no conclusive evidence supports this practice (3). Other new MRI techniques may reduce false-negative results and improve diagnostic sensitivity (15).

There may be other reasons for the high sensitivity of bone SPECT imaging in this study. Osteonecrosis of the

TABLE 1

Patients with Normal MRI Findings and Abnormal Bone SPECT Findings for Femoral Heads After Renal Transplantation

Patient no.	Sex	Age (y)	Time after transplantation (mo)	Interval between SPECT and MRI (d)	Side of hip	Pain	SPECT pattern	Final diagnosis
1	M	26	3.6	9	R	–	1	OSN*
					L	+	1	OSN†
2	M	53	1.6	3	R	+	1	OSN†
					L	+	1	OSN†
3	F	37	2.4	5	R	+	1	OSN*
					L	+	1	OSN*
4	F	53	1.4	1	R	+	1	OSN†
					L	+	1	OSN†
5	M	48	1.5	5	R	+	1	OSN†
					L	–	Normal	Normal
6	M	38	2.5	3	R	+	2	OSN†
					L	–	Normal	Normal
7	F	52	1.8	5	R	–	Normal	Normal
					L	+	1	OSN†
8	F	35	3.3	4	R	+	1	Normal
					L	–	1	Normal
9	F	49	3.4	2	R	+	1	Normal
					L	+	1	Normal
10	F	36	1.9	12	R	–	1	Normal
					L	+	1	Normal

*Confirmed by core decompression.

†Confirmed by total hip replacement arthroplasty.

1 = cold defect without surrounding increased uptake; OSN = osteonecrosis; 2 = cold defect with surrounding increased uptake.

femoral head may be more easily diagnosed by bone SPECT in renal allograft recipients than in patients with other risk factors. Because of the underlying renal osteodys-trophy, skeletal uptake of ^{99m}Tc-methylene diphosphonate is increased, and higher surrounding bone uptake may result in a more strongly contrasted cold defect of the necrotic femoral head. A prospective, comparative study of bone SPECT and MRI in patients other than renal allograft recipients may clarify this possibility further. As for the technical aspects, the triple-head camera used in our study is more efficient than a single- or dual-head camera for hip SPECT because of the higher counting rate with shorter imaging time.

In our results, the findings for 6 hips of 3 patients were considered false-positive because the symptoms later disappeared and osteonecrosis was not seen on follow-up imaging studies. In 1 patient, multifocal increased uptake in the distal femurs and proximal tibiae developed along with lesions on both femoral heads. Follow-up bone scintigraphy showed a gradual improvement of these abnormalities after the steroid dose was decreased. Although bone marrow pressure was not measured in these patients and tissues were not examined histopathologically, the lesions might have been a very early stage of reversible osteonecrosis or borderline necrosis (12,15). Koo et al. (15) reported that femoral heads with borderline necrosis showed increased bone marrow pressure and histopathologic changes but persis-

tently normal MRI findings. Therefore, reversible or sub-clinical early osteonecrosis might have been detected by bone SPECT in our study. A further study is needed to confirm the presence of subclinical osteonecrosis.

Because early detection is the most important factor for prevention of disease progression and for a more favorable outcome of osteonecrosis, our results suggest a beneficial role for bone SPECT in the initial screening of renal allo-graft recipients with painful hips. However, because the natural history of osteonecrosis is not well known, the efficacy of bone SPECT as a screening method and the impact of positive findings on an aggressive surgical ap-proach also need to be further elucidated.

A limitation of this study is that only patients with ab-normal bone SPECT findings for the femoral heads under-went MRI. Because of the referral bias in our study, unde-tected osteonecrosis in some patients with normal bone SPECT findings might have been detected if MRI had been performed. However, we performed clinical and radio-graphic follow-up for more than 1 y after the initial bone SPECT examination for all patients who did not undergo MRI. In these patients with normal bone SPECT findings, osteonecrosis did not develop, and all patients with osteo-necrosis were identified by bone SPECT. Therefore, in this case, the referral bias should not have influenced the con-clusions from the study.

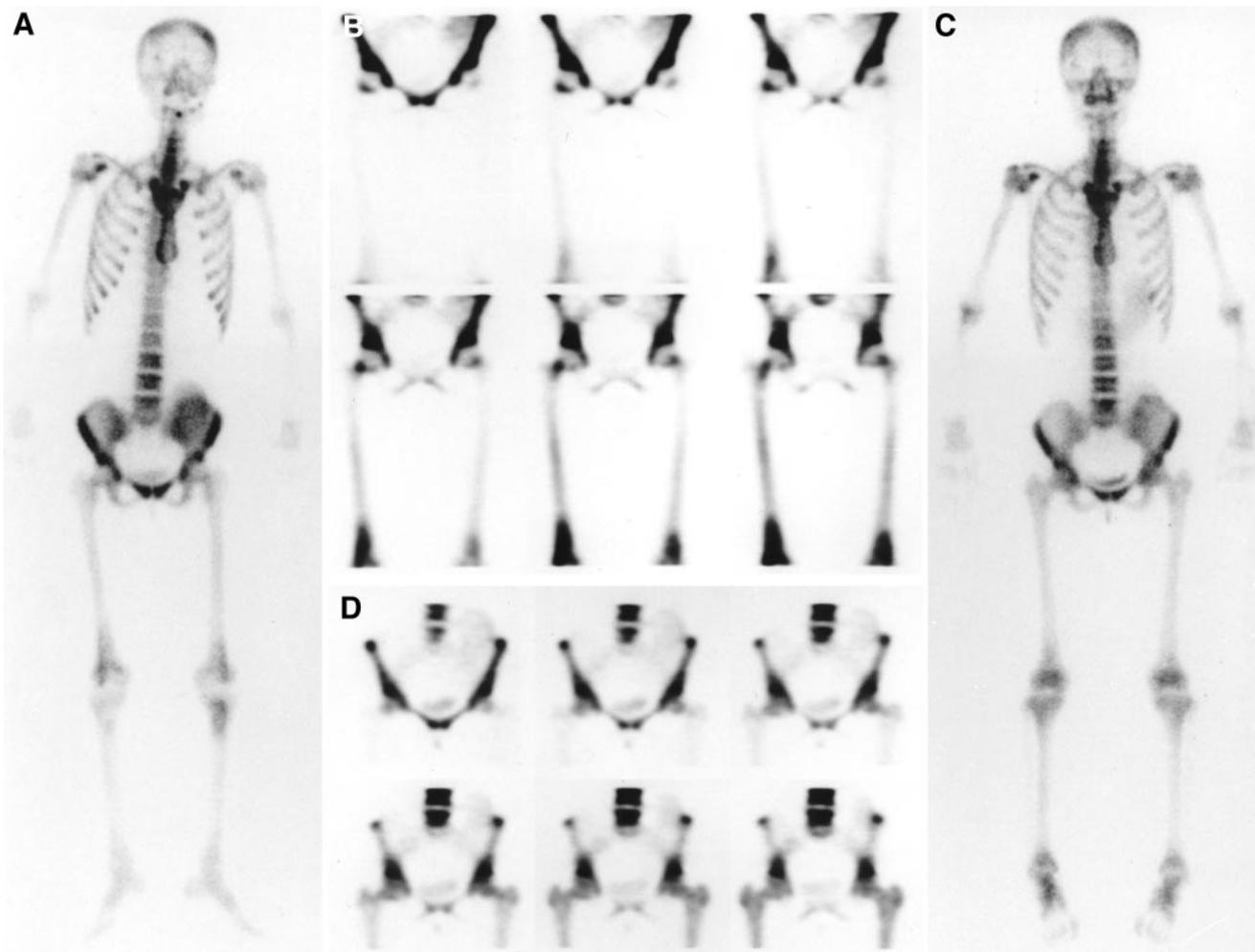


FIGURE 3. A 35-y-old female renal transplant recipient complained of bilateral hip pain. Whole-body bone scintigraphy (A) and SPECT (B) show decreased uptake in both femoral heads and increased uptake in both distal femurs and left proximal tibia, but initial MRI of both hips (not shown) and several follow-up MRI examinations until 1 y later showed normal findings. Follow-up bone scintigraphy (C) and SPECT (D) 2 y later show normalized uptake in both femoral heads, distal femurs, and left proximal tibia.

CONCLUSION

Bone SPECT is more sensitive than MRI in the detection of early osteonecrosis of the femoral heads after renal transplantation. Bone scintigraphy with SPECT should be used to diagnose osteonecrosis, particularly in patients with hip pain but normal radiographic findings after renal transplantation.

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