MUSCULOSKELETAL IMAGING

Iran J Radiol. 2015 January; 12(1): e11204. DOI: 10.5812/iranjradiol.11204

Published online 2015 January 12. **Research Article**

Metabolic Pattern of Asymptomatic Hip-Prosthesis by 18F-FDG-Positron-Emission-Tomography

Nermina Beslic [1]; Daniel Heber [2]; Rainer Walter Lipp [2]; Charlotte Sonneck-Koenne [3,*]; Peter Knoll [3]; Siroos Mirzaei [3]

[1]Department of Nuclear Medicine, Clinical Center University of Sarajevo, Bolnicka, Sarajevo, Bosnia and Herzegovina
[2]Department of Radiology, Medical University of Graz, Austria
[3]Department of Nuclear Medicine with PET-Center, Wilhelminenspital, Montleart straße 37, 1160 Vienna, Austria

*Corresponding author: Charlotte Sonneck-Koenne, Department of Nuclear Medicine with PET-Center, Wilhelminenspital, Montleart straße 37, 1160 Vienna, Austria. Tel: +43-1491503608, Fax: +43-1491503609, E-mail: charlotte.sonneck-koenne@wienkav.at

Received: August 12, 2013; **Revised:** November 20, 2013; **Accepted:** January 10, 2014

Background: Joint replacement is a procedure with a major impact on the quality of life of patients with joint degenerative disease or traumatic injuries. However, some patients develop symptoms after the intervention caused by mechanical loosening or infection. Metabolic imaging by 18F-FDG-PET investigated in these patients isoften hampered by low specificity for diagnosis of possible septic vs. mechanical loosening. The reason for this shortcoming is to our opinion the unawareness of physiological remodeling processes that could be seen in asymptomatic patients.

Objectives: In order to overcome this drawback, we aimed to find out the physiological metabolic functional pattern in asymptomatic patients with implanted hip prosthesis

Patients and Methods: Twelve patients (6 males, 6 females); mean age 73 ± 7 (range 58 - 91) years were prospectively enrolled in the study. The patients were admitted to our department for oncological referral with implanted hip prostheses. All patients explained no symptoms with regard to their implanted prosthesis. The attenuation corrected images were used for analysis.

Results: Fourteen hip prostheses in 12 patients were visually analyzed. Seven out of 14 prostheses among 12 patients showed focal periprosthetic enhanced metabolism, two of which showed two sites of enhanced uptake; whereas, the remaining five prostheses showed singular hypermetabolic areas within the periprosthetic site. The remaining seven prostheses in the other five patients showed no periprosthetic-enhanced uptake.

Conclusion: Of the asymptomatic patients investigated, 58% showed focal enhanced periprosthetic glucose metabolism. This finding should be taken into consideration as a more probable unspecific metabolic pattern for correct interpretation of 18F-FDG-PET studies in patients with suspected septic loosening of the hip prosthesis.

*Keywords:*18F- FDG; PET; Arthroplasty; Prosthesis Loosening; Prosthesis Infection

1. Background

For decades, joint replacement has been a procedure with major impact on the quality of life in elderly patients with joint degenerative diseases or traumatic injuries. Unfortunately, some patients develop symptoms after surgical intervention. In the majority of patients, aseptic loosening due to biochemical reaction of the bone causes chronic pain developed at the site of arthroplasty. The second most frequent reason for chronic pain is infection of the prosthesis. Both entities have a very similar clinical appearance, but require different therapeutic approaches due to different pathophysiological substrates (1). Lack of a single imaging modality that could clearly differentiate between infections and loosening makes this problem a challenge in the routine workup of these patients.

There are multiple diagnostic tests used to distinguish between loosening and infection. Laboratory analysis, including white blood cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are not specific enough. Canner et al. found that out of fifty-two patients who had an infection following joint arthroplasty, only eight (15%) had leukocytosis (2). The ESR may remain elevated for months after an uncomplicated total hip replacement (3). CRP levels increase in a non-specific manner as a result of infectious, inflammatory or neoplastic disorders.

Conventional imaging methods are helpful in some situations when complications arise (4, 5), but their diagnostic potential in distinguishing loosening and inflammation are limited. CT is superior to radiography in imaging soft tissue abscesses (6); however, not a recommended diagnostic tool due to significant artifacts on the images at the location of the prosthesis that hamper the optimal interpretation of the results. Thus, non-attenuation-corrected images must be interpreted to avoid false-positive results if PET/CT is used for the evaluation of painful prosthesis (7). Aspiration biopsy of the joint was regarded as a gold standard, but it is not convenient for the patient and may not always be helpful in distinguishing the two above-mentioned pathological entities. A positive result can confirm infection, but a negative result cannot exclude it (8).

Nuclear medicine modalities offer several diagnostic methods that are dedicated to the diagnosis of infection and are not affected by orthopedic implants. Three-phase bone scintigraphy (TPBS) is widely accepted for the diagnosis of different pathological processes of the musculoskeletal system including detection of infection with a high sensitivity and limited specificity in the diagnosis of infected joint prostheses (9). It is noticeable that reported results of different studies dealing with the problem of painful joint prosthesis show variation, which is mostly due to different interpretation criteria applied (10, 11). TPBS, with an accuracy of about 50-70% can be performed as the modality of primary choice in these patients, but it should be combined with other diagnostic modalities (12).

White blood cell (WBC) scintigraphy labeled with 99mTc HMPAO or 111In-oxine or anti-granulocyte scintigraphy using 99mTc-labeled monoclonal antibodies (MoAb) or their fragments are frequently used nuclear medicine imaging modalities in the detection of infection and inflammation, but it is important to emphasize that neither of these imaging methods can reliably differentiate sterile inflammation from infection (13). Significant decrease in the accuracy of WBC imaging is caused by the fact that labeled leukocytes are accumulating both in infected tissue and in bone marrow (10). A combined study consisting of WBC imaging and complementary bone marrow (BM) imaging performed with radiolabeled sulphur colloid is based on the fact that both radiopharmaceuticals accumulate in marrow; whereas, WBCs accumulate in infection, but sulfur colloid does not. Although the combination of these two modalities increases the accuracy in the diagnosis of osteomyelitis up to 90%, pitfalls that could affect the results are not negligible (14).

18F-FDG-PET is a promising imaging modality for the evaluation of a variety of infectious and inflammatory processes (15). In addition, there are reports indicating that in the evaluation of inflammation or infection, 18F-FDG-PET is even more accurate than conventional nuclear medicine procedures (16). These features of 18F-FDG-PET diagnostic modalities encouraged many professionals to perform research on its applicability in patients with painful prostheses. However, the results of the studies dealing with the role of 18F-FDG-PET are so far rather inconclusive and need to be more clearly defined (12). According to Chacko et al., the intensity of uptake is not useful for separating the infected from the aseptically loosened device (17). The periprosthetic glucose metabolism could also be enhanced to certain degrees in normal cases, which have been addressed in another study (18), and could hamper the interpretation of the examination. The reason for this shortcoming is to our opinion the unawareness of physiological remodelling processes that could be seen in asymptomatic patients. The aim of this study was to demonstrate this "physiological" pattern and discuss the findings in the literature.

2. Objectives

In the present study, we aim to delineate different metabolic patterns in asymptomatic patients with hip prostheses and to improve the specificity of 18F-FDG-PET in patients with suspected septic loosening of hip prosthesis.

3. Patients and Methods

Twelve patients, (6 males, 6 females); mean age, 73 ± 7 (range, 58-91) years were enrolled prospectively into the study. The patients were admitted to our department for oncological referral with implanted hip prostheses. None of the patients expressed any symptoms in regard to their implanted prosthesis and none of them had hematological malignancies or any metabolic bone manifestation of the primary tumor. All patients gave their written consent. The PET studies were performed on a full ring PET-scanner (Siemens EXACT, Knoxville, USA) as described in earlier studies (19). The attenuation corrected images were analyzed visually in regard to the metabolic periprosthetic pattern.

4. Results

Fourteen hip prosthesis in 12 patients were visually analyzed. The results are summarized in Table 1. With findings

Table 1. Patient Characteristics [a]

Patient No.	Sex	Age, y	Prosthesis Side (L/R)	Time Since Implantation, y	Sites of Pathological Uptake
1	m	79	R	2	--
1	m	79	L	2	N
2	m	68	L	6	--
3	f	64	L	7	N
4	m	70	R	5	N
5	f	76	L	11	N, T
6	m	78	R	9	--
7	f	91	R	7	--
8	m	80	R	5	--
9	f	69	R	3	N
10	f	82	R	2	T, N
11	f	67	R	5	N
11	f	67	L	4	--
12	m	58	R	5	--

[a] T = trochanter, N = neck, m = male, f = female, L = left, R = right

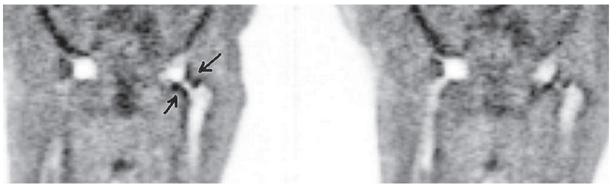

Figure 1. 18F-FDG-PET in patient number 1 (male, 79 years) with an asymptomatic 2-year history of bilateral hip prosthesis shows enhanced uptake in the left neck region (arrows).

related to periprosthetic enhanced uptake, Figure 1 demonstrates a case of a patient with asymptomatic hip prosthesis on both sides with enhanced uptake in the left neck region.

5. Discussion

One of the largest samples of patients with hip prosthesis examined with 18F-FDG-PET was reported by Reinartz and colleagues who compared PET with TPBS. The authors concluded that 18F-FDG-PET is a highly accurate diagnostic procedure to differentiate reliably between aseptic loosening and periprosthetic infection (18). They described, by a qualitative analysis, the different patterns of periprosthetic 18F-FDG uptake in different conditions, from normal to septic loosening 6 months after arthroplasty. Similar approaches have been done using 18F-Fluoride-PET (20).

18F-FDG-PET has great potential in detecting the infection, but in cases of increased aseptic loosening, periprosthetic uptake of 18F-FDG could be caused by wear-induced polyethylene particles and the subsequent growth of aggressive granulomatous tissue (16). Non-infectious inflammatory reactions around the neck of the prosthesis are common findings months or even years after surgery and they should not be interpreted as a finding suggestive of infection (21).

Application of SUV (standard uptake value) as a semi-quantitative parameter is usually a very important tool in the interpretation of oncological PET images, but it cannot be applied as a reliable criterion in inflammatory pathology due to low specificity, particularly not as a single criterion (10). Knowing the limitations of 18F-FDG-PET alone and taking into account the mechanism of its uptake in malignant tissues, leukocytes were labeled with 18F-FDG in order to increase its affinity to the inflamed tissue. Although the first results were promising, it was found that 18F-FDG was rapidly released from the leukocytes. Apart from that, these radiopharmaceuticals had other methodological disadvantages (22).

It has been suggested that the amount of increased 18F-FDG uptake is less important than the location of increased 18F-FDG uptake when this technique is used to diagnose periprosthetic infection in patients who had undergone prior hip arthroplasty (16). Uptake pattern seems to be of essential importance in the diagnosis of infection and is defined as very suggestive of infection if the 18F-FDG uptake between the bone and prosthesis at the level of the midshaft portion of the prosthesis is present (23, 24). This suggests that more standardized criteria for the interpretation of the 18F-FDG scan for the diagnosis of infection on the prosthesis placement should be defined and applied in practice.

Depending on the type of prosthesis and on other factors, hip prosthesis can show different metabolic patterns. Keeping in mind different metabolic patterns of periprosthetic 18F-FDG uptake in different conditions and the reliability of periprosthetic SUV-measurement with the new PET/CT devices, it seems to be of the utmost importance to find visual criteria that could be applied in these cases (18). In this study, we could demonstrate (Table 1) this pattern of hypermetabolic areas that could be defined more likely as normal and not caused by septic or aseptic loosening only on the neck and/or trochanteric area. Two patients who showed enhanced periprosthetic uptake in two regions, had a history of re-implantation in one case and a period longer than 10 years after the surgery in the second case. Interestingly, we could not observe focal enhanced glucose metabolism in the stem or tip region in any patient.

These findings are also of importance to rule out a suspected infection, as it was shown in a recent study where FDG-PET had a sensitivity of 100% and a negative predictive value of 100% (25). The study is limited by the fact that the patients could not provide information regarding the type of prosthesis, particularly whether they were cemented or not. No patient had a leukocytosis, but 8/12 patients--with or without periprosthetic-enhanced uptake--had an elevated CRP. Since they were all referred for oncological reasons, data was not taken into consideration.

The results of this study demonstrate a non-specific pattern of enhanced 18F-FDG-uptake in asymptomatic patients in the neck or trochanteric region after arthroplasty, which should be taken into consideration for correct interpretation of metabolic studies in patients with suspected septic loosening of the hip prosthesis.

Authors' Contributions

Study concept and design: Beslic, Mirzaei, and Heber; analysis and interpretation: Beslic, Heber, Knoll, and Soonneck-Koenne; critical revision of the manuscript for important intellectual content: Lipp, Sonneck-Koenne, Mirazei, and Heber; statistical analysis: Knoll

Financial Disclosure

Dr. Mirzaei and Dr. Knoll reported receiving EU grant (FP7). Dr. Mirzaei reported receiving honoraria from Merck and Novartis. Dr. Beslic, Dr. Heber, Dr. Lipp and Dr. Sonneck-Koenne have no relevant financial interests related to the material in the manuscript or otherwise.

References

1. Furnes O, Lie SA, Espehaug B, Vollset SE, Engesaeter LB, Havelin

LI. Hip disease and the prognosis of total hip replacements. A review of 53,698 primary total hip replacements reported to the Norwegian Arthroplasty Register 1987-99. *J Bone Joint Surg Br.* 2001;**83**(4):579–86.
2. Canner GC, Steinberg ME, Heppenstall RB, Balderston R. The infected hip after total hip arthroplasty. *J Bone Joint Surg Am.* 1984;**66**(9):1393–9.
3. Shih LY, Wu JJ, Yang DJ. Erythrocyte sedimentation rate and C-reactive protein values in patients with total hip arthroplasty. *Clin Orthop Relat Res.* 1987(225):238–46.
4. Weissman B, Sledge CB. *Orthopedic Radiology.*Philadelphia: Saunders; 1986.
5. Einsiedel T, Gebhard F, Bregolato I, Hiemeier A, Kinzl L, Schultheiss M. Proximal cement fixation in total hip arthroplasty--first results with a new stem design. *Int Orthop.* 2008;**32**(3):295–306.
6. Halpern BS, Dahlbom M, Waldherr C, Yap CS, Schiepers C, Silverman DH, et al. Cardiac pacemakers and central venous lines can induce focal artifacts on CT-corrected PET images. *J Nucl Med.* 2004;**45**(2):290–3.
7. Buckwalter KA, Parr JA, Choplin RH, Capello WN. Multichannel CT Imaging of Orthopedic Hardware and Implants. *Semin Musculoskelet Radiol.* 2006;**10**(1):86–97.
8. Fehring TK, Cohen B. Aspiration as a guide to sepsis in revision total hip arthroplasty. *J Arthroplasty.* 1996;**11**(5):543–7.
9. Segura AB, Munoz A, Brulles YR, Hernandez Hermoso JA, Diaz MC, Bajen Lazaro MT, et al. What is the role of bone scintigraphy in the diagnosis of infected joint prostheses? *Nucl Med Commun.* 2004;**25**(5):527–32.
10. Reinartz P. FDG-PET in patients with painful hip and knee arthroplasty: technical breakthrough or just more of the same. *Q J Nucl Med Mol Imaging.* 2009;**53**(1):41–50.
11. van der Bruggen W, Bleeker-Rovers CP, Boerman OC, Gotthardt M, Oyen WJ. PET and SPECT in osteomyelitis and prosthetic bone and joint infections: a systematic review. *Semin Nucl Med.* 2010;**40**(1):3–15.
12. Love C, Marwin SE, Palestro CJ. Nuclear medicine and the infected joint replacement. *Semin Nucl Med.* 2009;**39**(1):66–78.
13. Ruf J, Oeser C, Amthauer H. Clinical role of anti-granulocyte MoAb versus radiolabeled white blood cells. *Q J Nucl Med Mol Imaging.* 2010;**54**(6):599–616.
14. Palestro CJ, Love C, Tronco GG, Tomas MB, Rini JN. Combined labeled leukocyte and technetium 99m sulfur colloid bone marrow imaging for diagnosing musculoskeletal infection. *Radiographics.* 2006;**26**(3):859–70.
15. Zhuang H, Yu JQ, Alavi A. Applications of fluorodeoxyglucose-PET imaging in the detection of infection and inflammation and other benign disorders. *Radiol Clin North Am.* 2005;**43**(1):121–34.
16. Chacko TK, Zhuang H, Nakhoda KZ, Moussavian B, Alavi A. Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. *Nucl Med Commun.* 2003;**24**(6):615–24.
17. Chacko TK, Zhuang H, Stevenson K, Moussavian B, Alavi A. The importance of the location of fluorodeoxyglucose uptake in periprosthetic infection in painful hip prostheses. *Nucl Med Commun.* 2002;**23**(9):851–5.
18. Reinartz P, Mumme T, Hermanns B, Cremerius U, Wirtz DC, Schaefer WM, et al. Radionuclide imaging of the painful hip arthroplasty: positron-emission tomography versus triple-phase bone scanning. *J Bone Joint Surg Br.* 2005;**87**(4):465–70.
19. Ahmadzadehfar H, Rodrigues M, Zakavi R, Knoll P, Mirzaei S. Prognostic significance of the standardized uptake value of pre-therapeutic (18)F-FDG PET in patients with malignant lymphoma. *Med Oncol.* 2011;**28**(4):1570–6.
20. Kobayashi N, Inaba Y, Choe H, Ike H, Fujimaki H, Tezuka T, et al. Use of F-18 fluoride PET to differentiate septic from aseptic loosening in total hip arthroplasty patients. *Clin Nucl Med.* 2011;**36**(11):e156–61.
21. Kumar R, Basu S, Torigian D, Anand V, Zhuang H, Alavi A. Role of modern imaging techniques for diagnosis of infection in the era of 18F-fluorodeoxyglucose positron emission tomography. *Clin Microbiol Rev.* 2008;**21**(1):209–24.
22. Palestro CJ. In vivo leukocyte labeling: the quest continues. *J Nucl Med.* 2007;**48**(3):332–4.
23. Zhuang H, Chacko TK, Hickeson M, Stevenson K, Feng Q, Ponzo F, et al. Persistent non-specific FDG uptake on PET imaging following hip arthroplasty. *Eur J Nucl Med Mol Imaging.* 2002;**29**(10):1328–33.
24. Zhuang H, Yang H, Alavi A. Critical role of 18F-labeled fluorodeoxyglucose PET in the management of patients with arthroplasty. *Radiol Clin North Am.* 2007;**45**(4):711–8.
25. Chen SH, Ho KC, Hsieh PH, Lee MS, Yen TC. Potential clinical role of 18F FDG-PET/CT in detecting hip prosthesis infection: a study in patients undergoing two-stage revision arthroplasty with an interim spacer. *Q J Nucl Med Mol Imaging.* 2010;**54**(4):429–35.