Original Article

COMPARISON OF DIFFERENT DIAGNOSTIC MODALITIES IN EVALUATION OF INFECTION OF TOTAL HIP ARTHROPLASTY

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Summary

Loosening is the most common late complication of total hip arthroplasty. Although rare, low-grade infection often presents as prosthetic loosening and could be missed. There is controversy about the diagnostic value of bone scintigraphy and laboratory tests in patients suspected of having loosening. In this retrospective study, we evaluated the sensitivity and the specificity of different diagnostic modalities in patients suspected of having loosening of the hip arthroplasty. Seventeen patients (20 hips) with total hip arthroplasty and possible prosthetic loosening were examined with conventional radiography and three-phase bone scintigraphy. Results of microbiological examinations of joint aspiration and surgical specimens (9 patients), plus C-reactive protein level (CRP) and erythrocyte sedimentation rate (ESR) test, as well as clinical follow-up were evaluated in the twenty hips. Sensitivity, specificity and accuracy values were calculated. Five hips had septic, and three hips had aseptic loosening. In twelve cases, neither loosening nor infection was confirmed. For diagnosing infection with conventional radiography and bone scintigraphy, respectively, sensitivity values were 62.5% and 87.5%; specificity - 80% and 91.6%; and accuracy 85% and 90%. For ESR and CRP, respectively, sensitivity values were 60% and 100%; specificity - 100% and 70%; and accuracy - 86.7% and 75%. In a study population of patients suspected of having infected total hip replacements, three-phase bone scintigraphy performed better than conventional radiography, ESR and CRP tests.

Key words: scintigraphy, hip arthroplasty.

Introduction

Loosening is the most common late complication of total hip arthroplasty (THA) [1]. Although rare, low-grade infection often presents as prosthetic loosening and could be missed. After the considerable decrease from 9% in the initial series of Charnley [2], the reported rate of infection after primary implantation and revision arthroplasty of hip prostheses is between 1% and 4% [3]. Although rare, infection is a serious complication in reconstructive joint surgery.

The diagnosis of an infected hip endoprosthesis is usually made using clinical methods, radiographic techniques, and biopsy. However, there is no absolutely

precise diagnostic test. A complicating factor is that the accuracy of imaging investigations depends on the expertise of the interpreters [4, 5]. Moreover, the relative utility of bone scintigraphy and laboratory examinations is controversial [6, 7].

The aim of our retrospective study was to evaluate the diagnostic value of bone scintigraphy, C-reactive protein level (CRP) and erythrocyte sedimentation rate (ESR), in patients suspected of having aseptic or septic loosening of the hip arthroplasty.

Material and Methods

From the database of the Clinic of Orthopedics and Traumatology, 20 total hip arthroplasties, examined with bone scintigraphy, were reviewed retrospectively. The series included eleven females and six males, mean age 63.7±8.2 years (age range 51-81). Three arthroplasties were bilateral; five hips were scheduled for revision because of infection, and three because of aseptic loosening. In another nine cases, bone scintigraphy was performed for evaluation of periprosthetic remodeling after revision with impaction allografting. In three of the cases, patients complained of hip pain. The average time between the index surgery and bone scintigraphy was 3.3±4.6 years (range 0.5-16 years). The patients were evaluated clinically [1], radiographically [1, 8, 9], and scintigraphically [7]. Differential white blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and fibrinogen were measured shortly before the examination. ESR levels above 40 mm/hr were considered abnormal. CRP levels were considered abnormal according to the local laboratory standard (above 0.8 mg/dL). No patient received antibiotic treatment at the time of imaging. Demographic data on the patients in the series are shown in Table 1.

Imaging evaluation included standard radiographs and 99Tc-MDP bone scans.

Table 1. Characteristics of the patients in the series.

Parameter		**Results**
Demo-graphics	Age (yrs)	63.7 (51 to 81)
	Weight (kg)	73.9 (47 to 115)
	Height (cm)	166.3 (145 to 185)
	Gender (M/F; %)	6/11 (35.3%/64.7%)
Primary diagno-sis N,%	Osteoarthritis	14 (70%)
	Fracture	3 (15%)
	Osteonecrosis	2 (10%)
	Others	1 (5%)
Primary/Revision HA (N, %)		9/11 (45%/55%)
Involved hip (R/L, N, %)		15/5 (75%/25%)
Follow-up (yrs)		3.3 (0.5 to 16)

Conventional Radiography

Implant stability was assessed radiographically according to the criteria proposed by Engh et al. [8] for cementless, and by Harris and McGann [9] for cemented implants. Radiolucency was defined as a radiolucent line ≥2 mm and parallel to the implant. Subsidence was defined as a decrease of at least 5 mm in the distance between the top of the stem and the greater trochanter. Cup migration >5 mm was defined by measuring the distance from the teardrop line. The diagnosis of infection [3, 10] was rendered when at least one of the following criteria was present: rapid prosthetic migration (of at least 2 mm within 6-12 months), rapidly progressing periprosthetic osteolysis, and/or irregular periprosthetic osteolysis. The diagnosis of loosening (without infection) [1, 8, 9] was rendered when at least one of the following criteria was present: migration (of less than 5 mm), periprosthetic lucency (in a smooth area of 2 mm or greater in diameter), periosteal reaction (of the solid type), and/or cement fracture. In the patients with only one set of radiographs, the diagnosis of infection or loosening was based on the same morphologic criteria, without information regarding migration.

Bone Scintigraphy

Three-phase bone scintigraphy was performed with a gamma camera equipped with a low-energy, high-resolution, parallel-hole collimator by using a 20% window centered on the 140-keV photopeak after intravenous injection of 555-700 MBq of 99mTc-MDP (Methylene Diphosphonate). In the dynamic phase, images of the hip were acquired in a 3-second exposure up to 2 minutes after injection. The blood pool phase consisted of acquisition of a static spot image of the hip (anterior view) 5 minutes after intravenous tracer injection. The third phase (i.e. the bone mineral metabolism study) was performed 24 hours after injection, and anterior and posterior spot views of the hip were again obtained. The images were analyzed by a nuclear physician (T.P. and D.V.), blinded to the results from the other studies (radiographs and laboratory tests). The appearance (focal or diffuse) of the increased radionuclide uptake was described [6, 11]. Focally or diffusely increased periprosthetic uptake in all three phases of bone scintigraphy was considered diagnostic for infection. Increased radionuclide uptake limited to the third phase was considered to indicate a loosened but not infected total hip replacement.

Diagnosis of Infection

Our criterion for infection was based on detecting microorganisms in cultures. If no microorganisms were found, the detection of local abscess formation and the presence of neutrophilic granulocytes were also considered. In the eight hips revised, at the time of revision surgery, biopsy specimens were collected. Each was put in a separate, dry, sterile glass container and taken to the laboratory for immediate processing. Standard bacteriological techniques were used to identify isolates and determine antibiotic sensitivity. For eight of the 20 cases, results from the analysis of additional histologic specimens of capsular tissue were available. The final diagnosis of septic/aseptic loosening was based on surgical, histologic, laboratory, and bacteriologic data and follow-up. No infection was assumed to be present in patients who had negative microbiologic results at revision (for the eight revised hips); normal ESR, CRP level and white blood cell count; and improvement in their clinical symptoms for more than 6 months.

Statistical Analysis

The sensitivity of the different tests was defined as the number of true-positive results divided by the sum of true-positive and false-negative; specificity - as the number of true-negatives divided by the sum of true-negatives and false-positives; accuracy was defined as the sum of true-positives and true-negatives divided by the total number of cases.

Data were compared using a sign test. Statistical analysis was performed with the SPSS statistical package Version 10.0 (SPSS, Chicago, Illinois, USA). Significance was defined as a “p” value of <0.05.

Results

Five hips were diagnosed as having an infection on the basis of the correlation between positive pre- and intra-operative cultures, and laboratory and histological findings showing acute or chronic inflammation of tissue (Fig. 1); the appearance of the tissue intraoperatively; radiographic findings; and the clinical course. Three hips were diagnosed radiographically as septically loose. There were seven positive and thirteen negative bone scans. In four cases, bone scintigraphy yielded positive result for sepsis; on the other hand, one of the four hips with negative intraoperative culture was diagnosed as septic. Clinical, radiographic, and pre- and intra-operative findings showed aseptic loosening in three hips (two cups 2/15, 13.3%) and two stems (2/15, 13.3%) (Fig. 2). The sensitivity of conventional radiography was 62.5%; specificity was 80%, and accuracy 85%. The sensitivity of bone scintigraphy was 87.5%; specificity was 91.6%; and accuracy - 90%. The observed differences were not statistically significant.

Data were also evaluated with respect to the predictive value of ESR and CRP for independent evaluation of infection (Table 2). For ESR, there were three positive and twelve negative results. For CRP, there were eight positive and seven negative results. The mean ESR value for the 15 patients with measurement was 22.9 mm/H (range, 6 to 63 mm/H, SD ±19.5), and the mean value for CRP for the 16 patients with measurement was 1.84 mg/dL (range, 0.24 to 7.2 mg/dL, SD ±2.03). However, differences were not significant ($p>0.05$).

Differential white blood count and fibrinogen measurements did not show correlation with loosening (septic or aseptic).

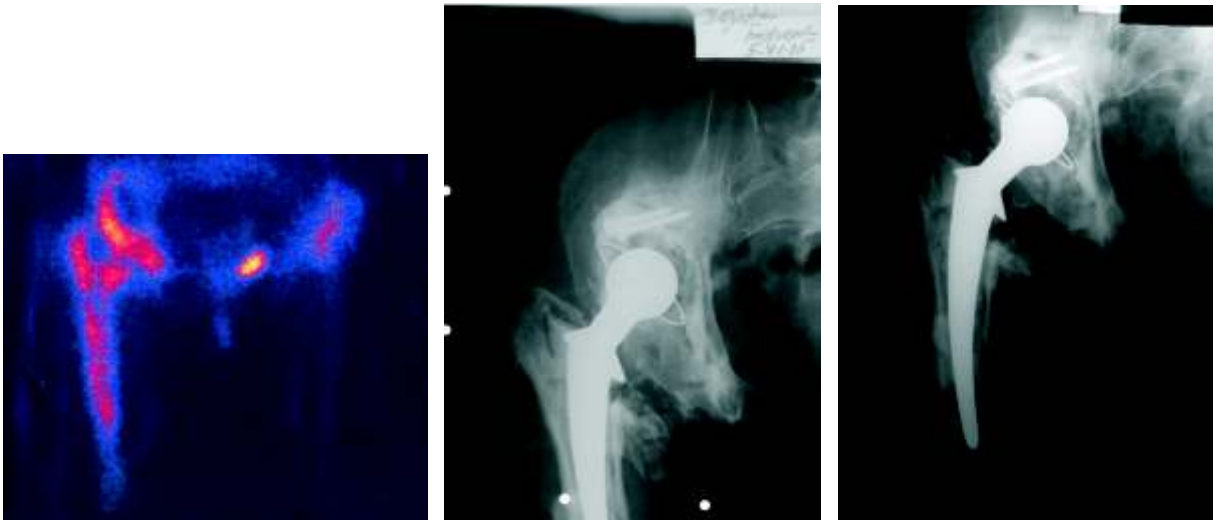

Figure 1. P.B, 57-year-old female 26 months after left total hip replacement. Infection was diagnosed by microbiological evaluation of a surgical specimen. Results of conventional radiography, bone scintigraphy, and ESR and CRP were true-positive. A) Bone scintigraphy. Increased radionuclide uptake. B), C) Conventional anteroposterior radiographs of the left hip show rapid development of osteolysis (arrows) at the bone-prosthesis and cement-bone interfaces. (B was obtained 6 months prior to C).

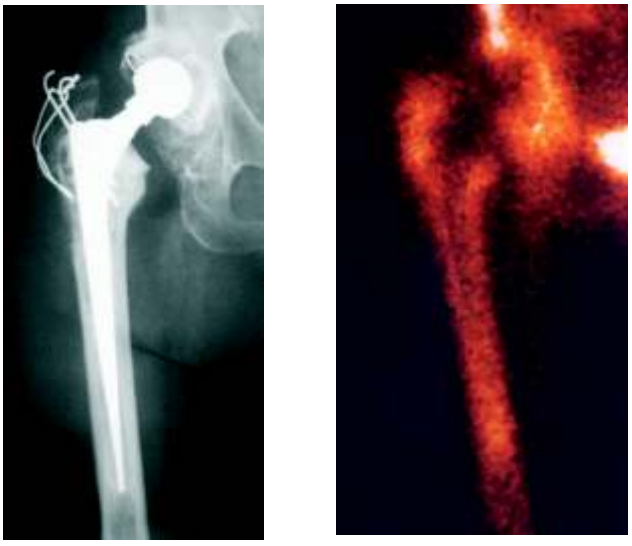

Figure 2. T.I., 67-year-old female 6 months after right revision total hip replacement with osteoplasty and cementing technique. Aseptic loosening of the cup. Result of conventional radiography was false-negative (A), whereas this of bone scintigraphy true-positive (B). ESR and CRP within normal range.

Table 2. Ability of different modalities to predict infection of hip arthroplasty.

	Sensitivity (%)	**Specificity** (%)	**Accuracy** (%)
Radiography	62.5	80.0	85.0
Scintigraphy	87.5	91.6	90.0
ESR	60.0	100.0	86.7
CSR	100.0	70.0	75.0

Discussion

Improvements in prosthetic materials and surgical techniques have led to marked decreases in the prevalence of infection and aseptic loosening in patients with hip replacements. Identifying the cause of loosening is important, as it will determine the extent of surgery required. In the presence of infection, implant removal and radical debridement of infected soft tissue and bone is often indicated. The use of bone grafts is controversial.

Radiographic diagnosis of infected hip arthroplasty versus aseptic loosening is difficult because there is considerable morphologic overlap between the two diagnoses. In aseptic loosening, wear debris (composed of polymethylmethacrylate, polyethylene, or metal) lead to macrophage activation, which in turn releases bone-resorbing products like interleukins and prostaglandin E2 [1]. This occurs in areas of progressive bone loss and granuloma formation, which may simulate abnormalities relating to infection. The course bone resorption takes in time, however, may serve as an important tool in differentiating an aseptic loosening from a septic one [11].

A negative bone scan suggested the absence of loosening. However, a positive result was regarded as controversial for the diagnosis of both aseptic and septic complications. Focally increased radionuclide uptake around the prosthesis is commonly considered to represent loosening, while diffusely increased uptake is commonly considered to represent infection [7]. However, infection may also be present in prostheses with focal uptake patterns [11].

We described a sensitivity of 87.5% and a specificity of 91.6% for bone scintigraphy in diagnosing infection. Itasaka et al. (2001) described a sensitivity of 83%, a specificity of 79%, and an accuracy of 79% [12]. Bone scintigraphy is of limited value in the diagnosis of loosening and infection in patients who present with it within 12 months after an arthroplasty procedure [13]. The inclusion of seven patients with less than one-year follow-up has probably had effects on our results.

Clinical examination, plain radiographs, and bone scintigraphy, as well as combined measurement of CRP, ESR can detect prosthetic loosening and differentiate between low-grade infection and mechanical instability. In Bulgarian literature, there are several studies on bone scintigraphy investigations of THA. Moreover, there are few publications discussing the value of laboratory findings in diagnosing loosening of hip arthroplasty. The results from current studies support the practice of intraoperative cultures, laboratory tests and bone scintigraphy in diagnosing infection of hip arthroplasty. Our study supports previous findings that bone scintigraphy as a method of diagnosing periprosthetic complications has a high sensitivity, and relatively good specificity and accuracy [7].

Our study has certain limitations. The prevalence of infection was low, and this was attributed to the specificity of the Clinic of Orthopedics and Traumatology and the relatively low rate of infection in prosthetic joint surgery. In addition, for obvious reasons, surgery with microbiological evaluation is normally not performed in all patients with a painful total joint replacement. Clinical follow-up sometimes has to be used for evaluation of possible hip infection, which was the case with twelve hips in our study.

Conclusion

Bone scintigraphy and laboratory tests are useful tools for detecting infection of total hip arthroplasty. Based on the results of our study, it may be concluded that ESR lacks sensitivity, but bone scintigraphy and CRP are accurate enough to predict a periprosthetic infection. However, only CRP can reliably exclude the absence of infection. In a situation in which bone scintigraphy, laboratory studies and clinical picture are equivocal, aspiration biopsy may be helpful in establishing periprosthetic infection.

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