



PET-CT 18F-PSMA 1007 in the staging of patients with prostate cancer prior to curative intent radiotherapy: a prospective observational study

PET-TC 18F-PSMA 1007 en la estadificación de pacientes con cáncer de próstata previo a la radioterapia con intención curativa: un estudio observacional prospectivo

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Abstract

Objective: The objective of our study was to assess whether there are staging changes in CaP with PET PSMA compared to standard diagnostic methods, and if these changes occurred, to understand how they altered the treatment of patients with an initial diagnosis of CaP and their relationship with the D'amico score.

Methods: We present a prospective observational study conducted on patients initially diagnosed with prostate cancer, who underwent standard staging studies alongside PET PSMA imaging.

Results: Forty patients diagnosed with prostate cancer were staged using standard diagnostic methods and PET PSMA. In 40% of the patients, initial staging changed based on the results obtained from PET PSMA. After PET PSMA, the uro-oncology committee decided to modify the initial treatment plan in 27.5% of the cases, including radiation boost targeting the extra-prostatic lesions detected by PET PSMA. When correlating the change in staging with PET PSMA versus the D'amico risk score, no changes were observed in the low-risk group, 19% in the intermediate-risk group, and 62% in the high-risk group. These differences were statistically significant ($X^2=9.2$; $df=2$; $p=0.01$).

Limitation and value: The study faced limitations in sample size and lack of long-term patient follow-up. However, it highlights key contributions: the promising evaluation of PET PSMA in staging, its influence on therapeutic decisions, and its association with the D'amico score.

Conclusion: PET PSMA showed substantial changes in CaP staging, particularly in higher-risk patients, suggesting its potential utility in guiding therapeutic decisions before radiotherapy.

Keywords:

Prostate cancer, PSMA, PET-CT, tomography

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Citation: Modina, P., Costa L., Arceluz M., Romero Acuña J., David C., Faccio F., et al. *PET-CT 18F-PSMA 1007 in the staging of patients with prostate cancer prior to curative intent radiotherapy: a prospective observational study.* *Rev Mex Urol.* 2024;84(2): 1-7

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Received: 10 de diciembre de 2023.

Accepted: 10 de mayo de 2024.



Resumen

Objetivo: El objetivo de nuestro estudio fue evaluar si existen cambios de estadificación en CaP con PET PSMA en comparación con los métodos diagnósticos estándar, y si estos cambios ocurrieron, comprender cómo alteraron el tratamiento de los pacientes con diagnóstico inicial de CaP y su relación con la puntuación de D'Amico.

Métodos: Presentamos un estudio observacional prospectivo realizado en pacientes con diagnóstico inicial de cáncer de próstata, a quienes se les realizaron estudios de estadificación estándar junto con imágenes PET PSMA.

Resultados: Cuarenta pacientes diagnosticados con cáncer de próstata fueron estadificados utilizando métodos de diagnóstico estándar y PET PSMA. En el 40 % de los pacientes la estadificación inicial cambió en función de los resultados obtenidos de la PET PSMA. Después del PET PSMA, el comité de urooncología decidió modificar el plan de tratamiento inicial en el 27.5 % de los casos, incluyendo un refuerzo de radiación dirigido a las lesiones extraprostáticas detectadas por el PET PSMA. Al correlacionar el cambio en la estadificación con PET PSMA versus la puntuación de riesgo de D'Amico, no se observaron cambios en el grupo de bajo riesgo, el 19 % en el grupo de riesgo intermedio y el 62 % en el grupo de alto riesgo. Estas diferencias fueron estadísticamente significativas ($\chi^2=9,2$; $g1=2$; $p=0,01$).

Limitación y valor: el estudio enfrentó limitaciones en el tamaño de la muestra y falta de seguimiento de los pacientes a largo plazo. Sin embargo, destaca contribuciones clave: la prometedora evaluación de PET PSMA en la estadificación, su influencia en las decisiones terapéuticas y su asociación con la puntuación de D'Amico.

Conclusión: PET PSMA mostró cambios sustanciales en la estadificación de CaP, particularmente en pacientes de mayor riesgo, lo que sugiere su utilidad potencial para guiar las decisiones terapéuticas antes de la radioterapia.

Palabras clave:

cáncer de próstata,
PSMA, PET-CT,
tomografía

Introduction

Prostate cancer (PCa) is one of the leading causes of cancer-related death in men worldwide.⁽¹⁾ PCa is the second most commonly diagnosed cancer in men, with an estimated 1.4 million diagnoses worldwide in 2020.⁽²⁾ Despite careful patient selection before treatment for PCa, post-treatment relapse with curative intent is frequent, partly due to the insufficient sensitivity and specificity of existing standard imaging modalities such as computed tomography (CT) and bone scintigraphy (BS) in detecting non-localized disease.⁽³⁾

Prostate-specific membrane antigen (PSMA) is a transmembrane glycoprotein that is highly overexpressed in almost all PCa cases, with expression levels increasing with higher tumor grade and stage. PSMA ligands are small molecules that bind to the active site of the extracellular domain of PSMA.⁽⁴⁾

Currently, studies have reported the use of PSMA PET in both primary staging and evaluation of biochemical recurrence; however, most published data focus on biochemical recurrence

of prostate cancer, which is currently the main indication for PSMA PET use.

The proPSMA study conducted in men with PCa undergoing staging prior to curative-intent therapy found that PET PSMA outperformed conventional imaging in detecting distant disease in high-risk patients.

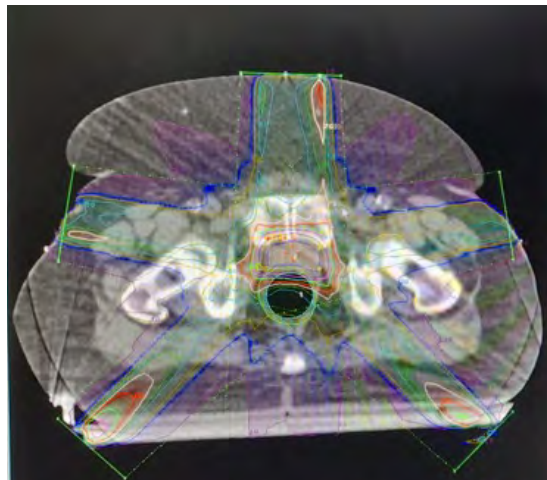
The objective of our study was to evaluate if there were changes in the staging of CaP using PSMA PET compared to standard diagnostic methods. Additionally, if changes occurred, we aimed to understand how these modifications impacted the treatment of patients with an initial diagnosis of CaP, particularly in relation to the D'Amico risk score.

Material and methods

A prospective observational study was conducted in patients with an initial diagnosis of PCa who underwent standard staging studies (CT and BS) and PSMA PET. Patients were eligible if they had histopathologically confirmed PCa by transrectal prostate biopsy and were being considered for curative-intent radiotherapy following staging with conventional diagnostic methods and PSMA PET. Patients were excluded if they had contraindications for PSMA PET. A focal increase in tracer uptake greater than the background and not associated with physiological uptake was considered a positive result for PSMA PET. The evaluated variables included age, International Society of Uro-pathology (ISUP) grade, clinical stage (TNM), prostate-specific antigen (PSA) level, D'Amico risk score,⁽⁵⁾ results of CT, BS, PSMA PET, and

treatment change. Intensity-modulated radiotherapy (IMRT) was administered, delivering 60 Gy to the prostate gland and 40 Gy to regional lymph nodes (Figure 1).

Figure 1: Axial planning image of IMRT in the prostate gland with a dose of 60 Gy



Treatment change was defined as an increase in the radiation dose (boost) by focal delivery of 60 Gy to suspected lesions of extraprostatic disease localized in the iliac chain (N1). Risk groups were defined according to D'Amico scores as low, intermediate, and high risk, respectively. Statistical analyses were performed using SPSS 28 software. Descriptive measures for quantitative variables included mean and standard deviation or median and quartiles 1 and 3. Absolute frequencies and percentages were used to describe qualitative variables. 95% confidence intervals (95% CI) were calculated. Proportions were compared using Pearson's chi-square test. The selected significance level was $\alpha = 0.05$.

Results

From October 2019 to August 2020, 40 patients diagnosed with PCa were staged using standard diagnostic methods and PSMA PET. Table 1 presents descriptive characteristics of the patients.

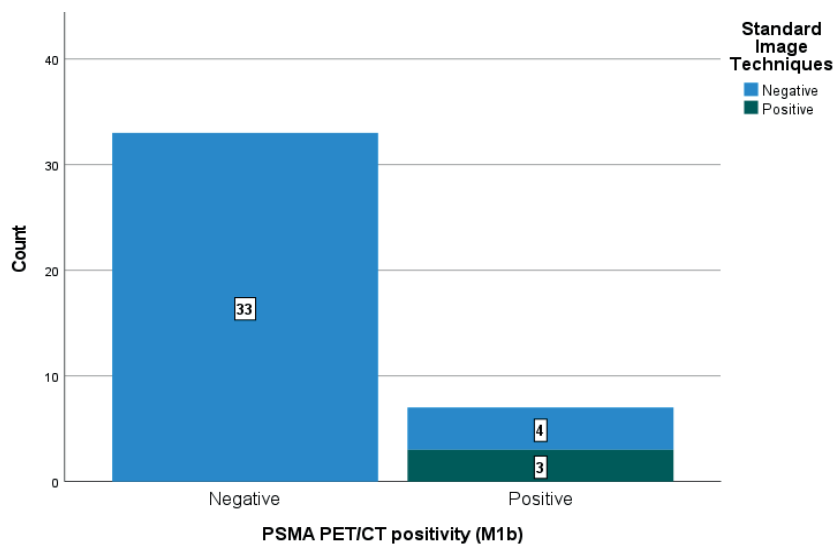
Table 1. Age distribution and urological profile of the patients

Variable	
Age (Mean ± SD) [years]	68.6 ± 7.6
ISUP % (N)	
1	7.5 (3)
2	15 (6)
3	37.5 (15)
4	30 (12)
5	10 (4)
D'amico Score % (N)	
Low risk	7.5 (3)
intermediate risk	40 (16)
High risk	52.5 (21)
PSA (Median (Q1-Q3)) [ng/ml]	10.2 (6.5-21.2)

In the 40 patients, 40% (n=16) of the initial stagings changed according to the results obtained

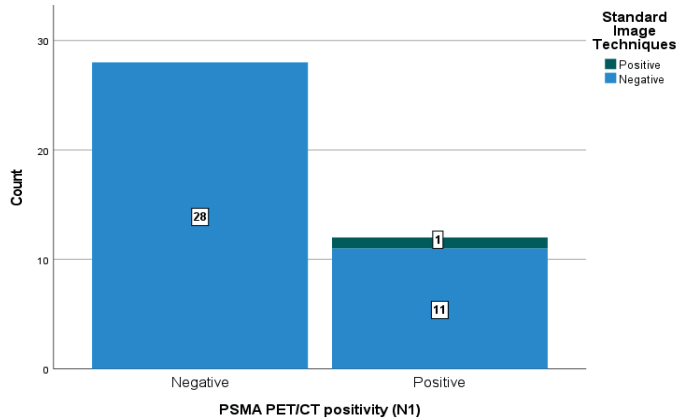
In the TNM classification, it was observed that, in the detection of bone metastases (M1b), out of 7 cases where the PET PSMA gave positive results, the standard methods were negative in 57% (n=4) of them (Figure 2).

Figure 2. M1b positivity of PET-CT PSMA versus standard methods



In addition, in the detection of locoregional adenopathies (N1), out of 12 cases where PET PSMA gave positive results, standard methods were negative in 92% (n=11) of them. (Figure 3).

Figure 3. N1 positivity of PET-CT PSMA versus standard methods

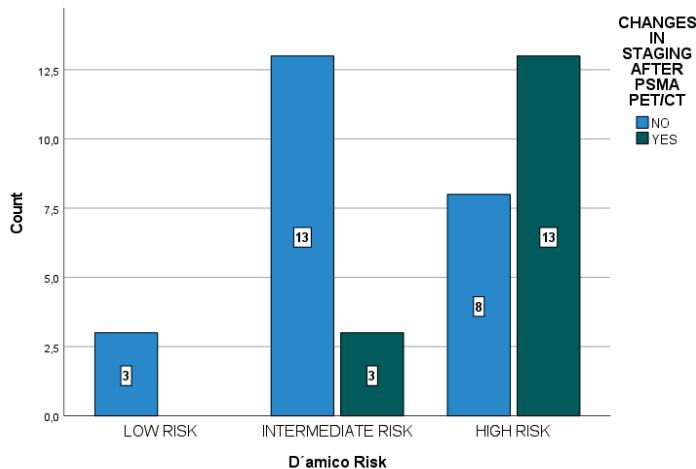


In the detection of non- locoregional adenopathies (M1a), out of 4 cases where the PET PSMA gave positive results, the standard methods were negative in 100% (n=4). Finally, the evaluation of visceral metastases (M1c) did not present positivity neither in PET PSMA nor in standard methods.

Following the PSMA PET, the uro-oncology committee decided that 27.5% (n=11) of the initial treatment plans should be modified based on the captured extra-prostatic images from the PSMA PET, leading to a radiation boost.

When correlating the change in staging from the PSMA PET with the D'Amico risk score, it was observed that there were no changes in the low-risk group, 19% changes in the intermediate-risk group, and 62% changes in the high-risk group. These differences were statistically significant ($\chi^2=9.2$; $df=2$; $p=0.01$) (see Figure 4).

Figure 4. Change in post-PSMA PET staging according to D'Amico Score categories



Discussion

The PET-PSMA is widely used for the evaluation of biochemical recurrence of PCa and has recently been employed for initial staging prior to treatment. A multicenter study evaluating the use of PSMA in initial staging of patients with negative bone scintigraphy showed that PET-PSMA yielded positive results in 17 patients, resulting in a sensitivity of 41.5 % (95 % CI: 26.7 %-57.8 %) and specificity of 90.9 % (95% CI: 79.3 %-96.6 %) for bone metastasis assessment.⁽⁶⁾ A retrospective study utilizing PET-PSMA for initial assessment of 206 PCa patients found a specificity of 93.5 % and a sensitivity of 38.2 % for detecting nodal disease.⁽⁷⁾ A multicenter clinical trial assessing the initial staging of PCa using conventional imaging and PET-PSMA demonstrated that PET-PSMA had a 27 % higher diagnostic accuracy than conventional imaging. He also showed lower sensitivity (38 % vs. 85 %) and specificity (91 % vs. 98 %) in favor of PET-PSMA.⁽³⁾ Our analysis was demonstrated the highest diagnostic accuracy of PET-PSMA compared to conventional imaging. Specifically, 57 % of positive bone findings on PET-PSMA (M1b) were negative on standard diagnostic methods. Additionally, in the detection of locoregional lymph nodes (N1), standard methods were negative in 92 % of the 12 cases where PET-PSMA yielded positive results. Similarly, in the detection of non-locoregional lymph nodes (M1a), standard methods were negative in 100 % of the 4 cases where PET-PSMA showed positive results.

The higher diagnostic accuracy of PET-PSMA has prompted the medical community to assess whether the increased positivity of the study changes therapeutic strategies. The proPSMA study found that conventional ima-

ging led to a change in treatment intention or modality in 15 % (95% CI: 10 %-22 %) of patients, compared to 28 % (95 % CI: 21 %-36 %) for those who underwent first-line PET-PSMA ($p=0.008$).⁽³⁾ In our study, the use of PET-PSMA resulted in a treatment modality change in 27.5 % of cases, supporting previous findings.

The proPSMA clinical trial only evaluated high-risk patients according to the D'Amico risk score and assessed treatment changes in this group. Our analysis not only included patients at high risk of recurrence after treatment but also incorporated those at intermediate and low risk of recurrence according to the D'Amico score. We observed 0 % changes in the low-risk group, 19 % changes in the intermediate-risk group, and 62% changes in the high-risk group ($\chi^2=9.2$; $df=2$; $p=0.01$).

The primary function of any imaging diagnostic test is to provide accurate results. Our study continues to demonstrate the unequivocal superiority of PET-PSMA compared to conventional imaging. This finding can be attributed to the high uptake and specificity of the PSMA radiotracer, enabling the identification of small-volume nodal or visceral disease and early bone metastases before lytic or blastic changes occur.

Conclusion

In our study, PET-PSMA demonstrated an initial staging change in 40% of cases. When comparing it with the D'Amico risk score, we observed that higher risk was associated with a higher probability of staging change. Based on our analysis, it can be inferred that PET-PSMA is a useful tool for staging patients at moderate and high risk prior to radiation therapy.

Conflict of interest

None of the authors have any conflicts of interest or financial ties to disclose.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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