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Médecine Nucléaire 39 (2015) 54–58
Médecine Nucléaire
Imagerie Fonctionnelle et Métabolique

General review

PET/CT in prostate cancer

TEP/TDM dans le cancer de la prostate

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Received 27 November 2014; accepted 6 January 2015
Available online 16 February 2015

Abstract

The aim of this short review is to delineate the role of positron emission tomography/computed tomography (PET/CT) in prostate cancer (PCa) diagnosis, staging and restaging the disease. Moreover, we will discuss the application of choline PET/CT in radiation and surgical salvage treatments and, finally, the advent of new radiopharmaceuticals will be briefly discussed.

Keywords: Prostate cancer; PET/CT; Imaging

Résumé

Le but de cette courte revue est de définir le rôle de la tomographie de positons couplée à la tomodensitométrie dans le diagnostic, le bilan d'extension et de récidive du cancer de la prostate. En outre sont discutées les applications de la TEP/TDM à la choline dans les traitements de rattrapage chirurgicaux et par radiothérapie, et brièvement l'arrivée de nouveaux radio-pharmaceutiques.

Mots clés : Cancer de la prostate ; TEP/TDM ; Imagerie

1. Introduction

PSA remains the least expensive and most largely used biomarker for screening and treatment monitoring of prostate cancer (PCa), however, the use of PSA has important limitations, mainly because it is not able to distinguish local from distant disease and cannot provide prognostic information on survival or treatment response [1].

In the last few years, the advent of new Molecular imaging methods, such as PET/CT and magnetic resonance (MR) may provide clinicians with useful information that can have an impact on the management of PCa patients. The ideal non-invasive imaging modality should have a strong clinical impact providing information regarding the best treatment modality personalised for each patient [2].

In the present review, we will provide an overview on the role of PET/CT with choline in prostate cancer detection, staging, restaging, treatment guide and response to treatment assessment.

2. PET/CT in primary PCa detection

PET/CT has a limited role in primary PCa detection due in particular to the low sensitivity and specificity. PET/CT is in most cases unable to discriminate cancer versus normal prostate or hyperplasia [3–7].

The first complete report in this field was been published by Farsad et al. in 36 patients who had biopsy-proven PCa,

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http://dx.doi.org/10.1016/j.mednuc.2015.01.001
0928-1258/

reporting a sensitivity and specificity of ^{11}C-choline PET/CT of 66% and 81% [8]. Subsequent studies have reported variable sensitivities and specificities, but with the constant finding of an overlap of choline uptake between benign and malignant changes [4,6,8,9].

3. PET/CT in prostate cancer staging

Staging prostate cancer is crucial to establish the correct treatment strategy. Preoperative nodal staging at initial diagnosis of PCa should guide surgical treatment decisions [10], while the assessment of distant metastases is crucial in patients with high-risk disease, in order to identify patients who might benefit the most from a curative intent treatment, and those who should receive systemic therapies as first-line treatment [11].

In lymph-nodal staging, Schiavina et al. showed that ^{11}C-choline PET/CT had low sensitivity, but high specificity (60% and 98%, respectively) for nodal staging in a population of 57 intermediate and high-risk patients [12]. Similar results have been also found by other authors [13].

Recently, Evangelista et al. [13] published a meta-analysis evaluating the role of PET/CT with choline in staging prostate cancer. The low sensitivity but high specificity of PET/CT has been confirmed. The authors concluded that choline PET/CT should be reserved to high and very high-risk patients according to nomograms to minimize the number of false negative results.

A prospective comparison of CT, MRI and ^{11}C-choline PET/CT for preoperative lymph node staging confirmed these findings for the three modalities. ^{11}C-choline PET/CT showed the best patient-based specificity, followed by DWI and CT [14].

Further studies are needed in order to identify the individuals who might benefit the most from choline PET/CT before primary treatment.

4. Bone metastasis assessment

PET/CT with choline can detect more skeletal lesions than bone scintigraphy. It has been shown that PET/CT choline could have a clinical impact, either as a first study or as a secondary study after a bone scan [15–17]. Considering that PET/CT is much more expensive compared to bone scans, in the near future, the cost-effectiveness of choline PET/CT should be investigated, especially in patient subgroups that would benefit from the higher sensitivity and specificity of PET/CT in comparison to bone scan.

5. Imaging biomarkers in prostate cancer restaging

PSA is the best way to follow up patients after primary treatment. Biochemical relapse is when a raise in PSA level is detected after primary treatment (PSA $>$ 0.2 ng/mL). Differentiation between the presence of local or distant relapse is critical to choose the proper treatment strategy [18]. The role of any imaging method should be to discriminate patients with local recurrence (who may benefit from local salvage treatment with curative intent), from those affected by distant failure (who are candidates for systemic therapy). The two main International Urologic Guidelines (NCSC and EUA) do not recommended any imaging modality to be routinely performed to identify the site of recurrence, in particular, when PSA values are low [11,19]. Therapeutic options after primary treatment are radiotherapy, complete or intermittent ADT, combination of ADT with 5-alfa-reductase inhibitors or early chemo-hormonal approaches [20]. In the last few years, works aimed at demonstrating a possible role of PET-guided salvage therapies have been published [21,22]. These papers underline the potential role of PET/CT imaging in restaging PCa and in guiding salvage therapies either with RT or surgery.

6. PSA and PSA kinetics

In the last few years, many studies have focused their attention on the possible correlation between the detection rate of ^{11}C-choline PET/CT and the serum PSA level. Krause et al. [23] demonstrated a significant and strict correlation between PET/CT detection rate and PSA serum levels in a population of sixty-three PCa patients with biochemical relapse (PSA mean 5.9 ng/mL) after primary treatment studied with ^{11}C-choline PET/CT. Again a strict relationship between PSA values and positive ^{11}C-choline PET/CT findings was confirmed later by Giovacchini et al. [24] in a large population of relapsed PCa patients, and by Castellucci et al. [25,26] who showed a strict relationship between the detection rate of ^{11}C-choline PET/CT and other PSA derivates, in particular PSA kinetics (PSA velocity and PSA doubling time).

According to these data, PSA kinetics should always be taken into consideration before performing a choline PET/CT in patients with biochemical failure because it is the most relevant factor for a PET/CT positive result, especially in the case of low PSA values.

7. PET/CT in prostate cancer recurrence

7.1. Local relapse

The sensitivity of choline PET/CT in detecting locally recurrent PCa is low, notably in the case of low PSA values [23–27]. The low accuracy of choline PET/CT is related to its limited spatial resolution and to its limited specificity since inflammation and normal prostatic residual tissue may show some uptake of choline.

Regarding local relapse, choline PET/CT has shown low sensitivity particularly in patients with low PSA values [23–27]. Kitajima et al. studied a population of 115 patients and reported a sensitivity, specificity and accuracy of 54, 92 and 65%, respectively, for ^{11}C-choline PET/CT while MR showed a sensitivity, specificity and accuracy of 88, 84 and 87% [28].

7.2. Lymph node relapse and tailored treatments

The detection of lymph node metastasis should guide the most appropriate treatment that may include tailored surgery or radiotherapy. Kitajima et al. showed a better accuracy of