CASUISTRY

\[ ^{11} \text{C-choline PET/CT and multiparametric MRI in patients with biochemical relapse of prostate cancer} \]

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KEYWORDS
\[ ^{11} \text{C-choline positron emission tomography/computed tomography; Multiparametric magnetic resonance imaging; Biochemical relapse; Prostate cancer} \]

Abstract

Clinic problem and case series: To assess the diagnostic usefulness of \[ ^{11} \text{C-choline PET/CT} \] vs. multi-parametric MRI in the prostate cancer relapse.

A retrospective study of 21 patients with prostate cancer treated initially with surgery (\( n = 12 \)), radiotherapy (\( n = 9 \)). PSA levels were increased (post-surgery: 3.3-3.6 ng/ml; post-radiotherapy: 2.4-8.8 ng/ml).

In an interval of time of 15 days all patients were underwent to: whole-body-dual-modality PET-CT carried out early after \[ ^{11} \text{C-choline (296±29 MBq)} \] injection, and multiparametric prostate MRI with paramagnetic intravenous contrast (using anatomical imaging sequences, diffusion-weighted imaging and dynamic contrast-enhanced imaging).

On the basis of our results, all patients were underwent to directed diagnosis and/or clinical, analytic and imaging follow-up.

In 15 patients (71.4\%) both procedures showed concordant results: 4 negative and 11 positive cases [7 local recurrences, 3 isolated pelvic lymph nodes (2 infracentimetric), 1 local relapse and only one M1 bone metastases].

The results were discordant in 6 patients (28.6\%): 3 local relapses in MRI with no PET significance, 1 local relapse in PET with no MRI significance. 2 bone metastases were identified with PET (out of the field-of-view of MRI).

Comment: \[ ^{11} \text{C-choline PET/CT} \] and multi-parametric MRI play a complementary role in the detection of local relapse in prostate cancer patients, with similar sensitivity for the detection of lymph involvement. Whole-body \[ ^{11} \text{C-choline PET/CT} \] technique is also useful for bone staging.

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Clinical problem with casuistry

Biochemical recurrence after prostatectomy is defined as the elevation of PSA > 0.2 ng/ml. The definition of biochemical recurrence after radiotherapy is more controversial, but an increase of 0.2 ng/ml in 6–12 months is accepted. It is important if the recurrence is local or there exists lymph node involvement or metastatic bone involvement or a combination between them, since it determines patient management, being able to consider radical therapy for local recurrence, but a systemic treatment, combined or not with systemic treatment is necessary for metastatic disease.

Prostate biopsy is the traditional method for detecting local recurrence; however, it is invasive, costly, and it has a relatively low but not negligible complication rate (such as infection). Moreover, the negative biopsy does not exclude local recurrence due to potential sampling error, so repeat biopsy is needed. Therefore, the biopsy is not recommended by the EAU in patients with PSA < 1 ng/ml.

In this casuistry, we compared the diagnostic usefulness of PET/CT with 11C-choline and multiparametric MRI in the detection of local recurrence, lymph node involvement, intrapelvic involvement in patients with biochemical recurrence of prostate cancer.

We included 21 patients with a history of prostate cancer, initially treated with surgery (n = 12) or radiotherapy (n = 9) who had increased PSA (postsurgery 0.3–3.6 ng/ml; postradiotherapy 2.4–8.8 ng/ml). All patients underwent: full body 'two phase' PET/CT study and multiparametric prostate MRI.

11C-choline has been synthesized in the cyclotron located in the same system. The tracer was administered with the intracamerical patient (296 ± 29 MBq) initiating the acquisition immediately. After performing CT of attenuation correction, 2 consecutive full body PET emission acquisition (9 steps/2 min) were carried out, without patient mobilization.

The multiparametric prostate MRI includes performing anatomical sequences, diffusion study, and dynamic study after administration of intravenous paramagnetic contrast.

The interpretation of PET/CT with 11C-choline was performed by 2 specialists in nuclear medicine. The prostate multiparametric MRI interpretation by 2 specialists in X-ray diagnosis. Both were evaluated blindly from the other examination. We performed analysis of the detection rate of PET/CT with 11C-choline and prostate multiparametric MRI.

From our results, all patients with both scans, or one of them positive, underwent directed diagnostic study and/or salvage treatment, performing clinical, analytical and imaging follow-up, between 12 and 18 months, revealing increased size or, alternatively, reduction or resolution of the lesion, associated with the reduction or normalization of PSA after therapy.

The patients with the 2 negative tests have reached the diagnosis of true negative, including the histological findings, post-biopsy, or the negative follow-up for at least 12–18 months, by means of diagnostic tests, without progression of the PSA level.

In 15 patients (71.4%) both examinations were concordant, 4 negative, and 11 positive: 7 local recurrences (5...
postradiotherapy, 2 postprostatectomy), 3 unique pelvic adenopathies (2 infracentimeter, 3 postprostatectomy), 1 local recurrentne, and 1 single bone metastasis (1 postradiotherapy).

In 6 patients (28.6%) both examinations were discordant: 3 local recurrences identified in MRI without significance in PET (3 postprostatectomy), 1 local recurrence identified in PET without significance in MRI (postradiotherapy) and 2 bone metastases identified in PET outside the field of MRI.

**Commentary**

Choline uptake is due to deregulation of choline in the tumor cells. Colin-kinase is an enzyme which is overexpressed in tumor cells. Overexpression of colin-kinase is independent of Ki67 in prostate tumors. 5

The MRI diffusion study, by means of modified T2-weighted sequences, provides information on the random motion of free water molecules. The diffusion is based on the fact that the restriction of water correlates with increased cellularity. The neoplastic tissue has a higher diffusion restriction, with low signal on the map of diffusion coefficient (ADC). In the dynamic study, after administration of intravenous contrast (gadolinium), the dynamics of contrast uptake and perfusion allows for the study of microvascular tissue, and indirectly of angiogenesis. 3 types of uptake curve have been described: type I progressive; type II plateau; and type III washing. The last 2 are associated with a neoplastic process.

This different biology means that there is no correlation between both techniques, as reflected in the first comparative studies. Thus, a superiority of multiparameter MRI over PET/CT with 18F-choline has been described in detecting local recurrence in patients with small lesions and low elevation of PSA (5–7 mm; PSA 0.8–1.4 ng/ml) but with similar sensitivity in >10 mm. 6

Our results are consistent with the findings described, and the 3 local recurrences identified postprostatectomy by means of multiparametric MRI have infracentimeter character (Fig. 1). Therefore, the spatial resolution of PET systems, around 7 mm, limits the sensitivity of the examination in detection of local recurrence. However,

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**Figure 1**  Patient with a history of prostate cancer treated with surgery 3 years ago having high PSA (1.5 ng/ml). (A) and (B) Dynamic study with intravenous paramagnetic contrast. Postprostatectomy changes with hyperintense nodular lesion in right posteroirateral vesicoureteral anastomosis, with initial rapid increased uptake curve, and late plateau-washing phase, highly suggestive of local recurrence.

**Figure 2**  Patient with a history of prostate cancer treated with radiotherapy 2 years ago having elevated PSA (2.8 ng/ml). (A) and (B) Axial early and late PET/CT imaging. Deposit of 11C-choline (SUVmax 2.0) in the middle third of the right prostate lobe showing cumulative dynamics in the late imaging (SUVmax 2.3), metabolic behavior suggestive of local recurrence.
local recurrence identified by means of PET/CT study with $^{11}$C-choline, without translation in MRI, was after radiotherapy (Fig. 2), probably related to signal changes that occur after this treatment in the prostate gland.

Detection of lymph node involvement is crucial in restaging of prostate cancer. The low negative predictive value of the analysis due to lesions of choline PET is related to the limitation of the technique in the detection of
microscopic lymph node infiltration. However, the scan shows a high positive predictive value, which facilitates performing appropriate treatments.

In our cases, both scans showed the same detection rate, even in the detection of lymph node infracentimeter infiltration (Fig. 3). Luboldt et al. performed a comparison between MRI and PET/CT with $^{11}$C-choline in the detection of bone metastases of prostate cancer, describing similar results between both techniques. Our results are consistent with these findings (Fig. 4), although it should be noted that PET/CT as whole-body scanning has allowed for the identification of metastatic bone lesions outside the field of MRI.

Therefore, this casuistry shows that PET/CT with $^{11}$C-choline and multiparametric MRI have a complementary role for the detection of local recurrence of prostate cancer, with similar sensitivity for the detection of lymph node infiltration. PET/CT with $^{11}$C-choline, as whole-body technique, allows for bone staging. Therefore, its combination is necessary for a better combination of compression in restaging of patients with prostate cancer recurrence.

For this reason, we believe that PET/MRI integrated teams, newly introduced, can play an important role in these patients, by obtaining optimal spatial and temporal data coregistration of PET and MRI, adding the benefits of both, additionally enabling a reduction of the radiation, by avoiding performance of CT study, as well as improvement in the management of patients, performing both examinations in a single session.

Conflict of interest

The authors declare that they have no conflict of interest.

References