## **Original Article**

# Screening with angiographic images prior to <sup>99m</sup>Tc-HMPAO labelled leukocyte scintigraphy in the diagnosis of periprosthetic infection<sup>\*</sup>



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#### ABSTRACT

*Aim:* To evaluate the impact of the angioscintigrapy of the three phase bone scan as screening method to rule out infection of the hip and knee prosthesis prior to performing the <sup>99m</sup>Tc-HMPAO leukocyte scintigraphy.

Material and methods: A total of 120 (70 women, 50 men; mean age  $71 \pm 11$  years) with clinical suspicion of hip (n = 63) or knee (n = 57) infection of the prosthesis and clinical suspicion of infection were evaluated prospectively. All patients underwent three-phase bone scan (angioscintigraphy, vascular and bone phase) and  $^{99\text{m}}\text{Tc-HMPAO-labeled}$  white blood cell scintigraphy. Final diagnosis of infection was made by microbiological documentation or clinical follow-up for at least 12 months.

Results: Eighteen out of 120 patients were diagnosed of infection of hip prosthesis (n = 10) or knee prosthesis (n = 8). The angioscintigraphy was positive in 15/18 infected cases and in 21/102 of the non-infected cases with a sensitivity of 83%, specificity of 79% and negative predictive value of 97%. Sensitivity and specificity of <sup>99m</sup>Tc-HMPAO leukocyte scintigraphy were 72% and 95%, respectively. If the leukocyte labeled scintigraphies had been used exclusively for patients with positive angioscintigraphy, this would have saved up to 70% of the <sup>99m</sup>Tc-HMPAO leukocyte scintigraphies performed. There were no cases of infection with positive labeled leukocyte scintigraphy and negative angioscintigraphy.

*Conclusion:* Angioscintigraphy (blood flow phase of bone scan) is a useful technique for screening for hip and knee joint prosthesis infection, significantly reducing the need for <sup>99m</sup>Tc-HMPAO leukocyte scintigraphy without affecting the sensitivity of the technique.

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# Cribado mediante angiogammagrafía previo a la realización de gammagrafía con leucocitos <sup>99m</sup>Tc-HMPAO en el diagnóstico de infección de prótesis articulares

RESUMEN

Objetivo: Analizar la utilidad de la fase angiogammagráfica de la gammagrafía ósea en 3 fases como posible método de cribado en el diagnóstico de infección de prótesis de cadera y de rodilla, previa a la realización de la gammagrafía con leucocitos marcados.

*Material y métodos:* Se analizaron prospectivamente 120 pacientes (70 mujeres y 50 hombres) con edad media de  $71 \pm 11$  años y sospecha clínica de infección de prótesis de cadera (n=63) o rodilla (n=57), a los que se realizó gammagrafía ósea en 3 fases (angiogammagrafía, fase vascular y fase ósea) y gammagrafía con leucocitos marcados con  $^{99}$ TC-HMPAO. El diagnóstico definitivo se realizó mediante estudio microbiológico o seguimiento clínico mínimo de 12 meses.

Resultados: Se estableció el diagnóstico de infección de la prótesis articular en 18/120 pacientes: 10 pacientes con prótesis de cadera y 8 pacientes con prótesis de rodilla. La angiogammagrafía fue positiva en 15/18 pacientes infectados y en 21/102 pacientes no infectados, mostrando una sensibilidad del 83%, una especificidad del 79% y un valor predictivo negativo del 97%. La gammagrafía con leucocitos marcados mostró una sensibilidad y una especificidad del 72 y del 95%, respectivamente. Si se realizara la gammagrafía con leucocitos marcados exclusivamente a los pacientes con angiogammagrafía positiva, se reduciría un 70% de gammagrafías con leucocitos practicadas. No hubo ningún caso de infección con gammagrafía con leucocitos marcados positiva y angiogammagrafía negativa.

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Conclusiones: La angiogammagrafía es una buena técnica de cribado de infección de prótesis articulares de cadera y rodilla, disminuyendo significativamente el número de gammagrafías con leucocitos marcados, sin afectar la sensibilidad de la técnica.

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#### Introduction

In developed countries the incidence of hip and knee arthroplasty has increased considerably in the last decade, especially as a result of population aging, biomedical technology and increased life expectancy in patients with chronic illness.<sup>1</sup> In the USA about 700,000 joint replacements are carried out on an annual basis.<sup>2</sup> In Spain it is estimated that up to 30,000 arthroplasty procedures are performed per year.<sup>1</sup>

Although prostheses increase the quality of life of patients, they may involve multiple complications, such as aseptic loosening or periprosthetic infection.<sup>3</sup> Infection is the most serious complication, with an incidence of 0.8–1.9% in knee replacements, and between 0.3% and 1.7% with hip arthroplasty.<sup>5</sup>

Patients with chronic diseases such as rheumatoid arthritis and diabetes, obese patients and patients with multiple previous surgical interventions are particularly affected by infection.<sup>6</sup> Up to about 70% of all prosthetic infections occur within the first 2 years of surgery,<sup>7</sup> the most common microorganisms being *Staphylococcus epidermidis* (31%) and *Staphylococcus aureus* (20%).<sup>8</sup>

A simple X-ray, the initial step for the evaluation of a painful prosthesis, is sufficient to identify the cause of pain in only 25% of cases. Therefore, in most patients other imaging methods to discern etiology are usually required. The presence of artifacts created by the metallic components of joint replacements limit the capabilities of CT and MRI scans. Arthrocentesis is an invasive technique and the results are frequently inconclusive, having a high false positive rate due to contamination and elevated false negative rate because of difficulties in obtaining a sufficient sample for diagnosis. Markers of inflammation such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have high sensitivity, but low specificity, and often cannot differentiate an aseptic loosening from an infection because levels may be elevated in both clinical situations.

Bone scintigraphy (BS) and scintigraphy with <sup>99m</sup>Tc-HMPAO labeled leukocytes (LS) are the most widely used imaging techniques in the study of joint replacements for the differential diagnosis between aseptic loosening and infection. The LS is highly sensitive and demonstrates specificity that can reach 80–100% when analyzed by an expert specialist or evaluated in conjunction <sup>99m</sup>Tc-colloid bone marrow scintigraphy which facilitates the differentiation between activation of bone marrow adjacent to the prosthesis from a true periprosthetic infection. <sup>11</sup>

It has been reported that the analysis of the three-phase BS has a high negative predictive value of 90–93% in detecting periprosthetic infection. <sup>12,13</sup> However, in most cases with aseptic loosening the blood pool phase and the bone phase in BS usually come up positive, so that the overall performance as a screening test is low. <sup>13</sup> So far the different phases of BS as a possible screening method for the diagnosis of infection of joint replacements have not been studied independently.

The aim of this paper is to analyze whether angiographic images may be useful as a screening method for the diagnosis of prosthetic joint infection, prior to LS.

### Material and methods

#### **Patients**

In this prospective study, 120 patients were studied consecutively (70 women and 50 men) with a mean age of  $71 \pm 11$  years,

with total hip (n=63) or knee (n=57) replacement. The average time since the replacement surgery was  $78\pm76$  months. The inclusion criterion was clinical suspicion of septic loosening of the prosthesis. ESR and CRP were determined, BS was performed in 3 phases and LS carried out in all patients. Normal values were 1-20 mm/h for ESR and 0-1 mg/dl for CRP. In patients undergoing replacement of the prosthesis, the definitive diagnosis was performed by sampling and subsequent microbiological analysis. In patients not undergoing surgery, infection was excluded from diagnosis when, during a clinical follow-up period of at least 12 months, in the absence of specific antibiotic treatment, no signs of active infection were found.

#### Microbiological analysis

An average of 8 periprosthetic samples were taken, if two or more samples were positive for the same organism results were considered positive for infection. Samples were collected by joint fluid aspiration, swab smears in standard culture medium and periprosthetic tissue biopsy.

#### Imaging techniques

In order to carry out the BS, an intravenous bolus injection 925 MBq of  $^{99m}\text{Tc-HMDP}$  was administered for study with the patient placed under the camera. The blood flow phase consisted of a dynamic study in anterior and posterior projection obtaining  $60\times1$  s images in word mode for 1 min with a  $128\times128$  matrix and at zoom 1. The detection field was focused on the prosthesis of study. Next, 2–4 min post-injection, 90 s static images were acquired without changing the position of the patient (blood pool phase). Finally, 2 h after injection, images were taken of the area of study in word mode for 300 s with a matrix of  $256\times256$  (bone phase).

For the LS autologous leukocytes were obtained from the patient for cell labeling with 185 MBq of <sup>99m</sup>Tc-HMPAO. Four hours after reinjection of the labeled leukocytes, 600 s images were taken in anterior and posterior projection for hip prostheses, and for knee replacements, from the anterior, posterior, and both lateral aspects.

#### Image interpretation

The evaluation of the BS and LS images was performed visually by 3 independent observers. Analyzing images of each phase (blood flow, blood pool and bone phase) of the BS independently, 2 categories (either positive or negative for periprosthetic infection) were considered. The GL was considered positive for infection when there was any extra-medullary periprosthetic uptake. If the three observers did not agree on the same result, either positive or negative for infection, the result coinciding with two observers was selected.

### Statistics

Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated using the standard methods. The variables were compared using the Student's t test for ESR and CRP and were considered to be statistically significant

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