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Original article

^{18}F-FDG PET/contrast enhanced CT in the standard follow-up of patients with lymphoma

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ABSTRACT

Aim: To assess the diagnostic accuracy of ^{18}F-FDG PET/contrast enhanced computed tomography (ceCT) in the detection of asymptomatic recurrences in patients with lymphoma.

Material and methods: Patients with lymphoma and clinical complete remission underwent ^{18}F-FDG PET/ceCT for standard follow-up.^{18}F-FDG PET and ceCT were evaluated blindly by two independent observers, and classified as positive or negative for recurrence. Additionally a combined evaluation of both techniques was performed.

The final diagnosis was established by histopathological analysis or a clinical follow-up longer than 6 months.

Statistical diagnostic parameters and concordance levels between both diagnostic techniques were calculated.

Results: A total of 114 explorations on 90 patients were analyzed. Only 4 patients were diagnosed as asymptomatic recurrence during the follow-up.

^{18}F-FDG PET/ceCT, ^{18}F-FDG PET and ceCT showed an association with the final diagnosis ($p = .002$ and $\chi^2 = 11.96$; $p < .001$ and $\chi^2 = 15.60$; $p = .001$ and $\chi^2 = 11.96$, respectively). The concordance between ^{18}F-FDG PET and ceCT was moderate/high and significant (Kappa = 0.672; $p < .001$).

A sensitivity and specificity of 50% and 88% was obtained for the ^{18}F-FDG PET/ceCT civ, 50% and 93% for the ^{18}F-FDG PET, and 50% and 91% for the ceCT.

Conclusion: The combined use of ^{18}F-FDG PET/ceCT did not offer any advantage compared to any isolated diagnostic technique in the detection of asymptomatic lymphoma recurrence.

^{18}F-FDG PET/TC con contraste intravenoso en el seguimiento estandarizado de pacientes con linfoma

Palabras clave:
Linfoma
^{18}F-FDG PET/TC con contraste intravenoso
Seguimiento estándar
Recidiva asintomática

RESUMEN

Objetivo: Valorar la capacidad diagnóstica de la ^{18}F-FDG PET/TC con contraste intravenoso (PET/TCciv) en la detección de recidivas asintomáticas de pacientes con linfoma.

Material y métodos: Se realizó una PET/TCciv en pacientes con linfoma para seguimiento estandarizado y en remisión completa clínica. Tanto la ^{18}F-FDG PET como la TCciv fueron evaluadas de forma independiente por 2 observadores y clasificadas como positiva o negativa para recurrencia. Adicionalmente se realizó una valoración combinada de ambas exploraciones.

El diagnóstico final se estableció por análisis histopatológico o seguimiento clínico superior a 6 meses.

Se calcularon los parámetros diagnósticos estadísticos y los niveles de concordancia entre ambas técnicas diagnósticas.

Resultados: Se analizaron un total de 114 exploraciones pertenecientes a 90 pacientes. Solo 4 pacientes fueron diagnosticados de recurrencia asintomática durante el seguimiento.

La ^{18}F-FDG PET/TCciv, la ^{18}F-FDG PET y la TCciv mostraron asociación con el diagnóstico final (p = 0,002 y $\chi^2 = 11,96$; p < 0,001 y $\chi^2 = 15,60$; p = 0,001 y $\chi^2 = 11,96$ respectivamente). La concordancia entre la ^{18}F-FDG PET y la TC civ fue moderada/alta y significativa (Kappa = 0,672; p < 0,001).

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Se obtuvo una sensibilidad y especificidad del 50% y 88% para la ^{18}F-FDG PET/TCciv, del 50% y 93% para la ^{18}F-FDG PET y del 50% y 91% para la TCciv.

Conclusión: El uso combinado de la ^{18}F-FDG PET/TCciv no ofreció ventaja con respecto a ambas técnicas por separado en la detección de recidiva asintomática por linfoma.

Introduction

Up to one third of patients with lymphoma will relapse after complete remission. This high incidence of relapse, justifies clinical surveillance, although the standard imaging follow-up is a debatable issue. Clinical symptoms are generally present in a majority of the cases before recurrence is diagnosed, especially in Hodgkin's lymphoma (HL) and in aggressive no Hodgkin's lymphoma (NHL), explaining that most recurrences are detected by the patient or the clinician.[1,2]

Despite current guidelines do not recommend imaging follow-up and recent studies state that there is a limited role for routine surveillance imaging, clinicians continue using a combination of clinical exploratory data combined with morphological imaging techniques while others use ^{18}F-FDG PET/CT based on its high diagnostic performance in the initial staging.[3–7]

In our institution, standard surveillance of patients with lymphoma was commonly performed using ceCT. When PET/CT technique became available, hematologists argued that, even with the excellent diagnostic performance of PET/CT, there was no sufficient evidence to substitute ceCT and so both studies should be performed on every patient. In order to avoid duplicating appointments, reduce costs and patient exposure to radiation, conventional imaging follow-up of patients with lymphoma was performed by a hybrid full diagnostic imaging (^{18}F-FDG PET/ceCT), yearly in the first 5 years after remission, for any type of lymphoma, and biyearly afterwards until the 10th year in aggressive lymphomas and 15 years in indolent ones.

Based on the absence of previous reported experience, the aim of the present work was to evaluate all the data obtained in a full hybrid diagnostic procedure (PET/ceCT) in order to establish the role of ^{18}F-FDG PET/ceCT, ^{18}F-FDG PET and ceCT in the detection of asymptomatic recurrence and incorporate this practice-based evidence in the clinical management of our patients with lymphoma.

Material and methods

Patients

For the present study, a retrospective analysis of ^{18}F-FDG PET/ceCT, from January 2007 to January 2015, in patients with lymphoma in complete remission for standard surveillance was conducted. The selection criteria were: complete response (CR) after the end of treatment with a previous negative PET/CT and ceCT and clinical remission during 12 months after CR.

The final diagnosis was established by histopathological analysis or clinical-radiological follow-up longer than 6 months after the ^{18}F-FDG PET/ceCT included in the analysis (named as target PET/CT). Those patients with out diagnostic confirmation were excluded.

Finally, 90 patients (30 with HL and 60 with NHL) were included. The patient's stage at diagnosis was: I-A (6), II-A (18), II-B (8), III-A (8), III-B (7), IV-A (23), IV-B (23) and cutaneous (2).

PET/ceCT acquisition

Patients were asked to fast for at least 6 h before undergoing PET/ceCT and had glucose levels under 160 mg/ml. All the patients received an intravenous injection of 370 MBq (10 mCi) of ^{18}F-FDG. Data acquisitions by an integrated PET/CT system (DSTE 16 s; GE Medical Systems) were performed 1 h after FDG injection from the head to the proximal legs following a standardized procedure for PET and ceCT described in a previous work.[8]

Image interpretation

PET and ceCT images were blinded and independently reviewed by a nuclear medicine physician and a radiologist.

A PET study was classified as positive and indicative of recurrence when at least one lesion with a metabolic rate superior to the reference background activity and not explained by reactive-inflammatory phenomena was seen, or a finding with doubtful interpretation in which its nature could not be defined.

In the ceCT scan, a study was listed as positive when at least one abnormal location of new apparition and not explained by another process, was found.

Furthermore, a combined and integrated PET and ceCT interpretation was obtained, classifying as positive when positivity was described with at least one diagnostic technique, either PET or ceCT.

Statistical analysis

Statistical analysis was performed using SPSS for windows software (version 22.0). All statistical tests were two-sided with a significance level of $p < 0.05$. Categorical variables were summarized as frequencies and percentages.

The association between ^{18}F-FDG PET/ceCT, ^{18}F-FDG PET and ceCT with the final diagnosis (recurrence or not) was examined using Pearson Chi-squared-test. Cohen's kappa test was used to report the concordance between ^{18}F-FDG PET and ceCT, classifying the results as poor (<0.20), weak (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80) and very good (0.81–1.00). Statistical diagnostic measures were also obtained.

Results

A total of 114 explorations in 90 patients were analyzed. A patient-basis analysis was performed.

Only 4 patients were clinically diagnosed on asymptomatic recurrence. 2 of them showed true positive (TP) and the others false negative (FN) cePET/CT.

The TP corresponded to an axillary low-grade B lymphoma recurrence (Fig. 1) and a follicular NHL with supra and infra-diafragmatic lymph node involvement. The FN was a cervical peripheral T-cell lymphoma recurrence, confirmed by an amigdalar biopsy and a cutaneous diffuse large B-cell lymphoma (DLBCL) in a patient with a previous diagnosis of testicular peripheric T-cell lymphoma.