Rev Esp Med Nucl Imagen Mol. 2018;37(3):163–171

Special collaboration

Cardiac ^{18}F-FDG PET/CT procedure for the diagnosis of prosthetic endocarditis and intracardiac devices☆

S. Aguadé Bruix[a,e,f,*], A. Roque Pérez[b,d,f], H. Cuéllar Calabria[b,d,f], M.N. Pizzi[c,e,f]

[a] Servicio de Medicina Nuclear, Hospital Universitari Vall d'Hebron, Barcelona, Spain
[b] Servicio de Radiología, Hospital Universitari Vall d'Hebron, Barcelona, Spain
[c] Servicio de Cardiología, Hospital Universitari Vall d'Hebron, Barcelona, Spain
[d] IDI: Institut de Diagnòstic per la Imatge, Barcelona, Spain
[e] VHIR: Vall d'Hebron Institut de Recerca, Barcelona, Spain
[f] Universitat Autònoma de Barcelona, Barcelona, Spain

ARTICLE INFO

Article history:
Received 11 January 2018
Accepted 23 January 2018
Available online 5 April 2018

Keywords:
PET/CT
^{18}F-FDG
Infective endocarditis
Prosthetic valves
Intracardiac devices
Myocardial suppression uptake

ABSTRACT

Infective endocarditis (IE) is a serious condition with a poor prognosis, its mortality unchanged significantly despite diagnostic and therapeutic advances in the last 30 years. The diagnostic ability of the modified Duke criteria in prosthetic endocarditis and/or devices does not exceed 50%, so new tools are necessary for the diagnosis of this entity in this context. The ^{18}F-FDG PET/CTA combines a highly sensitive technique to detect inflammatory-infectious activity with a technique with high anatomical resolution to assess the structural lesions associated with endocarditis. With a diagnostic sensitivity between 91% and 97%, this hybrid technique has become a useful diagnostic tool for patients with prosthetic valves or devices and suspicion of IE, becoming a major criterion in the diagnostic algorithm of current guidelines. This excellent diagnostic capacity ability depends directly on the quality of the obtained exploration and the knowledge at the time of interpreting the images.

The aim of this review is to describe and standardize the methodology of cardiac ^{18}F-FDG PET/CTA in the diagnosis of endocarditis in prosthetic valves and intracardiac devices, with special emphasis on the particularities of the patient's preparation, the PET and CT acquisition procedures, and the subsequent imaging postprocessing and interpretation.

Metodología de la PET/TC con ^{18}F-FDG cardíaca para el diagnóstico de la endocarditis protésica y de dispositivos intracardíacos

Palabras clave:
PET/TC
^{18}F-FDG
Endocarditis infecciosa
Válvulas protésicas
Dispositivos intracardíacos
Frenación miocárdica

RESUMEN

La endocarditis infecciosa (EI) es una patología grave y con mal pronóstico cuya mortalidad no se ha modificado significativamente a pesar de los avances en su diagnóstico y tratamiento en los últimos 30 años. La capacidad diagnóstica de los criterios de Duke modificados en la endocarditis protésica y/o de dispositivos no supera el 50%, por lo que se hacen necesarias nuevas herramientas para el diagnóstico de esta entidad en dicho contexto. La ^{18}F-FDG PET/aTC combina una técnica con gran sensibilidad para detectar actividad inflamatoria-infecciosa y una técnica con gran resolución anatómica para valorar las lesiones estructurales asociadas a la endocarditis. Con una sensibilidad diagnóstica entre el 91 y el 97%, esta técnica híbrida se ha convertido en una herramienta de diagnóstico útil en la sospecha de EI de pacientes con válvulas protésicas o dispositivos, convirtiéndose en un criterio mayor en el algoritmo diagnóstico de las guías actuales. Esta excelente capacidad diagnóstica depende de forma directa de la calidad de la exploración obtenida y del conocimiento a la hora de interpretar las imágenes.

El objetivo de esta revisión es describir y estandarizar la metodología de la ^{18}F-FDG-PET/aTC cardíaca en el diagnóstico de endocarditis protésica y de dispositivos intracardíacos, haciendo especial énfasis en las particularidades de la preparación del paciente, de la adquisición de los estudios PET y TC, y del posterior posprocesado e interpretación de las imágenes.

☆ Please cite this article as: Aguadé Bruix S, Roque Pérez A, Cuéllar Calabria H, Pizzi MN. Metodología de la PET/TC con ^{18}F-FDG cardíaca para el diagnóstico de la endocarditis protésica y de dispositivos intracardíacos. Rev Esp Med Nucl Imagen Mol. 2018;37:163–171.

* Corresponding author.
E-mail address: saguade@vhebron.net (S. Aguadé Bruix).

Introduction

Infectious endocarditis (IE) is a severe disease with a poor prognosis. In addition, the mortality rate has not changed significantly over time despite advances in diagnosis and treatment in the last 30 years.[1] Around 20% of patients with IE have prosthetic heart valves and/or intracardiac devices which are a predisposing factor for the development of infection, making these patients a special population group with a different epidemiological profile and higher mortality. Although the diagnostic ability of the modified Duke criteria is acceptable for the global diagnosis of endocarditis, the diagnostic sensitivity of these critiera in patients with prosthesis and/or intracardiac devices is less than 50%. Therefore, new tools are needed for the diagnosis of IE in this setting.

Positron emission tomography plus computerized tomography (PET/CT) with ^{18}F-fluorodeoxyglucose (FDG) combines the great sensitivity of PET for detecting inflammatory-infectious activity with CT, which has great anatomical resolution for the evaluation of structural lesions associated with endocarditis, especially if the latter is cardiac angiotomography (aCT). The diagnostic sensitivity of PET combined with aCT (PET/aCT) ranges from 91 to 97%, with its main indication being high clinical suspicion of IE due to possible rejection of a prosthetic valve according to the modified Duke criteria.[2,3] The European guidelines for the management of IE have included the results of both PET/CT and aCT alone as major diagnostic criteria for prosthetic IE since 2015.[4]

Although clinical practice guidelines still do not strongly recommend PET/CT in the case of device infection, there is acceptable evidence of its utility.[3] The diagnostic sensitivity of PET/aCT is practically 100% for the diagnosis of infection of the generator and/or extravascular indwelling leads, while it is more limited for evaluating the intravascular and/or intracardiac route of the electrodes.[3]

Cardiac PET/CT studies should not be considered as a reduced version of an oncologic PET/CT study. The diagnostic capacity of these studies largely depends on the quality of the procedure taking into account that it requires the study of structures in movement such as the cardiac structures and the need to achieve adequate anatomical resolution. These aspects carry a series of particularities related to patient preparation and image acquisition (in both PET and CT/aCT), the use of intravenous contrast and the processing and presentation of the studies, all aiming to improve the visualization of the cardiac structures and facilitate the correct interpretation of the images obtained. These considerations are essential since an inadequate acquisition technique may lead to difficulties in study interpretation and diagnostic errors. However, to date, there is no standardized method to perform cardiac PET/CT for the diagnosis of prosthetic and/or intracardiac device endocarditis.

Background

Images of glucidic metabolism obtained with PET/CT are based on ^{18}F-FDG. After intravenous introduction of this radiotracer into body, it enters cells by diffusion facilitated by glucose-specific transporter proteins (GLUT). Within the cells ^{18}F-FDG is phosphorylated by hexokinase and glucokinase enzymes converting into ^{18}F-FDG-6-phosphate. Reversion of the phosphorylation reaction is catalyzed by the glucose-6-phosphatase enzyme which, in turn, is inhibited by insulin. Once phosphorylated, deoxyglucose remains trapped inside the cells for a time inversely proportional to the concentration of glucose-6-phosphate and clearly greater than the semidecay period of ^{18}F since it cannot follow the metabolic pathways of glucose (catabolic: glucolytic pathway or anabolic: glucogenogenesis) due to this deoxygenation.[5]

Metabolism of the myocardium

Of all the cells in the organism the cardiomyocytes have a special metabolism which is adapted to their high energy requirements. The heart is an aerobic organ which requires a continuous supply of oxygen and metabolic substrates to correctly maintain its function. In normal physiological conditions (adequate oxygen and substrate supply), the heart produces adenosine triphosphate (ATP) from the beta oxidation of fatty acids. However, it can rapidly change energy substrates according to changes in arterial oxygen concentrations, energy substrates and certain neurohormonal factors.

When there are elevated fatty acid levels and low insulin levels, the myocardium only metabolizes small quantities of glucose. Nonetheless, after a glucose overload such as that occuring in the post-prandial period or during the administration of glucose solutions, the heart adjusts its metabolic values and uses glucose as the primary source of energy. This adjustment is mainly mediated by insulin and its antilipolytic effects since insulin receptors are increased, producing an overexpression of specific GLUT-4 transporters of the muscle cells (including the cardiomyocytes).[6]

To the contrary, during periods of prolonged fasting the glucose levels fall, with an important reduction in the activity of insulin receptors together with GLUT-4 transporters (dependent on insulin). In this setting, myocardial cells use fatty acids as the first metabolic substrate.

Metabolism of inflammatory cells

Inflammatory cells take up ^{18}F-FDG due to the elevated rate of glycolysis and overexpression of the number of GLUT-1 and GLUT-3 glucose membrane transporters independently of insulin stimulation. Numerous cytokines and growth factors act on these inflammatory cells (mainly macrophages and leucocytes) transforming them into activated cells, and this activation provokes an increase in the expression and affinity of glucose transporters leading to a greater production of glycolytic enzymes such as hexokinase. In turn, this produces an increase in the uptake of ^{18}F-FDG proportional to the grade of cellular activation in the inflammed tissues, being greater according to the number of neutrophils and macrophages.[7] However, this increase is also potentiated by hyperemia and an increase in tissue diffusion in the inflammed tissues.

Patient preparation

The first difficulty encountered in studies aimed at evaluating inflammation/infection of cardiac structures is the suppression of basal physiologic glucidic metabolism of the myocardium present in many subjects which translates into elevated myocardial uptake of ^{18}F-FDG. This physiological uptake of the myocardium interferes with visualization of the cardiac structures and hinders corre ct interpretation of the images, potentially masking pathological uptakes, or to the contrary, leading to erroneous interpretation of zones of physiological uptake as pathological uptake. This is the main reason for the need to suppress the physiological use of ^{18}F-FDG by the myocardium with adequate patient preparation prior to the PET/CT study.

Taking into account the presence of an independent mechanism of glucose incorporation for cardiomyocytes (GLUT-4) and for inflammatory cells (GLUT-1 and GLUT-3), the myocardial uptake of ^{18}F-FDG can be blocked without affecting the uptake of the inflammatory cells. To do this different combined actions must be performed with the objective of suppressing the physiological uptake of cardiomyocytes prior to the administration of ^{18}F-FDG.