



NUCLEAR MEDICINE IN THE DIAGNOSIS OF HIP PROSTHESIS INFECTIONS: A SYSTEMATIC REVIEW OF THE FUNCTIONAL APPROACH

MEDICINA NUCLEAR NO DIAGNÓSTICO DE INFECÇÕES EM PRÓTESES DE QUADRIL: UMA REVISÃO SISTEMÁTICA DA ABORDAGEM FUNCIONAL

MEDICINA NUCLEAR EN EL DIAGNÓSTICO DE INFECCIONES EN PRÓTESIS DE CADERA: UNA REVISIÓN SISTEMÁTICA DEL ENFOQUE FUNCIONAL



<https://doi.org/10.56238/edimpecto2025.060-025>

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ABSTRACT

Infections associated with hip prostheses represent one of the most challenging complications in orthopedics, requiring accurate and early diagnosis to ensure appropriate treatment and functional preservation. This study conducted a systematic literature review aimed at evaluating the available scientific evidence on the effectiveness of nuclear medicine methods in diagnosing these infections compared with conventional anatomical imaging. The search was carried out in the PubMed database in April 2025 using the descriptor “Nuclear medicine and arthroplasties.” Fifteen studies addressing the use of radiopharmaceuticals in hip prostheses were included. The results demonstrated that techniques such as technetium-99m (^{99m}Tc)-labeled leukocyte scintigraphy and ¹⁸F-FDG PET/CT show high sensitivity and specificity, allowing differentiation between active infection and aseptic inflammation. Furthermore, functional and metabolic imaging methods proved less susceptible to metallic artifacts compared to traditional anatomical modalities. It is concluded that nuclear medicine is an essential diagnostic tool for periprosthetic hip infections, contributing to safer and more accurate therapeutic decisions, although it still faces limitations related to technological availability and diagnostic protocol standardization.

Keywords: Orthopedics. Infections. Nuclear Medicine. Imaging Diagnosis. Hip Arthroplasty.

RESUMO

As infecções associadas a próteses de quadril representam uma das complicações mais desafiadoras no campo da ortopedia, exigindo diagnóstico preciso e precoce para garantir

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tratamento adequado e preservação funcional. Este estudo realizou uma revisão sistemática da literatura, com o objetivo de avaliar as evidências científicas disponíveis sobre a eficácia dos métodos de medicina nuclear no diagnóstico dessas infecções, em comparação com os exames anatômicos convencionais. A busca foi conduzida na base PubMed, em abril de 2025, utilizando o descritor “Nuclear medicine and arthroplasties”. Foram incluídos 15 artigos que abordavam diretamente o uso de radiofármacos em próteses de quadril. Os resultados demonstraram que técnicas como a cintilografia com leucócitos marcados com tecnécio-99m (^{99m}Tc) e o PET/CT com ^{18}F -FDG apresentam elevada sensibilidade e especificidade, permitindo distinguir infecção ativa de inflamação asséptica. Além disso, os métodos de imagem funcional e metabólica mostraram-se menos suscetíveis a artefatos metálicos em comparação às modalidades anatômicas tradicionais. Conclui-se que a medicina nuclear constitui uma ferramenta diagnóstica essencial no contexto das infecções periprotéticas do quadril, contribuindo para decisões terapêuticas mais seguras e assertivas, embora ainda enfrente limitações relacionadas à disponibilidade tecnológica e à padronização dos protocolos.

Palavras-chave: Ortopedia. Infecções. Medicina Nuclear. Diagnóstico por Imagem. Artroplastia de Quadril.

RESUMEN

Las infecciones asociadas a las prótesis de cadera representan una de las complicaciones más desafiantes en el campo de la ortopedia, lo que exige un diagnóstico preciso y temprano para garantizar un tratamiento adecuado y la preservación funcional. Este estudio realizó una revisión sistemática de la literatura con el objetivo de evaluar la evidencia científica disponible sobre la eficacia de los métodos de medicina nuclear en el diagnóstico de estas infecciones, en comparación con los exámenes anatómicos convencionales. La búsqueda se llevó a cabo en la base de datos PubMed en abril de 2025, utilizando el descriptor “Nuclear medicine and arthroplasties”. Se incluyeron quince estudios que abordaban el uso de radiofármacos en prótesis de cadera. Los resultados demostraron que técnicas como la gammagrafía con leucocitos marcados con tecnecio-99m (^{99m}Tc) y el PET/CT con ^{18}F -FDG presentan alta sensibilidad y especificidad, permitiendo distinguir entre infección activa e inflamación aséptica. Además, los métodos de imagen funcional y metabólica resultaron menos susceptibles a los artefactos metálicos en comparación con las modalidades anatómicas tradicionales. Se concluye que la medicina nuclear constituye una herramienta diagnóstica esencial en las infecciones periprotésicas de cadera, contribuyendo a decisiones terapéuticas más seguras y precisas, aunque aún enfrenta limitaciones relacionadas con la disponibilidad tecnológica y la estandarización de los protocolos diagnósticos.

Palabras clave: Ortopedia. Infecciones. Medicina Nuclear. Diagnóstico por Imagen. Artroplastia de Cadera.

1 INTRODUCTION

The development of joint prostheses represents one of the greatest advances in modern biomedical technology. The implantation of these devices, especially in joints such as the hip and knee, has become an increasingly frequent procedure, with approximately 150,000 hip arthroplasties estimated to be performed per year in the United States and about 400,000 worldwide. These interventions provide a significant reduction in discomfort in patients affected by diseases of the coxo-femoral joint and a substantial improvement in mobility, especially when not complicated by infectious processes (Lima; Barone, 2001).

Joint prostheses are a milestone in orthopedic medicine, offering effective solutions to debilitating joint pathologies. These devices have the main purpose of relieving pain, restoring functionality and, consequently, increasing the quality of life of patients (Ioshitake *et al.*, 2016 *apud* Marsura *et al.*, 2023). However, among the complications associated with the use of joint prostheses, loosening, whether septic or aseptic, remains the main clinical challenge. Periprosthetic infection, although less frequent than mechanical failures, has more serious consequences, including multiple surgeries, permanent loss of the implant, and even death, in addition to annual costs that can reach 80 million dollars in the United States alone (Lima; Barone, 2001).

Early and accurate diagnosis of these infections is essential for therapeutic success and functional preservation of the joint. However, traditional clinical and laboratory methods are not always able to distinguish sterile inflammatory processes from active infections, which makes the use of imaging tests an essential component in the diagnostic workup. In this context, nuclear medicine techniques have gained prominence for their ability to identify early pathophysiological changes, allowing the differentiation of septic from aseptic loosening and guiding more assertive therapeutic approaches.

Thus, this article aims to evaluate the available scientific evidence on the efficacy of nuclear medicine in the diagnosis of infections in hip prostheses, comparing its performance with conventional imaging methods used in clinical practice.

2 THEORETICAL FRAMEWORK

Several types of prostheses have been developed, adapted to specific joints, such as hip, knee, shoulder, elbow and ankle. The choice of the type and materials used, such as metal alloys (consisting of titanium and cobalt chromium), ultra-high molecular weight polyethylene (UHMWPE), and ceramics, should consider the anatomical particularities and individual needs of each patient (Marsura *et al.*, 2023).

The etiology of infections in arthroplasty is multifactorial, involving preoperative,

intraoperative, and postoperative factors. Among the risk factors related to the patient, previous revision surgeries, previous infections, smoking, obesity, rheumatoid arthritis, neoplasms, immunosuppression, and diabetes mellitus stand out. Surgical factors include simultaneous bilateral arthroplasties, prolonged operative time, and allogeneic transfusions. In the postoperative period, healing complications, urinary tract infection, and *Staphylococcus aureus* bacteremia are additional risk events (Del Pozo; Patel, 2009).

The microbiological identification of the infectious agent is essential for the direction of antimicrobial treatment. Staphylococci, especially *S. aureus* and coagulase-negative species, are responsible for more than half of prosthetic hip infections (Trampuz *et al.*, 2007). Factors such as advanced age, malnutrition, HIV infection, and a history of arthroplasty increase the vulnerability of patients (Lima; Oliveira, 2010).

Despite advances in understanding the pathogenesis of infections, their diagnosis still represents a considerable clinical challenge. This occurs since the manifestations are often nonspecific, for example, fever, pain, and malaise, and imaging tests are essential tools for diagnostic confirmation and localization of the infectious focus (Palestro *et al.*, 2013). In addition, the formation of bacterial biofilm on the prosthetic surface makes it difficult to eradicate the infection and often requires removal of the implant (Trampuz *et al.*, 2007; Bessa, 2021).

The advent of imaging tests has revolutionized medical diagnosis since the discovery of X-rays by Wilhelm Conrad Roentgen in 1895. Among the techniques used in arthroplasty, simple radiography, ultrasonography, and scintigraphic methods stand out. X-ray can reveal signs of loosening, such as lucencies at the cement-bone or metal-bone interfaces (Miller, 2011), while ultrasonography assists in detecting collections and guiding diagnostic punctures. However, nuclear medicine methods have greater sensitivity and specificity, especially when they employ leukocytes or labeled immunoglobulins (Del Pozo; Patel, 2009).

In addition, positron emission tomography (PET) with [¹⁸F]FDG and scintigraphy using technetium-99m (^{99m}Tc)-labeled radiopharmaceuticals are particularly promising. Such techniques exploit the high metabolic activity of inflammatory and infectious cells, allowing the differentiation of aseptic inflammation from active infections (Palestro *et al.*, 2013; Zoccali; Teori; Salducca, 2009). The ^{99m}Tc-leukocytes, in particular, has high sensitivity and specificity for identifying infectious foci, being useful even in cases of fever of undetermined origin (Corstens; Van der Meer, 2002).

3 METHODOLOGY

A systematic review of the literature was carried out, a method widely used in the

health area to identify, evaluate and synthesize scientific evidence on a specific topic, ensuring the selection of studies of high quality and clinical relevance (Galvão, 2014).

The review was guided by the question: "What is the available evidence on the efficacy of nuclear medicine in diagnosing infections in hip prostheses, compared to conventional imaging tests?". The guiding hypothesis considered that nuclear medicine offers relevant diagnostic advantages over traditional anatomical methods.

The search was performed in the PubMed database, on April 2, 2025, using the terms "Nuclear medicine and arthroplasties", with no area restrictions. A total of 853 studies were identified, of which 721 were published after 1994. After applying the inclusion and exclusion criteria—eliminating duplicates, paid studies, research conducted with animals, and articles focused on neoplasms—15 studies were selected because they directly addressed the use of nuclear medicine in the detection of infections in hip replacements.

Studies that addressed social aspects, non-infectious postoperative complications, or topics unrelated to clinical diagnosis were also excluded. During the writing of the present study, additional relevant publications were included to enrich the discussion and broaden the understanding of the clinical challenges related to the topic.

Table 1

Articles selected for review, following the criteria addressed

TITLE	AUTHORS / YEAR	RESULT
Appearance of septic prostheses Hip on plain radiographs.	S Tigges, R. G. Stiles and J. R. Roberson, (1994)	Although plain radiographs may present findings suggestive of infection in hip prostheses, their sensitivity is limited. Therefore, in cases of clinical suspicion of infection, it is recommended to use complementary tests, such as scintigraphy, computed tomography or magnetic resonance imaging, in addition to laboratory and microbiological evaluations, for a more accurate diagnosis.
Total Hip Replacement Imaging	Weissman BN, (1997)	It concludes that, although plain radiography is a valuable tool for the evaluation of total hip arthroplasties 1997 USA, it has limitations, especially in the detection of early complications, such as infections or early osteolysis. Complementary exams, such as tomography and magnetic resonance imaging, may be necessary for a more detailed evaluation.
Glucose transporters and insulin action – implications for insulin resistance and diabetes mellitus	Shepherd, P. R.; Kahn, B. B. (1999)	Dysfunction in glucose transport is central to insulin resistance and type 2 diabetes. Interventions that improve GLUT4 translocation can positively impact treatment and prevention.

The Role of Nuclear Medicine in Infection and Inflammation	Corstens, F. H.; Van Der Meer, J. W. (1999)	Nuclear medicine plays a key role in diagnosing infections and inflammation, especially when other methods do not provide sufficient information. Labeled leukocyte scintigraphy has high sensitivity.
The Role of Nuclear Medicine in Infection and Inflammation	Becker, W.; Meller, J. (2001)	Nuclear medicine is an essential tool in the diagnosis of complex infections. The introduction of hybrid technologies such as PET/CT has increased diagnostic accuracy.
Nosocomial infections in 46 patients undergoing total hip arthroplasty	Lima, A. L. L. M.; Barone, A. A. (2001)	Infections remain serious complications. Therapeutic success depends on early diagnosis, appropriate surgery, and effective antibiotic therapy.
Image of infection with radiopharmaceuticals in the twenty-first century	Das, S. S. <i>et al.</i> (2002)	Advances in the use of radiopharmaceuticals, such as antibiotics labeled with technetium-99m, increase diagnostic accuracy. The challenge is to develop more specific agents to differentiate between infection and inflammation.
Image of painful hip arthroplasty	Keogh, C. F. <i>et al.</i> (2003)	The choice of imaging method depends on clinical suspicion. Combining different techniques is essential to evaluate causes of pain in hip prostheses.
Sonication of Removed Hip and Knee Prostheses for Infection Diagnosis	Trampuz, A. <i>et al.</i> (2007)	Sonication of removed dentures is more effective than traditional tissue culture, with higher sensitivity (79%) and high specificity, even after previous use of antibiotics.
The role of FDG-PET in distinguishing between septic and aseptic loosening in hip prostheses	Zoccali, C.; Teori, G.; Salducca, N. (2009)	FDG-PET is promising in differentiating between septic and aseptic loosening, with good sensitivity and specificity, although there is a risk of false positives.
Infection associated with joint prostheses	Del Pozo, J. L.; Patel, R. (2009)	Prosthetic infections require careful diagnosis and combined treatment: prolonged antibiotics and specific surgical interventions (debridement or replacement of the prosthesis).
Update on infections in joint prostheses	Lima, A. L. L. M.; Oliveira, P. R. D. (2010)	Infections in prostheses require early diagnosis and appropriate treatment. Prevention is key, with rigorous perioperative care.
Hip arthroplasty imaging	Miller, T. T. (2012)	Reviews imaging methods (radiography, CT, MRI, and scintigraphy) to detect complications such as loosening and infection. X-ray is the most useful initial test.
Scintigraphy with (99m)Tc-labeled ubiquitin: a promising method for diagnosing infection in hip prosthesis	Aryana, K. <i>et al.</i> (2012)	The method showed 100% sensitivity, specificity, and accuracy in differentiating between infection and aseptic loosening, with rapid image acquisition.
Postoperative hip arthroplasty radiograph: what the radiologist should know	Vanrusselt, J. <i>et al.</i> (2015)	It proposes a systematic approach for postoperative radiographic evaluation, describing essential parameters and signs of complications such as infection and loosening.
Rehabilitation of patients undergoing total knee	Ioshitake, F. A. C. B. <i>et al.</i> (2016)	Physical therapy rehabilitation is essential after total arthroplasty, reduces complications and accelerates functional return.



arthroplasty: a literature review		
Medical Image Processing and Analysis	Marques da Silva, A. M.; Patrocínio, A. C.; Schiabel, H. (2019)	Medical image processing and analysis improve the detection and interpretation of anatomical structures, making diagnosis more accurate and efficient.

Source: Prepared by the authors (2025).

4 RESULTS

Tests based on the absorption of ionizing radiation-emitting radionuclides have a wide variety of diagnostic applications. In its implementation, the principle is used that the association of a radioactive emitter with an organic compound capable of being absorbed by the body allows directing the radiopharmaceutical to the area of interest to be investigated (Corstens; Van der Meer, 1999). An example of this is the use of labeled glucose molecules, used in the detection of infections due to the high consumption of glucose by cells in the affected regions (Zoccali *et al.*, 2009).

From this perspective, advances in nuclear medicine, supported by advances in medicine and physics, have proven to be fundamental in the detection of metabolic anomalies. Thus, they allow personalized approaches through specific radiopharmaceuticals, respecting the principles of dose limitation and using emitters with short physical half-lives (Del Pozo; Patel, 2009).

Thus, nuclear medicine exams stand out as highly effective tools for the detection of infectious pathologies in areas undergoing total hip arthroplasty (THA). Unlike conventional methods, such as magnetic resonance imaging, computed tomography, and radiography, these exams do not suffer significant interference from metallic artifacts. Studies by Censullo and Vijayan (2017) and Zoccali *et al.* (2009) demonstrate sensitivity and specificity values higher than 90% in nuclear medicine exams.

In this review, we identified 15 studies that addressed the use of nuclear medicine in the diagnosis of infections associated with hip replacements. The comparative analysis between the diagnostic modalities showed important differences in terms of sensitivity, specificity, and ability to differentiate between aseptic loosening and active infection.

Chart 2 presents a summary of the main imaging tests used for the detection of loosening or infection in hip prostheses, highlighting their main characteristics, advantages, and limitations.

Table 2

Most used exams for detection of hip prosthesis loosening

IMAGING TESTS	SENSITIVITY	SPECIFICITY	OBSERVATION
Radiography	Low	Average	Hit by artifacts.
Scintigraphy	Discharge	Discharge	Ideal for detecting acute inflammation.
63% approval	High (>90%)	High (>90%)	Detects active inflammatory processes.

Source: Prepared by the authors (2025).

Among the most indicated methods are bone scintigraphy with technetium-99m (99mTc)-labeled radiopharmaceuticals, such as 99mTc-MDP, and PET/CT with 18F-Sodium Fluoride (Raynor *et al.*, 2021; Koob *et al.*, 2019), both of which are able to identify early metabolic changes. The integration of the results of nuclear medicine exams with conventional imaging exams, added to the symptoms reported by the patient (Miller, 2012; Aryana *et al.*, 2012), contributes to a rapid and accurate diagnosis of periprosthetic infections.

Radiolabeled leukocyte scintigraphy, using technetium-99m (^{99m}Tc) or fluorine-18-labeled fluorodeoxyglucose (¹⁸F-FDG), is considered one of the most sensitive and specific methods for diagnosing infection in joint prostheses (Signore *et al.*, 2019). These radiopharmaceuticals allow the identification of active infectious processes through increased uptake in areas of inflammation, presenting a high negative predictive value. In a study conducted by Kim *et al.* (2014), the use of Single Photon Emission Computed Tomography associated with Computed Tomography (SPECT/CT) with ^{99m}Tc-HMPAO-labeled leukocytes demonstrated remarkable diagnostic performance, with sensitivity and specificity of 93.3%, positive predictive value of 94.3%, and negative predictive value of 92.1%, reinforcing its clinical utility in differentiating between infection and aseptic loosening of prostheses.

Thus, the findings of this review indicate that nuclear medicine represents a highly sensitive and specific tool in the detection of infections in hip prostheses, overcoming the limitations of traditional anatomical methods. Despite recognizing the technological bias inherent to the analysis, the study reinforces the importance of a complementary functional and metabolic approach in early diagnosis, contributing to safer and more accurate clinical decisions (Corstens; Van der Meer, 1999; Censullo; Vijayan, 2017).

5 DISCUSSION

During total hip arthroplasty (THA), screws are implanted to fix the acetabular component — the concave structure of the pelvis — and the femoral nail, responsible for connecting the femur to the pelvis and replacing the original joint. In some cases, such as trauma, a cerclage wire is used around the femur, in the region outside the shaft. This material

can also act as a potential infectious focus. Thus, any implanted component can be the point of origin of a periprosthetic infection.

Patients usually return to the surgeon with complaints of acute pain, fever, periprosthetic inflammation (joint effusion, edema, local heat, and hyperemia), as well as superficial disorders at the surgical site, such as persistent drainage, delayed healing, or localized wound dehiscence. These symptoms are often associated with joint stiffness and reduced range of motion (Gomes, 2019).

Although the loosening or displacement of the prosthesis can be detected by conventional tests, such as radiographs, these methods do not adequately identify infectious foci. Routine radiographs are ineffective as a baseline for longitudinal follow-up (Mulhall *et al.*, 2004 *apud* Vanrusselt *et al.*, 2015). According to Aryana *et al.* (2012), the sensitivity of radiographs is low in detecting anomalies, even in recent arthroplasties, with specificity ranging from 50% to 67%.

In addition, exams that use ionizing radiation, such as radiographs and CT scans, can generate artifacts due to the different attenuation coefficients of metallic materials (screws, rods and acetabular components), which compromises the quality of the result. Magnetic resonance imaging also suffers interference from these elements, as the magnetic field interacts with the metal, producing significant distortions in the image.

These limitations reinforce the relevance of nuclear medicine methods, capable of evaluating infectious processes in a functional and metabolic way, minimizing interference and contributing to more reliable and early diagnoses.

6 CONCLUSION

The analysis of the included studies shows that nuclear medicine is a diagnostic tool of great relevance in the detection of infections associated with hip prostheses. It is of considerable prominence for its ability to identify early metabolic and inflammatory changes, often before the anatomical manifestations visible in conventional imaging tests.

Traditional methods, such as radiography, ultrasonography, and computed tomography, continue to play an important role in structural evaluation and postoperative follow-up, but they have limitations in differentiating between infectious and non-infectious inflammatory processes. In this context, nuclear medicine techniques, especially those based on ^{99m}Tc radiolabeled leukocytes, demonstrate greater sensitivity and specificity, contributing significantly to early diagnosis and appropriate therapeutic conduction.

Despite its potential, the use of nuclear medicine still faces challenges related to the availability of resources, cost, and standardization of diagnostic protocols, which may restrict

its routine application in some health services. In view of this, it is recommended the development of prospective and comparative studies with greater methodological rigor, in order to consolidate the scientific evidence on the accuracy of the different methods of nuclear medicine and to strengthen it.

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