

# Advancement in pelvic cancer imaging: choline PET/CT in developing countries

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**SUMMARY** Introduction: Prostate cancer is the second most common cancer among men. Despite its early diagnosis and improved curative treatments, the rate of recurrence remains high, with one in two cases relapsing within ten years. Positron Emission Tomography (PET) with a radiotracer is most commonly used in prostate cancer. Indeed, prostate cancer is one of the malignancies known to have an increased metabolism of phosphatidylcholine, an essential component of the cell membrane, by increasing the level of choline kinase and increasing the rate of choline incorporation.

The aim of this study is to determine the role of Choline Positron Emission Tomography (choline PET/CT) in prostate cancer through our experience and a literature review.

Methods: This is a retrospective study carried out at the Sheikh Khalifa Hospital over 2 years from January 18, 2019, to January 31, 2021. The inclusion criteria were any patient with histologically confirmed prostate cancer who had undergone choline PET/CT in the Department of Nuclear Medicine.

Results: During the study period the Nuclear Medicine Department performed (n=60) choline PET scans. The average age of patients is 67 years with extremes of 52 and 82 years.

The average PSA level was 125 [0-1800]. The main indication was in the context of a biological relapse assessment, followed by an evaluation of the therapeutic response and in the context of an initial extension assessment. PET was able to detect local and/or distant lesions in 80% of patients in our series.

Conclusion: As there is no PET scans with Prostate-Specific Membrane Antigen (PSMA) in Morocco, choline PET is an alternative that has allowed better therapeutic management of our patients and thus the improvement of their prognosis.

**Key words:** prostate cancer, positron emission tomography, Choline, recurrence.

## INTRODUCTION

Prostate cancer is the second most common cancer among men. Its prevalence is clearly on the rise due to screening by Prostate-Specific Antigen (PSA) testing. However, despite early diagnosis and improved curative treatments, the recurrence rate remains high, with one in two cases of relapse after ten years. This may be related to the initial under-staging of morphological imaging studies, especially the evaluation of lymph node involvement. In the extension workup of high-risk cancers, choline Positron Emission Tomography (PET) can detect metastatic nodes larger than 5 mm, especially those located outside the curage territory.

Indeed, prostate cancer is one of the malignant tumours known to have an increased metabolism of phosphatidylcholine, an essential component of the cell membrane, by increasing the level of choline kinase and increasing the rate of choline incorporation. Choline derivatives, mainly 18F-fluoro-methyl choline (18F-FCH) were developed about 15 years ago and studied on animals and then on humans. This radiotracer has also shown promising results for the detection of tumour recurrence during the elevation of serum Prostate-Specific Antigen (PSA) after curative treatment (PSA>0.2 ng/ml after radical prostatectomy and PSA>2 ng/ml after external radiotherapy) [1, 2].

## PATIENTS AND METHODS

This is a retrospective study conducted at Sheikh Khalifa Hospital over 2 years from January 18, 2019, to January 31, 2021.

The inclusion criteria were any patient with histologically confirmed prostate cancer who had a choline PET scan performed at the nuclear medicine department.

The examination was standardized for all patients and was performed in two steps. After injection of the adequate dose of the radiotracer 18F-Choline (4 MBq/kg)

During the first stage, a dynamic acquisition centered on the pelvis was performed two minutes after administration of the radiotracer. It consisted of the realization of 10 images lasting

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one minute per image, followed by a scan from the skull to mid-thigh lasting 2 min 30 s.

The second step is started sixty (60) minutes after the injection of the radiotracer. It is coupled with a CT scan for correlation of attenuation and anatomical location.

## RESULTS

During the study period, the Department of Nuclear Medicine performed (n=60) choline PET scans. The main indication was in the framework of a biological relapse assessment, followed by an evaluation of the therapeutic response and in the framework of an initial extension assessment.

The average age of patients was 67 years with extremes of 52 and 82 years.

The median PSA level was 125 of [0-1800].

Choline PET did not show any abnormality in 20% of cases, prostatic lesions were detected in 35% of cases.

Metabolically active prostatic uptake associated with either lymph node involvement in 5% or bone involvement in 13.3% of cases was found. It should be noted that PET revealed isolated bone locations in 8 patients in our series.

## DISCUSSION

The contribution of 18FDG PET/CT can be useful in aggressive and dedifferentiated cancers, but its contribution is limited in most prostate cancers that express little Glut-1 transporter and concentrate little or no FDG.

The availability of tracers other than 18f-Fluorodeoxyglucose (FDG) suggests new opportunities for the diagnosis and management of Prostate Cancer (PCa). The use of different radiopharmaceuticals, such as radiolabeled choline, or radiolabeled ligands of Prostate-Specific Membrane Antigen (PSMA), has a significant impact in various clinical settings, from initial staging to the detection of a biochemical recurrence, enabling personalized treatment planning, and Metastasis-Directed Therapy (MDT) [3, 4]

The development of 18F-choline analogs currently allows PET/CT examinations to be performed in centers that do not have a cyclotron. The diagnostic value of 18F-FCH PET/CT in the initial workup has not been validated to date, as the results of the various published studies are contradictory [1]

Such an approach relies on the diagnostic performance of the imaging modalities used to detect the real extent and location of metastases. Many studies on PCa patients have been conducted using PET/CT [5,6], but most clinical protocols consider Magnetic Resonance Imaging (MRI) the principal imaging modality for staging and restaging of patients with PCa.

Behesthi and colleagues [7] evaluated the value of 18F-FCH PET/CT in the preoperative phase of intermediate- and high-risk patients with prostate cancer. The authors evaluated 132 prostate cancer patients with an intermediate or high risk of extra capsular disease. A total of 912 lymph nodes were

examined histopathologically, and analysis revealed a sensitivity of 45% with a specificity of 96%. The latter is similar regardless of the size of the nodes, whereas the sensitivity reaches 66% for nodes with a diameter of 5 mm or more.

Therefore, the authors concluded that 18F-FCH PET/CT have a limited value in the detection of malignant lymph nodes less than 5 mm in diameter [8]. Nevertheless, this examination, although imperfect, since it does not detect micro-metastases, is the most efficient non-invasive examination [9, 10].

Similarly, other studies have shown that there is a good correlation between the intra-prostatic tumor location of choline and the analysis of the prostatectomy specimen when the size is greater than 5 mm below this value, there is a high risk of false negative. It has also been reported that the intensity of choline uptake is independent of the aggressiveness of cancer, whether it is the Gleason score or the PSA level. Moreover, moderate SUV values could be responsible for false positives as the distinction between malignant and benign lesions is not formal for values with a cut-off of 3. Therefore, it is not recommended to perform a PET-choline scan as a first-line test for the initial diagnosis of intra-prostate cancer. On the other hand, PET-choline is of interest to guide biopsies when these have been previously negative. The most hypermetabolic site is cancer [11].

When biochemical recurrence is observed in patients, accurate determination of local *versus* metastatic disease is crucial for therapeutic management. Several studies have shown that 11C-Choline and 18F-FCH PET/CT is useful in detecting recurrence in patients with relapsed PSA for values ranging from 1 ng/ml [12] to 5 ng/ml. However, a threshold PSA value for which prostate cancer patients should be referred for PET/CT has not yet been established [13].

In a large prospective study, Cimitan's team [14] identified prostate cancer recurrence with 18F-FCH PET/CT in 53 out of 100 patients with relapsed PSA; however, 89% of patients with likely false-negative scans had a serum PSA level <4 ng/dl, which translates into lower sensitivity of 18F-FCH for detection of recurrent prostate cancer if the PSA was low. These results were supported by Krause's team who reported that choline PET/CT, has a low sensitivity in patients with PSA less than 4 to 5 ng/ml. Indeed, according to Krause et al. there is a linear relationship between the absolute PSA value and the identification of the relapse site [15].

According to the French Association of Urology (FAU), the indication of 18F-Fluorocholine (F-choline) Positron Emission Tomography (PET) is currently retained in the search for bone metastases of prostate cancer. A growing number of studies report interesting results in the diagnosis of extraskeletal relapse in patients previously treated for localized cancer.

It should be noted that there are no contraindications to the performance of the examination; therefore, there is no particular preparation of the patient. However, it is important not to initiate androgen suppression before a PET choline examination, as the effectiveness of androgen blockade will result in a drop in the PSA level and, at the same time, in the disappearance of

hypermetabolic foci, with the risk of decreasing the contribution of the PET choline examination. Similarly, it is preferable not to modify the hormonal therapy of a patient who has become resistant to castration before the PET scan [16].

## CONCLUSION

In our context, given the unavailability of other radiotracers such as prostate membrane specific antigen PSMA, choline PET remains the examination of choice for the detection of recurrences, particularly lymph node recurrences, and as part of an extensive assessment of oligometastatic disease,

thus modifying the therapeutic management and inevitably improving the prognosis of our patients.

## COMPETING INTERESTS

The authors declare no competing interests.

## AUTHORS' CONTRIBUTIONS

All the authors participated in the writing of the article and the bibliographical research concerning the case described. They also declare having read and approved the final version of the manuscript.

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