European Journal of Clinical Pharmacy

Print ISSN: 2385-409X **Online ISSN**: 3105-0409

Website: https://farmclin.com/

Original Research Article

Diagnostic performance of 99mTc PSMA SPECT/CT in assessment of prostatic carcinoma

Article History:

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Received: 14-10-2025
Revised: 11-11-2025
Accepted: 23-12-2025
Published: 30-12-2025

Abstract: ***Objective:*** The aim of this study was to assess the diagnostic performance of 99mTc-PSMA SPECT/CT in assessment of prostate cancer, and to correlate its findings with the findings of conventional imaging and various patient factors to discover if it is useful in staging, restaging and detection of recurrence in patients with loco-regional prostatic carcinoma. ***Patients and methods***: We prospectively analyzed PSMA SPECT/CT scans of 64 adult male patients presented with elevated total PSA level and pathologically proven prostatic adenocarcinoma. In all, 38 patients were referred for primary staging, 16 patients for restaging after Androgen Deprivation therapy and 10 patients for detection of recurrence. Whole body SPECT/CT imaging was carried out 3 to 4 h after intravenous administration of 740 MBq (20 mCi) [99mTc]Tc-HYNIC- iPSMA. Images were evaluated visually. ***Results:*** Molecular imaging by 99mTc PSMA SPECT/CT identified T2 stage in 64% of our studied cases showing excellent agreement with T staging detected by conventional imaging with Kappa Value (K)=0.864. Higher TNM stages detected by Tc PSMA (IVA & IVB) were significantly associated with very high risk classification and ISUP grades 4&5($p \leq 0.001$). Also, we found that N1&M1 status were predominantly classified as very high risk with p=0.02 &0.03 respectively. statistically significant associations were observed between 99mTc PSMA SPECT/CT findings and patient factors including Gleason's scores, ISUP grades, risk classification and PSA grades with p value 0.001. In comparative analysis, 99mTc PSMA SPECT/CT had higher sensitivity compared to conventional imaging in detection of regional LN metastases with moderate agreement (K=0.63). Also, 99mTc PSMA SPECT/CT has been detected bone metastases more reliably than bone scans with moderate agreement (k=0.69). Among 16 patients underwent ADT 14 patients had positive 99mTc PSMA findings with significant association between imaging results and therapy response($p<0.001$). Also, among 10 patients referred for biochemical recurrence 7patients had positive findings on 99mTc PSMA with a statistically significant association $p<0.001$. ***Conclusion:*** The findings of this study demonstrate that 99mTc-PSMA SPECT/CT is an effective imaging modality for identifying significant stages of prostate cancer aiding in informed treatment decision-making. The study also emphasizes the potential for 99mTc PSMA to serve as a cost-effective alternative to PSMA PET imaging particularly in regions with limited access to PET/CT systems or PSMA PET tracers.

Keywords: Prostate cancer, 99mTc-PSMA SPECT/CT, conventional imaging.

INTRODUCTION

In the last few years, the use of 68Ga-PSMA PET/CT in the initial staging of prostate cancer could make a significant impact on therapy. It was proven to be more sensitive and specific in the detection of prostate cancer compared to current conventional imaging modalities [1]. Although it is superior over 99mTc–PSMA SPECT/CT in terms of the number of detected lesions, there was no statistically significant difference in terms of localization of abnormality in patients with PSA

level of >0.5ng/ml [2]. This improvement in PET/CT images over SPECT/CT images comes at a significant price increase. As a result of current advances in detector technologies and reconstruction algorithms, the spatial resolution of SPECT images is rapidly approaching that of PET images, without a decrease in sensitivity [3]. Improvements of SPECT/CT together with novel technetium chemistry, will provide as high a level of functional and anatomical information as is attainable by PET/CT. All of the above developments are expected to increase the demand for and utility of technetium radiopharmaceuticals and their kits [4].
The aim of this prospective cross- sectiona*l study is to assess the diagnostic performance of 99mTc-PSMA SPECT/CT in assessment of prostate cancer and correlate its findings with the findings of conventional imaging to discover if it is useful in staging, restaging, and detection of recurrence in patients with prostatic carcinoma.

MATERIAL AND METHODS

Patients and methods

Study population

Our study included 64 adult male patients presented with elevated total
PSA level and pathologically proven prostatic adenocarcinoma who were
referred to perform 99mTc-PSMA SPECT/CT for purpose of initial staging or evaluation of therapy response or detection of recurrence. Our study performed at south Egypt cancer Institute during the period from June 2022 till December 2023. Patients who have normal PSA or those with not available imaging data were excluded. All these patients provided a written consent to expose the data that has been used for research purpose. Causes of referral of the studied patients are demonstrated in figure 1

The age of the patient, the total PSA level and conventional imaging results detected within one month prior to scan were documented. The available Gleason's score and ISUP grade among studied cases were also documented.

Classification of patients

According to risk classification: We classified our patients according to NCCN guidelines lastly updated at 2023 into intermediate, high and very high risk groups.

According to their PSA level they were categorized into two groups, PSA level ≤20 ng/ml and > 20 ng/ml.

According to the biopsy International society of Urologic Pathology (ISUP) grading system, we classified the patients into 5 grade groups.

According to the T-stage the patients were categorized according to the conventional imaging results into

- T2 "tumor localized to the prostate",
- T3 "patients revealing either extra-prostatic extension or seminal vesicles invasion"
- T4 "patients with tumor invasion to the nearby structures".

Study protocol

Patient preparation:

- Patient should be encouraged to drink enough water
- patients were instructed to void immediately prior to study initiation

Preparation of 99mTc PSMA and quality control:
We used 99mTc-HYNIC-iPSMA which is a novel tracer for detection of prostate cancer. 6-hydrasinonicotinamide (HYNIC) is a compound used to attach tecnetium-99m to the inhibitor of prostate specific membrane antigen. The kit of HYNIC-iPSMA-Sn, after being reconstituted with 1.0 mL of 0.2 M phosphate buffer solution (pH 7.0), followed by the addition of 1.0 mL of a sterile, bacterial endotoxin-free solution of sodium pertechnetate (99mTcO4Na) and incubation for 15 minutes in boiling water, gives an aqueous, transparent solution of 99mTc-HYNIC-iPSMA, whose pH is 6.5-7.5, which is appropriate for intravenous administration & Its nuclear properties correspond to those of Tc-99m.

The radiochemical purity (RCP) of 99mTc-HYNIC-PSMA was analyzed using a high performance liquid chromatography system.

99mTc PSMA SPECT/CT acquisition:

99mTc-PSMA SPECT/CT imaging was performed by a dual head gamma camera (Siemens; Symbia T). Three to four hours after IV administration of approximately 740 MBq (20 mCi) of 99mTc-PSMA, whole-body images were acquired in the supine position. SPECT/CT images for the pelvic regions were also added. Siemens software was applied to review planar and fusion SPECT/CT images.

Image interpretation

The images were evaluated visually by two experienced nuclear physicians. When the two physicians disagreed, a consensus was reached through discussion. Furthermore, the locations of abnormal uptake will be correlated with lesions detected by conventional imaging.

Standard reference of imaging results

Owing to ethical and practical reasons, not all lesions can receive pathology results. All available information, including pathology, 99mTc-MDP bone scans, CT, MRI, and clinical data, was used as a standard reference.

Statistical analysis

Data analysis was performed by SPSS software, version 25 (SPSS Inc., PASW statistics for windows version 25. Chicago: SPSS Inc.). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for nonnormally distributed data and mean± Standard deviation for normally distributed data after testing normality using Kolmogrov-Smirnov test.

The significance of the obtained results was judged at the (≤0.05) level.

• Chi-Square, Fisher exact test, Monte Carlo tests were used to
compare qualitative data between groups as appropriate

• One Way ANOVA test was used to compare more than 2
independent groups with Post Hoc Tukey test to detect pair-wise
comparison

• Interclass correlation was used to assess agreement between
continuous variables and good agreement was detected if interclass
correlation more than 0.7.

Results

Baseline characteristics

We studied 64 men referred for 99mTc PSMA SPECT/CT with elevated PSA and pathologically proven prostate cancer. The cause of referral was primary staging in 38 (59.4%) patients, Therapy response evaluation in 16 (25%) patients and biochemical recurrence in 10 (15.6%) patients.

The distribution of clinical data of the studied patients are shown in tables 1, 2 and 3:

The mean age of participants was (71.09 + 6.32) years (range: 59–83 years). The median PSA level was 100 ng/mL (range: 2.1–530 ng/mL), Grades 4 and 5 were most common representing 58.4% (28/48) of cases. Sixteen patients lacked documented Gleason scores. Most patients were classified as very high risk (54.7%), while intermediate and high risk classification represented in 14.1% and 31.3% of cases respectively. Most patients were classified as T2 (67.2%), while T3 and T4 stages were detected in 6.3% and 10.9% of cases, respectively. Inconclusive findings occurred in 15.6% of patients.

Findings from 99TcPSMA SPECT/CT:

Table 4 summarizes the findings showing:

40.6% of patients had prostate lesions only

31.3% had prostate lesions with positive regional LNs and distant mets

10.9% had prostate lesions with distant metastases-no regional LNs

9.4% had prostate lesions with positive regional LNs –and no distant mets

7.8% of our studied cases were negative for PSMA avid lesions T-Staging by Molecular Imaging (99mTc-PSMA) and its agreement with T staging by conventional imaging Molecular imaging identified T2 stage in 64% of our studied cases showing excellent agreement with T staging detected by conventional imaging with an interclass correlation of 0.969 (95% CI: 0.949–0.981) (Kappa value =0.864) as shown in tables 5, 6 Correlation of primary staging with ISUP Grade and Risk classification among 38 patients who were referred for primary staging.

Higher TNM stages detected by 99mTc PSMA (IVA & IVB) were significantly associated with very high risk classification and ISUP grades 4&5(p≤ 0.001) as shown in tables 7, 8 Also, N1&M1 status were predominantly classified as very high risk with p=0.02 &0.03 respectively as shown in tables 9, 10

Relation between 99mTc-PSMA findings and Gleason score, ISUP score, risk classification, PSA grade among studied cases (n=64) statistically significant associations observed between 99mTc PSMA+ findings and patient factors including Gleason's scores, ISUP grades, risk classification and PSA grades with p value 0.001 as shown in table 11

Comparative analysis

99Tc PSMA SPECT/CT had higher sensitivity compared to conventional imaging in detection of regional LN metastases with moderate agreement (K=0.63) as shown in table 12

Also, 99Tc PSMA SPECT/CT has been detected bone metastases more reliably than bone scans with moderate agreement (k=0.69) as shown in table 13.

Therapy response and recurrence detection

Among 16 patients underwent ADT 14 patients had positive 99mTc PSMA findings with significant association between imaging results and therapy response(p<0.001) as shown in table 14

Also, among 10 patients referred for biochemical recurrence 7patients had positive findings on 99mTc PSMA with a statistically significant association p<0.001 as shown in table 15

Discussion

Prostate cancer remains a significant health concern, and accurate diagnostic imaging is crucial for effective management. The assessment of prostatic carcinoma using technetium-99m
(99mTc) prostate-specific membrane antigen (PSMA) single photon
emission computed tomography/computed tomography (SPECT/CT) has
garnered increasing attention in recent years [5].

The aim of our study is to assess the diagnostic performance of 99mTc-PSMA SPECT/CT in assessment of prostate cancer and correlate its findings with the findings of conventional imaging to discover if it is useful in staging, restaging, and detection of recurrence in patients with prostatic carcinoma. We found an excellent agreement in T staging between 99mTc PSMA and conventional findings, with an interclass correlation of 0.969 (95% CI = 0.949 - 0.981) and Kappa value 0.864. Statistically significant associations were also observed between 99mTc-PSMA findings and Gleason scores, ISUP grades, risk classifications, PSA grades ($p<0.001$), and bone scan findings ($p<0.001$), highlighting the tracer's potential for improving clinical decision-making in prostate cancer management. We also found a statistically significant association.

between 99mTc-HYNIC- PSMA findings and restaging after administration of androgen deprivation therapy (ADT). Additionally, there was a significant correlation between 99mTc-PSMA findings and biochemical recurrence. Research indicates that there is a moderate correlation between 99mTc-PSMA uptake in the prostate and biopsy grade, presence of metastases, and PSA levels. This correlation is vital for tailoring treatment plans and improving prognostic accuracy.

The overarching goal of our study is to determine the utility of 99mTc-HYNIC-PSMA SPECT/CT in staging, restaging, and detecting recurrence in patients diagnosed with prostatic carcinoma.

In contrast, the study done by Werner et al., (2020) [6] which was investigating 99mTc-PSMA-I&S-SPECT/CT in prostate cancer imaging focuses on evaluating the performance of 99mTc-PSMA-I&S SPECT/CT for imaging prostate cancer across a broader patient population.

This study examines its diagnostic utility in various clinical scenarios, including primary staging, biochemical recurrence assessment, and restaging of advanced recurrent prostate cancer. The objective is to establish the sensitivity, specificity, and overall diagnostic accuracy of 99mTc-PSMA-I&S SPECT/CT in these contexts, with a particular emphasis on the detection rates of PSMA-positive lesions at different PSA levels.

In our study there were 48 patients graded according to the International Society of Urologic Pathology (ISUP), it was found that 34 patients (58.4%) had grades 4 and 5, while the remaining patients were classified as grades 1,2and 3. Notably, 16 patients were unable to provide documented Gleason scores and ISUP grades. The findings from the 99mTc-HYNIC-PSMA SPECT/CT indicated that 26 patients (40.7%) had positive prostate lesions without any regional lymph node or distant metastases, whereas 20 patients (31.3%) presented with positive prostate lesions alongside positive regional LNs and distant metastases.

In contrast, the study by Werner et al., (2020) [6] retrospectively evaluated 210 outpatients with prostate cancer using 99mTc-PSMA-I&S SPECT/CT, revealing a higher detection rate of PSMA-positive lesions in 65.2% of patients. The distribution of these lesions was primarily in lymph nodes (59%), bone (42%), and the prostate or prostatic fossa (28%). The study highlighted that the detection rates for biochemical recurrence (BCR) increased significantly with PSA levels, from 20% at PSA levels below 1 ng/mL to 82.9% and 100% at levels above 4 ng/Ml and 10 ng/mL, respectively.

In our study we demonstrate the effectiveness of molecular imaging using 99mTc-HYNIC- PSMA in assessing the T stage of prostate cancer among the studied cases. T2 stage emerged as the most prevalent, with 41 patients (64.1%) classified within this category. Among the 38 patients referred for primary staging who underwent TNM staging via 99mTc PSMA, a significant proportion was identified with advanced disease stages: 13 patients (34.2%) were classified as stage IVB, while 11 patients were categorized as stage IIIA. In analysis of the N staging in relation to risk classification, the findings revealed that for patients with N0; 30.7% have intermediate risk, 42.3% high risk and 26.9% very high risk and for cases with N1; 100% have very high risk classification.

Further analysis of the M staging revealed that among patients classified as M0; 32% have intermediate risk, 68% high risk and 0% very high risk and for cases with M1; 100% have very high risk classification.

The TNM staging results indicated that cases with stage II coincides with intermediate risk, cases with stage IIIA, IVA coincides with high risk and IVB that coincides with very high risk classification. Additionally, the TNM staging showed that stages II and IIIA coincide with grades 1,2&3 and stages IVA and IVB coincide with grades 4 and 5. Our study also found an excellent agreement in T staging between 99mTc PSMA and conventional loco-regional findings, with an interclass correlation of 0.969 (95% CI = 0.949 - 0.981) kappa value 0.864.

Statistically significant associations were observed between 99mTc- PSMA findings and Gleason scores, ISUP grades, risk classifications, PSA grades ($p<0.001$), and bone scan findings ($p<0.001$), highlighting the tracer's potential for improving

clinical decision-making in prostate cancer management.

These findings align with the overall trend of increasing risk associated with higher T and N stages, demonstrating the utility of 99mTc- PSMA in stratifying patients based on disease severity.

Similarly, Research by Zhang et al., (2022) [7] demonstrated that 99mTc-PSMA SPECT/CT outperformed 99mTc-MDP SPECT/CT in detecting bone metastases, particularly in patients with lower PSA levels.

Their findings indicated that 99mTc-PSMA not only provided superior sensitivity and specificity but also contributed to changes in treatment strategies for 14.9% of patients. This is consistent with our study's results,
which showed moderate agreement between 99mTc-HYNIC- PSMA SPECT/CT findings and bone scan findings with kappa value 0.69 Where 99mTc-PSMA scans revealed that 42 patients (65.6%) from the total sample of this study had free scans in comparison to 35 patients (54.7%)

who had free bone scans, while the rest of the 99mTc PSMA scans (34.4% from the total sample) revealed positive bone lesions. Among the negative PSMA patients, there were five patients (7.8% from the total sample) who previously had equivocal bone lesions in the bone scan, this means that 99mTc-PSMA SPECT/CT scan could exclude bone metastases these patients. On the other hand, there were 2 negative PSMA patients who previously had multiple bone lesions in the bone scan. These two patients previously underwent bone scan and revealed multiple bony metastases, then they received ADT and 99mTc-PSMA scan was scheduled one week later which showed no PSMA uptake in the previously detected bony lesions. It was assumed that this discordance is due to modulation of PSMA receptors by ADT therapy initiation [8].

Together, these studies underscore the growing consensus on the value of 99mTc PSMA in enhancing the diagnostic accuracy and management of prostate cancer patients.

The findings from our study indicate a statistically significant association between 99mTc-HYNIC-PSMA findings and restaging after administration of androgen deprivation therapy (ADT). Among the patients who received therapy, 14 patients (87.5%) exhibited positive 99mTc-PSMA findings, while only two patients (12.5%) were negative for PSMA-avid lesions (Explanation of this finding has been described above). Additionally, there was a significant correlation between 99mTc PSMA findings and biochemical recurrence; specifically, among patients
experiencing recurrence, 7 patients (70%) tested positive for recurrence,
whereas 3 patients (30%) were negative. These results suggest that 99mTc-HYNIC- PSMA imaging can effectively predict therapeutic response and recurrence in prostate cancer patients, underscoring its potential role in guiding treatment decisions.

Our findings regarding the relationship between 99mTc-PSMA imaging and restaging after ADT agree with the findings of the study of Werner et al., (2020) [6] which highlighted that patients undergoing ADT exhibited a higher detection rate of PSMA-positive lesions, with a detection rate of 90.3% compared to 70.7% in those not receiving ADT
($P = 0.0029$). This reinforces the notion that 99mTc-PSMA is particularly effective in identifying patients who are likely to respond to therapy. Furthermore, other studies, such as those by García-Pérez et al., (2018) [9] have also demonstrated a strong correlation between positive 99mTc PSMA findings and biochemical recurrence, with detection rates
significantly increasing in patients with higher PSA levels.

This is consistent with our findings, as both studies emphasize the importance of 99mTc PSMA in monitoring disease progression and guiding therapeutic strategies. According to our data 99mTc-HYNIC PSMA SPECT/CT seems to have a potential role in staging and restaging prostate cancer patients.

Figure 2 shows a case of 83 years old patient presented with pathologically proven prostatic carcinoma and elevated PSA level performed 99mTc-PSMA SPECT/CT for primary staging.

Total serum PSA level= 235.7 ng/ml
T stage detected by diagnostic CT: as T4
Risk classification: High risk
Figure 3 shows a case of A 62 years old patient presented with pathologically proven prostatic carcinoma and elevated PSA performed 99mTc-PSMA SPECT/CT for primary staging.
Total serum PSA level= 185.6 ng/ml
Gleason score 3+3=6, ISUP grade 1
T stage detected by MRI as T2
Risk classification: High risk

Limitations

1. Potential for false-positive and false-negative results: As with
any imaging modality, 99mTc-PSMA SPECT/CT may be subject to
false-positive and false-negative results, which may lead to over- or
underestimation of disease extent.
2. Potential for selection bias: The study included

patients with
elevated PSA levels and pathologically proven prostate cancer.
This selection process may limit the generalizability of the findings to the broader population of patients with suspected prostate cancer.

3. Potential for confounding factors: The study did not account for potential confounding factors, such as comorbidities, previous treatments, or other clinical variables, which may influence the interpretation of 99mTc-PSMA SPECT/CT findings.

4. Lack of long-term follow-up: The study did not report long-term outcomes, such as overall survival or progression-free survival, which are important endpoints for evaluating the clinical utility of 99mTc-PSMA SPECT/CT in prostate cancer management (make this one the last point).

Conclusion

1. The findings of this study demonstrate that 99mTc-PSMA
SPECT/CT is an effective imaging modality for identifying
significant stages of prostate cancer and stratifying patients based
on disease severity.
2. While variations in lesion detection between imaging modalities
were observed, 99mTc-PSMA SPECT/CT provides comprehensive
disease assessment, aiding in informed treatment decision-making.
3. Furthermore, the study highlights its potential as a cost-effective
alternative to PSMA PET imaging, particularly in regions with
limited access to PET/CT systems or PSMA PET tracers. This
positions 99mTc-PSMA SPECT/CT as a valuable tool for
expanding diagnostic and therapeutic capabilities in resource constrained
settings.

Recommendations

1. Incorporate 99mTc PSMA Imaging in Initial Diagnostic Workup 99mTc PSMA SPECT/CT should be routinely integrated into the diagnostic
.
evaluation for patients with prostate cancer due to its strong correlation with ISUP grades, T staging, and risk classification. This imaging modality significantly enhances the accuracy of staging and risk stratification, enabling more personalized and effective treatment strategies.

2. Implement 99mTc PSMA Imaging in Biochemical Recurrence

Detection Given the association between 99mTc PSMA findings and biochemical recurrence, this imaging technique is highly recommended for patients experiencing rising PSA levels following initial treatment. Early detection of recurrence allows fortimely therapeutic interventions and better long-term outcomes.

3. Utilize 99mTc PSMA Imaging to Monitor Therapy Response

The demonstrated relationship between positive 99mTc PSMA findings and response to androgen deprivation therapy (ADT) supports its use in monitoring treatment efficacy. Regular imaging assessments can help identify non-responders early, ensuring prompt adjustments to therapeutic plans.

4. Adopt a Patient-Centric Approach

Engage patients in discussions about the role of 99mTc PSMA imaging in their diagnostic and treatment processes. Educating patients on how imaging results guide clinical decisions can empower them and enhance their participation in managing their disease.

5. Provide Education and Training for Healthcare Professionals Training programs should be developed for clinicians and healthcare providers to familiarize them with the clinical utility of 99mTc PSMA imaging. Proper training ensures optimal application of this advanced imaging technique and maximizes its benefits in clinical practice.

6. Encourage Further Research and Validation

Larger, multi-center studies are necessary to validate the findings of this study across more diverse populations. Future research should also explore the combined use of 99mTc PSMA imaging with other diagnostic tools, such as MRI and PET, to further
improve diagnostic accuracy and treatment planning

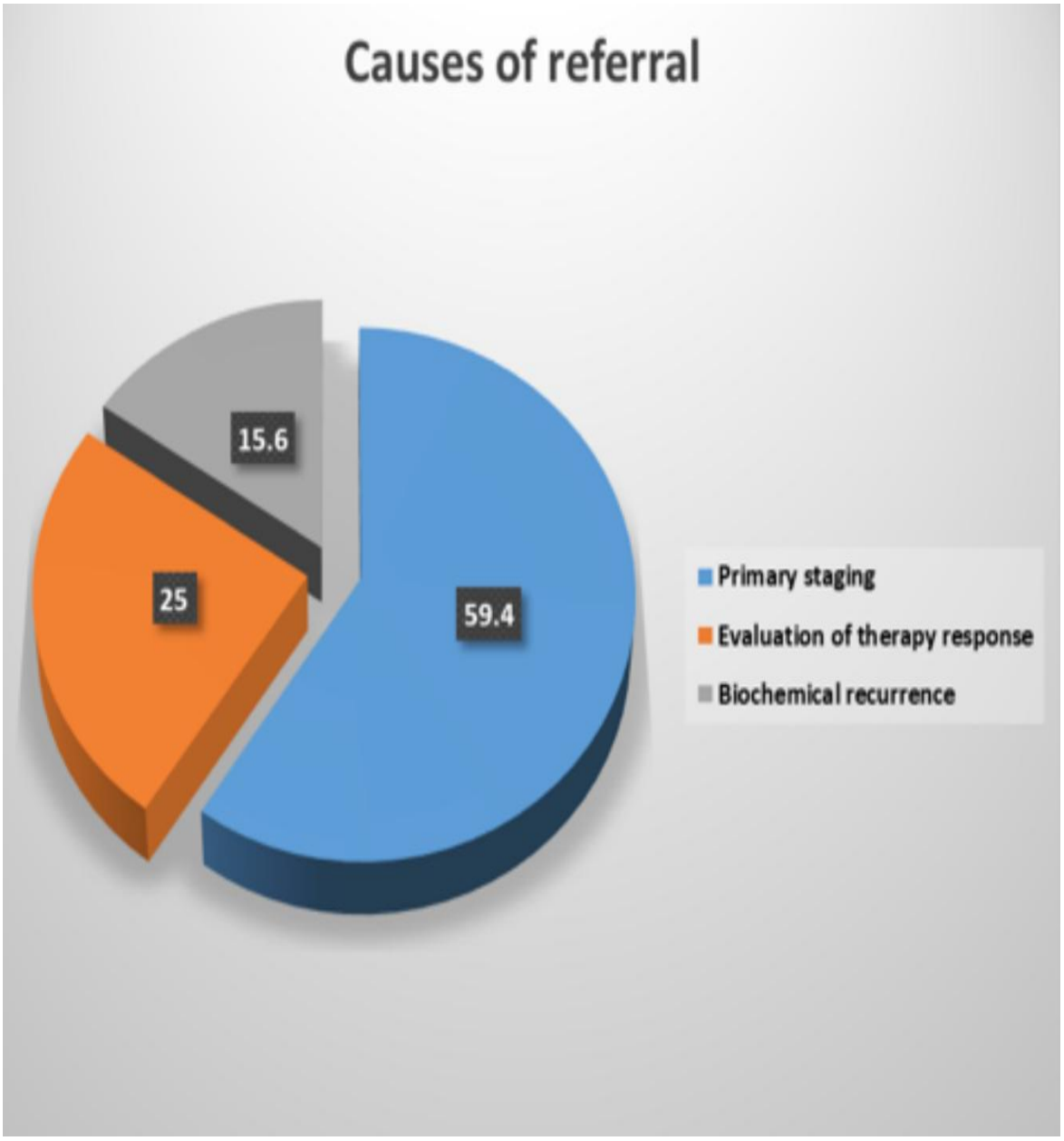

Figure 1 shows causes of referral among studied patients

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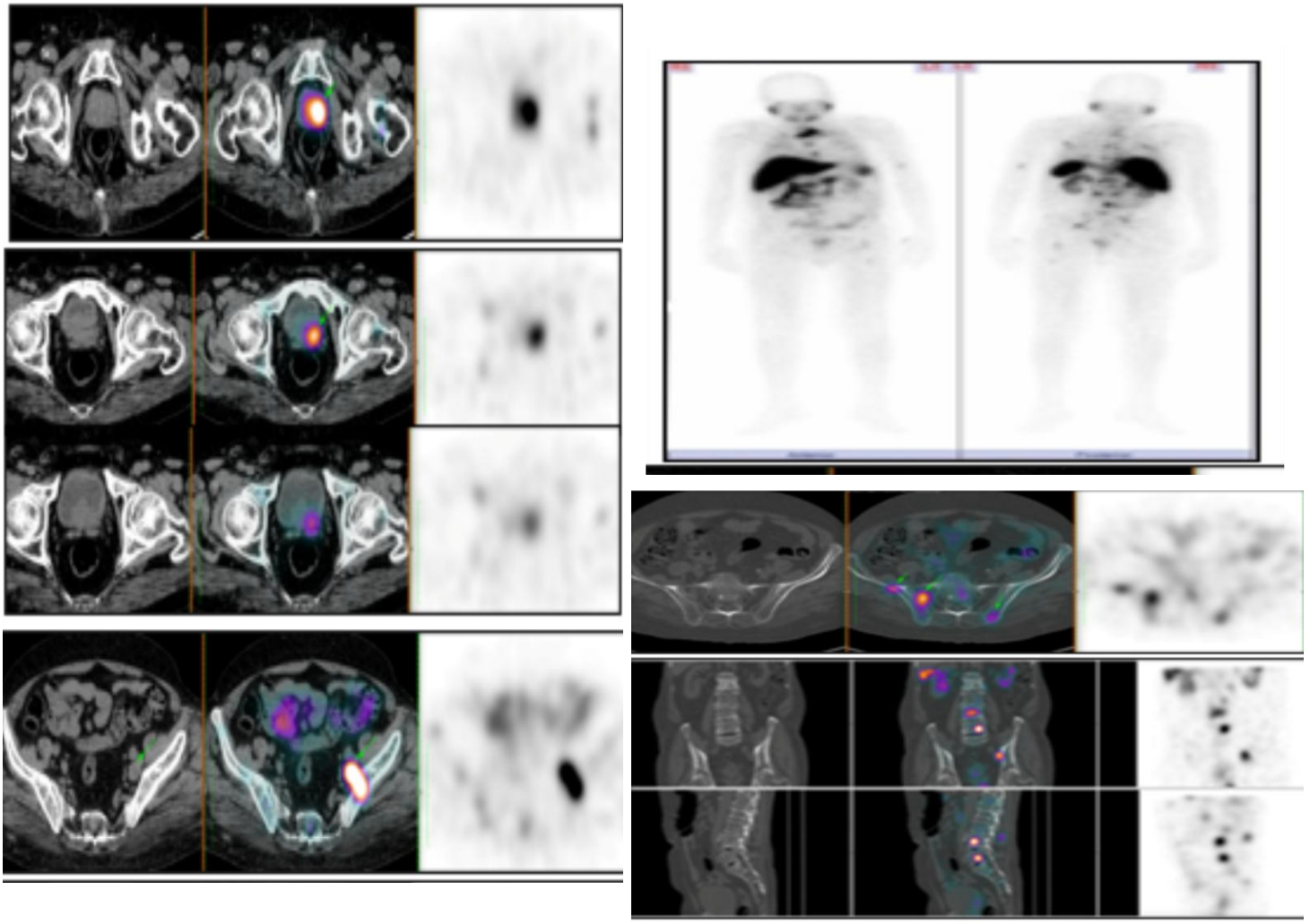

Figure 2. 99mTc PSMA SPECT/CT trans axial view(abdomen window)(A) trans-axial, coronal and sagittal views(bone window) (B) of the pelvis and planar anterior and posterior view (c) show PSMA avid prostatic lesion involving the transitional and peripheral zone of the gland at the left side with infiltration of the left seminal vesicle and urinary bladder wall.

PSMA avid metastatic pelvic lymph nodes including left external iliac and pre-vesical LNs.
Multiple PSMA avid metastatic sclerotic osseous lesions involving most of the lumber vertebrae, left iliac bone and proximal shaft of left femur. 99mTc-PSMA SPECT/CT staging T4N1M1b, Stage VIB. Staging based on AJCC manual 8th ed., 2017.

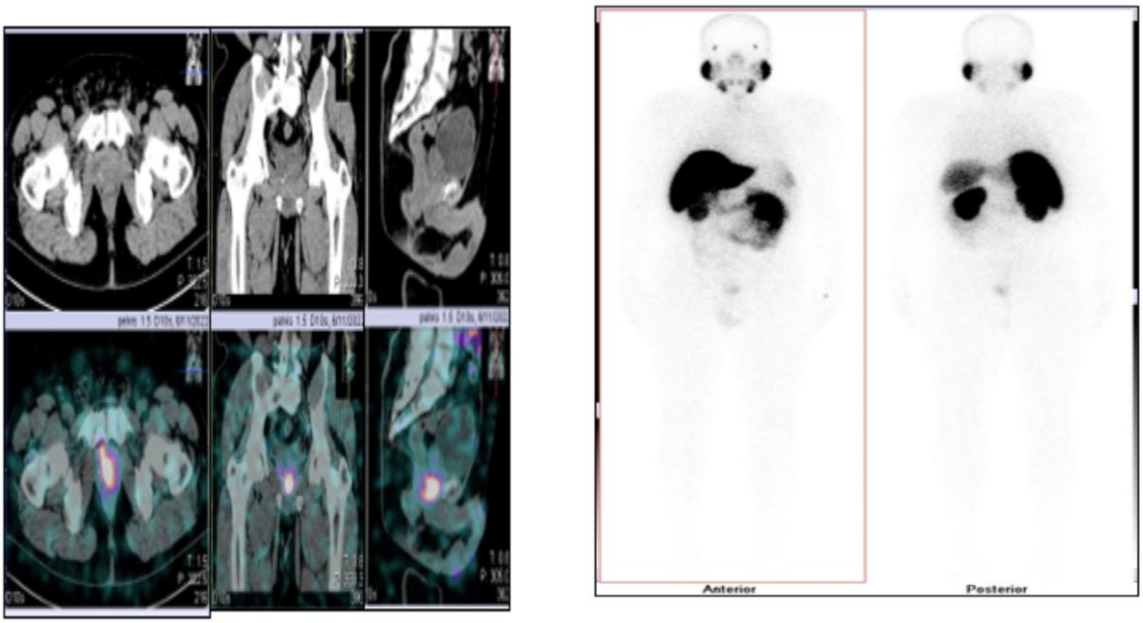

Figure 3. 99mTc PSMA SPECT/CT trans-axial, coronal and sagittal views (A) of the pelvis and planar anterior and posterior view(B) show Active PSMA uptake was seen at the prostatic gland involving the right peripheral and transitional zone of the mid gland and apex.
No evidence of PSMA avid pelvic lymph nodes.
No evidence of PSMA avid osseous deposits.

99mTc-PSMA SPECT/CT staging T2N0M0, Stage IIIA. Staging based on AJCC manual 8th ed., 2017. Gleason score 3+3, PSA 185.

Table (1): Age of the studied cases (n=64)

	Total number =64
Age/years Mean±SD (min-max)	71.09±6.32 (59-83)

Table (2): Gleason score, ISUP grade, Total PSA and risk classification among studied cases (n=64)

	N	**%**
Gleason's Score - *Median (min-max)*	8 (6 -10)	
ISUP grade	N=48	
- Grade 1	6	12.5
- Grade 2	8	16.7
- Grade 3	6	12.5
- Grade 4	14	29.2
- Grade 5	14	29.2
Total PSA (ng/ml)	100 (2.1 – 530)	
- ≤20	23	35.9
- >20	41	64.1
Risk classification.	N=64	
- Intermediate	9	14.1
- High	20	31.3
- Very high	35	54.7

Table (3): T stage as detected by conventional imaging (CT or MRI or TRUS) among studied cases (n=64)

	N	%
T2	43	67.2
T3	4	6.3
T4	7	10.9
Inconclusive findings	10	15.6
Total	64	100.0

Table (4): ^{99m}Tc-PSMA SPECT/CT findings of the studied cases (n=64)

^{99m}Tc PSMA SPECT/CT findings	N=64	%
Negative for PSMA avid lesions	5	7.8
Positive prostate lesion with no regional LNs or distant metastases.	26	40.6
Positive prostatic lesion, positive regional LNS with distant metastases	20	31.3`
Positive prostate lesion with positive regional LNS & no distant metastases	6	9.4
Positive prostate lesion with distant metastasis –no regional LNs	7	10.9

Table (5): T stage as detected by molecular imaging (^{99m}Tc-PSMA)

	N	%
Negative for recurrence	3	4.7
T1	2	3.1
T2	41	64.1
T3	4	6.3
T4	7	10.9
Tr	7	10.9
Total	64	100.0

Table (6): Kappa agreement of T staging between ^{99m}Tc-PSMA & conventional loco-regional findings

	T stage
ICC (95%CI)	0.969 (0.949-0.981)
Kappa value	0.864

ICC: Interclass correlation, CI: Confidence interval

Table (7): Relation between Stages detected by ^{99m}Tc-PSMA and risk classification among 38 patients who referred for primary staging (n=38)

	^{99m}Tc-PSMA				Test of significance
	Stage II	Stage IIIA	Stage IVA	Stage IVB	
	n(%)	n(%)	n(%)	n(%)	
Risk classification					
- Intermediate	8 (100)	0	0	0	$\chi^{2MC} = 38.1$
- High	0	11 (100)	0	0	P ≤ **0.001***
- Very high	0	0	6 (100)	13 (100)	

Table (8): Relation between disease stage detected by ^{99m}Tc-PSMA and ISUP grade among 38 patients who referred for primary staging (n=38)

	^{99m}Tc-PSMA (TNM staging)				Test of significance
	Stage II	Stage IIIA	Stage IVA	Stage IVB	
	n(%)	n(%)	n(%)	n(%)	
ISUP grade					
- Grade 1	0	6 (54.5)	0	0	χ^{2MC} = 93.8
- Grade 2	2 (12.5)	5 (45.5)	0	0	P ≤ **0.001***
- Grade 3	6 (87.5)	0	0	0	
- Grade 4	0	0	6 (100)	2 (15.4)	
- Grade 5	0	0	0	11(84.6)	

χ^{2}: Chi-Square test, MC: Monte Carlo test. *: significant p ≤ 0.05.

Table (9): Relation between N staging by ^{99m}Tc-PSMA and risk classification among 38 patients who were referred for primary staging (n=38)

	^{99m}Tc-PSMA		Test of significance
	N0	N1	
	n (%)	n (%)	
Risk classification			
- Intermediate	8 (30.8%)	0	FET
- High	11 (42.3%)	0	P= **0.03***
- Very high	7(26.9%)	12 (100%)	

FET: Fisher's Exact Test. *: significant p ≤ 0.05.

Table (10): Relation between M staging detected by ^{99m}Tc-PSMA and risk classification among 38 patients who referred for primary staging (n=38)

	^{99m}Tc-PSMA		Test of significance
	M0	M1	
	n (%)	n (%)	
Risk classification			FET
- Intermediate	8 (32.0%)	0	P= **0.02***
- High	17 (68.0%)	0	
- Very high	0	13 (100.0%)	

FET: Fisher's Exact Test. *: significant p ≤ 0.05.

Table (11): Relation between ^{99m}Tc-PSMA findings and Gleason score, ISUP score, risk classification, PSA grade among studied cases (n=64)

	^{99m}Tc-PSMA					Test of significance
	0 Negative for PSMA avid lesions	**1 Positive prostate, no regional LNs or distant metastases**	**2 Positive prostate, positive regional LNS with distant metastases**	**3 Positive prostate, positive regional LNS & no distant metastases**	**4 Positive prostate, no regional LNs with distant metastases**	
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	
Gleason score Mean ±SD	8 ± 1.0	7.9 ± 1.2	9.0 ± 0.9 ^{ab}	7.0 ± 0 ^{bac}	9.0 ± 0.1^{cb}	F= 4.8 P= **0.003***
ISUP grade - 1 - 2 - 3 - 4 - 5	 0 1 (33.3) 0 1 (33.3) 1 (33.3)	 6 (23.1) 1 (3.8) 6 (23.1) 11 (65.4) 2 (7.7)	 0 0 0 2 (33.3) 4 (66.7)	 0 6 (100) 0 0 0	 0 0 0 0 7 (100)	χ^{2MC} = 65.2 P ≤ **0.001***
Risk classification - Intermediate - High - Very high	 2 (40) 1 (20) 2(40)	 13 (50) 13 (50) 0	 0 0 20 (100)	 0 0 6 (100)	 0 0 7 (100)	χ^{2MC}= 18.2 P= **0.001***
PSA grade - ≤20 ng/ml - >20 ng/ml	 5 (100) 0	 15 (57.7) 11 (42.3)	 3 (15) 17 (85)	 0 6 (100)	 0 7 (100)	χ^{2MC} = 25.4 P ≤ **0.001***
PSA grade *(ng/ml)* *Median (min – max)*	3 (2.1- 20)	17.5 (2.3-220)	90 (10 – 320)	115 (102 – 170)	340 (200- 530)	KW= 26.3 P ≤ **0.001***

F; One Way ANOVA test, χ^2= Chi-Square test, MC: Monte Carlo test, KW: Kruskal Wallis test *: significant p ≤ 0.05

Similar superscripted letters denote significant difference between studied groups within same row by Post Hoc Tukey test

Table (12): Comparison between conventional locoregional imaging and ^{99m}Tc-PSMA in detection of regional LN metastases.

Regional LN metastases	Conventional locoregional imaging N (%)	^{99m}Tc-PSMA SPECT CT N (%)	Value of Kappa
Negative	40 (62.5%)	41 (64.1%)	
Positive	24 (37.5%)	23 (33.9%)	
Total	**64 (100%)**	**64 (100%)**	**0.63**

Table (13): Comparison between bone scan and ^{99m}Tc-PSMA in detection of bone metastases.

Bone metastases	Bone scan N (%)	^{99m}Tc-PSMA SPECT CT N (%)	Value of Kappa
Free	35 (54.7%)	42 (65.6%)	**0.69**
Positive	24 (37.5%)	22 (34.4%)	
Equivocal	5 (7.8%)	0	
Total	**64 (100%)**	**64 (100%)**	

Table (14): Relation between ^{99m}Tc-PSMA findings and response to androgen deprivation therapy among studied cases

	^{99m}Tc-PSMA		Test of significance
	Negative N(%)	Positive N(%)	
Androgen Deprivation Therapy -ve (n=48) +ve(n=16)	 0 2 (12.5)	 48 (100.0) 14 (87.5)	 χ^2=17.9 P<0.001*

*statistically significant, χ^2: Chi-Square calculator test

Table (15): Relation between ^{99m}Tc-PSMA findings and detection of recurrence among studied cases who referred for biochemical recurrence.

Recurrence by ^{99m}Tc-PSMA	Biochemical recurrence		Test of significance
	Negative N(%)	Positive N(%)	
-ve	54(100)	3(30)	χ^2= 26.8
+ve	0(0.0)	7(70)	P < 0.001*

χ^2: Chi-Square calculator test

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