^{18}F FDG PET-CT in Evaluation of Prostate Cancer – Experience at NINMAS

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ABSTRACT

Background: Fluorine-18 Fluorodeoxyglucose positron emission tomography-computed tomography (18F FDG PET-CT) is the most widely used oncologic imaging tool. However, due to some limitations and with the advent of newer disease-specific tracers 18F FDG is not routinely recommended in prostate cancer. However, in a developing country like Bangladesh with a growing cancer burden and where 18F FDG is an available tracer, we have tried to describe our experience in detecting the extent of disease in PCa.

Methods: Retrospectively reviewed data of 18F FDG PET-CT of total 25 prostate cancer patients referred to National Institute of Nuclear Medicine and Allied Sciences (NINMAS) from February, 2021 to August, 2023 were included. Each patient's PET-CT findings were reviewed in relation with histologic grade, Gleason's score and serum PSA level.

Results: Among the 25 patients with two patients came for baseline scan. 23 patients came for follow up evaluation with mean time for follow up from diagnosis being 26.8 months and all of them received treatment according to stage and standard guideline. In thirteen patients (52%) 18F FDG PET scan was negative with mean PSA 4.2 ng/ml and most of them (85%) were in grade group 2 and 3 with low Gleason's score (6 to 7). 18F FDG PET was positive in 12 patients (48%) including the two patients who came for baseline staging with mean PSA 145.46 ng/ml. Those two patients had isolated focal hypermetabolic lesion in prostate. Rest of the 10 patients with positive PET scan found high serum PSA level (mean PSA 167.67 ng/ml) with Gleason's score 8 to 10 and histologically all patients had poorly differentiated adenocarcinoma.

Conclusion: 18F FDG PET-CT can detect presence of disease in prostate cancer in follow up cases with raised PSA level and with high grade group or Gleason's score at the time of diagnosis. 18F FDG PET-CT can be a valuable tool for diagnosis of recurrence/metastases and follow up of prostate cancer in a cost-effective way in a developing country like Bangladesh.

18F FDG PET-CT effectively detects prostate cancer in high-grade cases, providing a cost-effective method for recurrence and metastatic diagnosis in developing countries like Bangladesh.

Keywords: Prostate cancer, ^{18}F FDG PET-CT, Biochemical recurrence.

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INTRODUCTION

In developing countries, prostate cancer (PCa) is the most prevalent non-cutaneous cancer and second most common cause of cancer-related mortality that affects men in older age group (1, 2). There are around 1.3–1.5 million PCa patients in Bangladesh, however only 0.2 million of them received a diagnosis each year (Strategy, 2009–15; Global Burden National Cancer Control of Disease Study, 2013) (3). Despite major advances, Current diagnostic techniques are not accurate enough to manage the condition effectively. Particularly, improved techniques are required to locate disease foci inside the prostate at the time of primary diagnosis, locate metastatic sites at that time, locate recurrent disease foci upon biochemical recurrence (BCR) following primary treatment, and quantify disease response in relation to the underlying biology. The return of measurable PSA is known as BCR, but it does not guarantee that a patient will experience a clinically significant recurrence or death from their illness. Studies have shown that only about 30% of patients with BCR following primary surgery experience a clinical recurrence (4).

According to current guidelines, disease staging with conventional imaging modality, which includes whole-body bone scintigraphy and CT or MRI of the abdomen and pelvis, is advised for patients with BCR and intermediate-to high-risk PCa (5,6).However, these techniques often underestimate the extent of metastatic illness. Lesions smaller than the 8–10 mm threshold are often missed by anatomical imaging modalities like CT or MRI, which diagnose metastatic illness only based on

morphological markers (7,8).In contrast, regions with benign degenerative alterations may be misinterpreted for osteoblastic osseous metastases on a bone scan, while malignant lytic bone lesions may show minimal uptake (9).Various alternative imaging approaches have been introduced in response to the unmet requirement for precise localization and staging of primary and recurrent PCa. At this point, the PET-CT has been the most thoroughly investigated and promising. Combining these sets allows functional imaging to be added to high-resolution 3D anatomical reconstructions (10).

Walker et al. said that novel PET radiotracers, such as 11C/18F Choline and ^{18}FFluciclovine, have been developed because of to the limitations of FDG in PCa. These radiotracers target different components of tumor metabolism, instead of glucose uptake. More recently, and with more success, radiotracers that target the prostate-specific membrane antigen (PSMA) have been introduced. In early clinical investigations, even more recent PSMA targeted tracers appear promising and continue to be released. In addition, ^{18}F labeled sodium fluoride (NaF) can be used to identify bone metastases, while ^{68}GaDOTATATE can identify advanced neuroendocrine prostate tumors (11).

However, because of a few drawbacks and the introduction of more recent disease-specific tracers, ^{18}F FDG PET-CT is not routinely advised in the case of PCa. In Bangladesh, where cancer rates are increasing and ^{18}F FDG is available the experiences in determining the disease extent in referred patients are shared.

PATIENTS AND METHODS

This retrospective study was conducted at the PET-CT division in National Institute of Nuclear Medicine & Allied Sciences (NINMAS), Dhaka. Patients' records were collected from the record section after obtaining proper permission. A total of 25 patients with PCa referred to NINMAS from February, 2021 to August, 2023for either baseline scan, treatment response evaluation or to detect recurrence. The demographic characteristics of histopathological grading as well as Gleason's score, serum PSA level and PET-CT characteristics were analyzed.

RESULTS

This study included a total of 25 patients, whose mean age was 70±7.8 years. All of the patients underwent treatment in accordance with stage and standard guidelines. Two patients came for a baseline scan, which indicates an early stage of the disease, and 23 patients came for a follow-up evaluation. The mean follow-up period from diagnosis was 26.8 months.

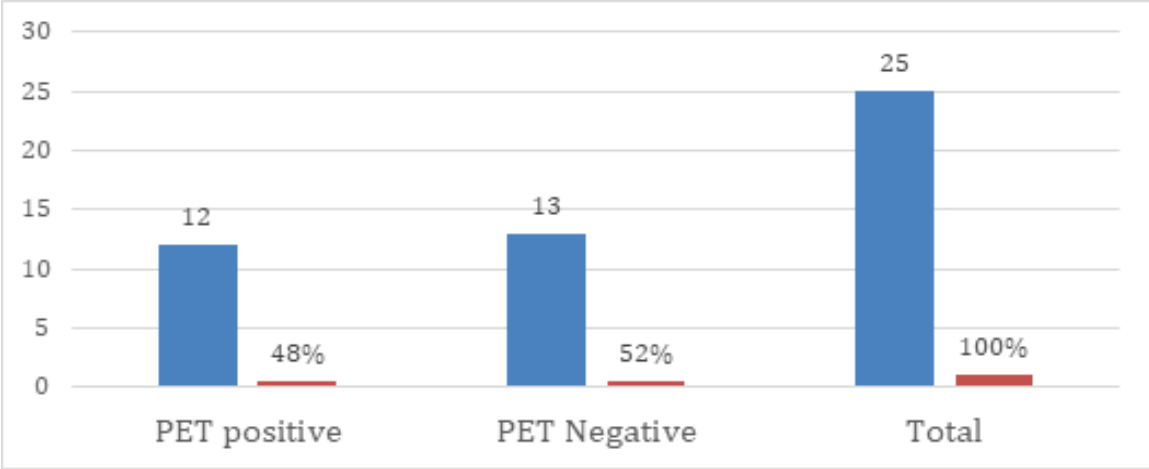

Figure 1: PET-CT scans of the patients under study revealed both positive and negative results.

With PSA levels and Gleason's scores of 66.2 ng/ml, 6.6 ng/ml, and 8 (6), two patients with baseline scans exhibited focal hypermetabolic lesions in the prostate without any distant metastases. The majority of the patients (85%) were in grading groups 2 and 3 with low Gleason's scores (6 to 7), and thirteen patients (52%), had a negative 18F FDG PET scan with a mean PSA of 4.2 ng/ml. Twelve patients (48%), including the two who arrived for baseline staging and had elevated serum PSA levels (mean PSA 145.46 ng/ml), had ^{18}F FDG PET results.

The SUVmax of the primary tumor in the two individuals' isolated focal hypermetabolic lesions in the prostate was high (11.3 and 12.6, respectively). Gleason's scores for the remaining ten patients with positive PET scans ranged from 8 to 10, indicating elevated blood PSA levels (mean PSA 167.67 ng/ml). Every patient had a poorly differentiated adenocarcinoma, according to histology. Six of the ten patients show involvement in more than one site. Seven individuals had lymph nodes as the most common site of metastases, with six patients having bone metastases. Three individuals experienced prostate bed recurrence, and one of them experienced isolated prostate bed recurrence. One patient had peritoneal and rectal infiltrations with nodal metastases, and another patient had liver metastases in addition to bone and lymph node metastases.

Table 1: Histopathological, biochemical, therapy pattern/method, and PET-CT results of the patients (n= 25)

Sl.	Age (years)	Surgery -Yes (√) /No (x)	CT- Yes (√) /No (x)	RT-Yes(√) /No (x)	ADT- Yes(√) /No(x)	Gleason's score	Grade	Follow up period (months)	PSA	PET-Positive (√)	PET-Negative (x)	Sites of positive lesions
1	67	x	√	x	√	8	4	12	73.2	√		prostate, skeleton
2	67	x	√	x	x	8	4	27	5.49	√		lymph nodes, skeleton
3	62	√	x	√	x	9	5	44	54.15	√		lymph nodes, liver, skeleton
4	69	√	x	√	x	9	4	84	1.62	√		prostate bed, lymph node, skeleton
5	69	√	√	x	x	10	5	13	11.8	√		prostate bed, lymph node, skeleton
6	52	√	√	√	x	8	4	18	12.2	√		lymph nodes
7	68	x	√	x	x	8	4		49.8	√		skeleton
8	72	x	√	√	√	8	4	58	269	√		lymph nodes, rectum and peritoneum
9	85	√	x	x	x	9	5	2	9.5	√		prostate bed
10	78	√	√	x	x	8	4	14	1190	√		lymph nodes
11	86	x	x	x	x	8	4	-	62.2	√		prostate
12	74	x	x	x	x	6	2	-	6.66	√		prostate
13	68	√	x	x	√	7	2	2	0.05		x	
14	73	x	√	√	x	7	2	36	0.12		x	
15	65	√	x	√	√	8	4	90	11.4		x	
16	73	x	√	√	x	7	2	100	4.94		x	
17	68	x	x	x	√	6	2	3	0.95		x	
18	65	√	x	x	√	6	2	7	9.1		x	
19	55	√	x	√	x	6	2	28	0.01		x	
20	70	x	√	x	x	7	2	8	0.158		x	
21	65	√	x	x	x	7	2	8	1.51		x	
22	77	√	√	x	√	8	4	18	0.16		x	
23	67	√	√	√	x	5	1	86	0.008		x	
24	80	x	x	x	x	7	2	9	26		x	
25	75	x	x	x	√	7	3	5	0.21		x	

*CT-Chemotherapy, RT-Radiotherapy, ADT- Androgen deprivation therapy

Table 2: Histopathological grade and Gleason's score at the time of diagnosis

Types of cancer	Histopathological Gleason's Score of prostate carcinomas	N=25 Number (%)
Low Grade Cancer	6 or less	05(20%)
Medium Grade cancer	3+4=7	06(24%)
Medium Grade Cancer with more abnormal cell	4+3=7	01(04%)
High Grade Cancer	8	09 (36%)
High Grade Cancer	9-10	04 (16%)

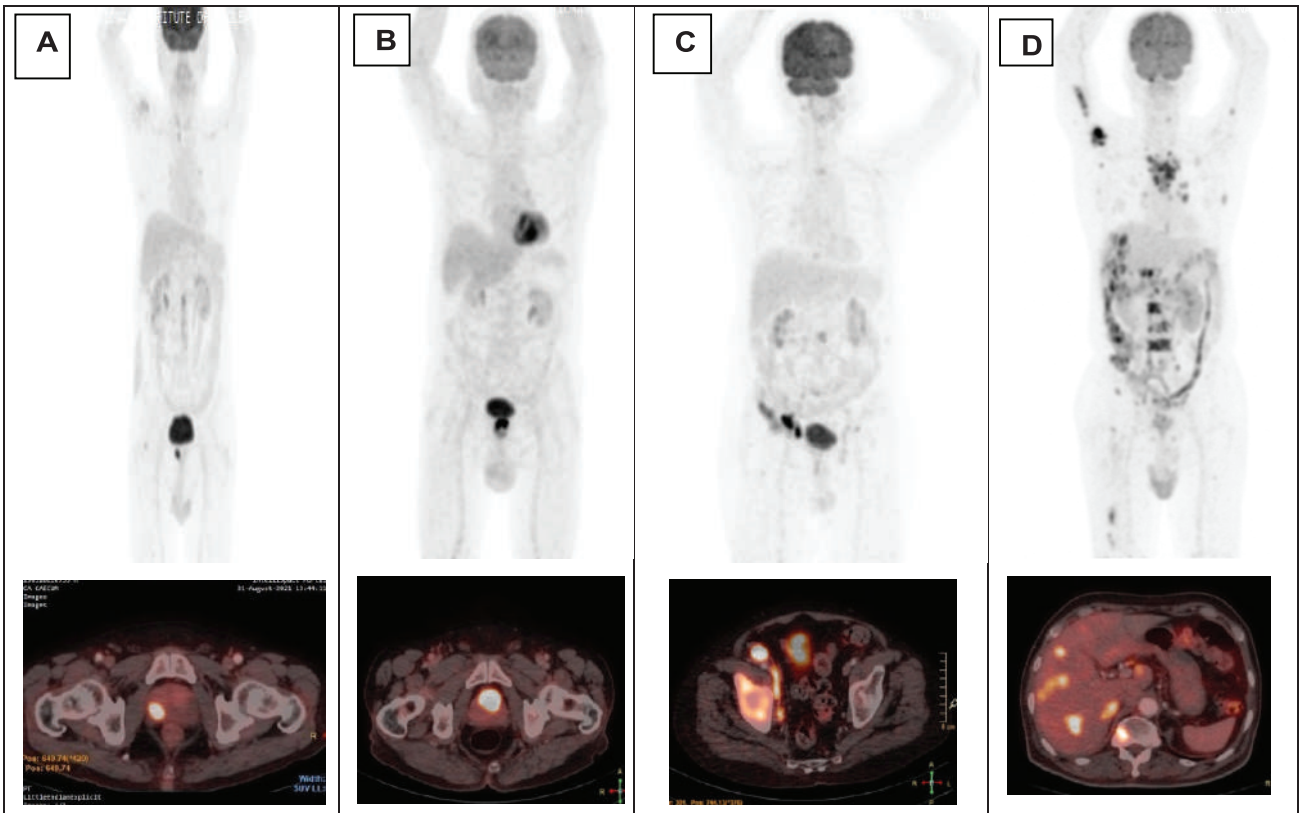

Figure: A) Maximum Intensity Projection (MIP) and Trans- axial fused PET-CT image of a 74 years old male patient having hypermetabolic lesion in prostate with PSA 6.66 ng/ml at baseline scan (Grade 2; Gleason's score 6).

Figure: B) MIP and Trans- axial fused PET-CT image of a 85 years old male patient having isolated hypermetabolic lesion in prostate with PSA 9.5 ng/ml at follow up scan with Grade 5 and Gleason's score 10.

Figure: C) MIP and Trans-axial fused PET-CT image of a 69 years old male patient having hypermetabolic metastases in bone and pelvic lymph nodes with PSA 11.8 ng/ml; Grade 5 and Gleason's score 10.

Figure: D) MIP and Trans- axial fused PET-CT image of a 62 years old male patient having extensive hypermetabolic metastatic lesions involving liver, lymph nodes and skeleton with PSA 54.1 ng/ml Grade 5 and Gleason's score 9.

Figure 2: PET-CT findings (Maximum Intensity Projection-MIP and Tans-axial fused PET-CT images) of four representative cases with serum PSA level and Gleason's score

DISCUSSION

The diagnosis of PCa is typically based on blind, systemic biopsies taken under ultrasound guidance when the condition is suspected due to elevated prostate-specific antigen (PSA) or abnormal digital rectal examination; however, multiparametric MRI (mpMRI) only indirectly shows tumor aggressiveness. Jadvar H et al. reported that molecular imaging with PET-CT has been widely explored over the last several decades to localize and assess disease extent (13). ^{18}F FDG is the most commonly used PET radiotracer used to assess neoplastic disorders generally; the tumors absorb FDG more readily than glucose, indicating more metabolic activity and tumor aggressiveness (14).

Early detection of PCa is important because cancer confined to the prostate gland is often curable. The diagnosis of PCa is usually based on blind, systemic biopsies taken under ultrasound guidance when the condition is suspected due to elevated prostate-specific antigen (PSA) or abnormal digital rectal examination. The sensitivity of ultrasound is limited. However, tumor aggressiveness is only indirectly shown by multiparametric MRI (mpMRI). Jadvar H et al. reported that to localize and assess disease extent, molecular imaging with PET-CT has been widely explored over the last several decades (13). ^{18}F FDG is the most widely used PET radiotracer used to assess neoplastic disorders generally. An analog of glucose, FDG is absorbed more readily in tumors, indicating more metabolic activity and tumor aggressiveness (14).

According to our findings, the majority of PCa patients mean age was 70±7.8 years, with rates declining both above and below that age range. It is generally considered a cancer of the elderly, and the median age of presentation is 68 years, which is consistent with our study (15).

Out of the 25 patients in this study, two underwent a baseline scan following diagnosis, and the PET-CT scan revealed positive results limited to the prostate bed. One of them had a high Gleason score, and both had elevated PSA values. Jadvar H et al. reported that 18F FDG PET-CT has demonstrated limited utility in the relevant natural history of PCa because most early cases of PCa exhibit poor glucose metabolism (13). On the other hand, the study by Liu Y presented findings from a retrospective study indicating that while ^{18}F FDG PET-CT is generally not effective for detecting primary PCa, it may be beneficial for initial staging in specific subgroups with elevated serum PSA levels (16).

One of ^{18}F FDG PET-CT's main uses in cancer has been to objectively evaluate how well different treatments are working at different stages of the disease's clinical management, including neoadjuvant, adjuvant, primary, or palliative settings. Overall, there is a paucity of information on the use of ^{18}F FDG PET-CT in imaging to assess treatment response in patients with metastatic prostate cancer. With androgen deprivation therapy (ADT) or chemotherapy, FDG uptake in metastatic lesions tends to decrease; however, individual lesions may exhibit mixed changes, the overall changes may be inconsistent with changes in serum PSA levels or circulating tumor cells, and most importantly, depend on the response criteria used (12). In our study, 23 patients came for follow-up evaluation with a mean time for follow-up from diagnosis being 26.8 months, and all of them received treatment according to the stage of the disease and standard guidelines. Eight patients were removed from androgen deprivation therapy, with six patients negative and two having positive PET-CT findings. GiovacchiniG et al. also reported that the accuracy of ^{18}F FDG PET-CT scans declines after receiving ADT (17).

Thirteen patients (52%) had negative 18F-FDG PET scan with a mean PSA of 4.2 ng/ml, and most of them (85%) were in grade groups 2 and 3 with low Gleason's scores (6 to 7). Evangelista et al. reported that patients with a PSA value greater than 2 ng/mL had a higher 18F FDG PET-CT detection rate for all disease sites; this rate plateaued at 80–85% for PSA values greater than 10 ng/mL (18). In this study, ten patients with positive PET scans found high serum PSA levels (mean PSA 166.7 ng/ml) with Gleason's scores of 8 to 10.

Piert M et al. compared the tumor-to-background PET SUV ratios with prostatectomy Gleason's scores. They found significantly higher tumor-to-background SUV

ratios in high Gleason score lesions (Gleason ≥4 + 3) versus lower Gleason's score lesions (Gleason ≤3 + 4) (19). In this study, three patients with positive PET scans were found with Gleason's scores of 9, 9, and 10 after prostatectomy.

Our result additionally highlights the value of using ^{18}F FDG PET scans following initial treatment with androgen deprivation therapy or radical prostatectomy in disease progression to metastases, in recurrence, in treatment resistance, etc. Published data supports that ^{18}F FDG PET-CT, together with bone scans, PSMA, MRI, CT, and other imaging modalities, has been widely utilized to monitor the results of treatment and surveillance in PCa (20).

Increased glucose metabolism is one of the dedifferentiation mechanisms that can be detected by an ^{18}F FDG PET scan. The Warburg phenomenon describes the overconsumption of glucose via aerobic glycolysis by cancer cells, even when there is enough oxygen present. Although other cancer cell types experience the Warburg effect early in their transformation phase, PCa cells only transition to a higher glycolytic rate when they have progressed. According to preclinical research, patients with metastatic castration-resistant prostate cancer can experience metabolic glucose reprogramming and become resistant to treatments that target the androgen receptor (AR) (21). The Gleason score and PSA are linked with the diagnostic value of ^{18}F FDG PET-CT (22).

^{18}F FDG PET-CT plays a valuable role in the diagnosis of recurrence/metastases and follow-up of PCa in a cost-effective way. However, aggressive PCa results in increased glucose metabolism, which enables the tumors to be detected by ^{18}F FDG PET-CT. The Gleason score and PSA are linked with the diagnostic value of ^{18}F FDG PET-CT (22).

Our study has some limitations. The main limitation is its retrospective nature. Also, no prognostic evaluation was made. Moreover, the response to different treatments at a specific time period was not evaluated. These limitations arise from some crucial factors, e.g., the scarcity of PET-CT centers leading to an overflow of patients and schedule overload. So patients cannot always be evaluated at a defined time period. But all these limitations can be overlooked in the weight of the value of this study, as this is the first study that can serve as an important tool for the clinician about the usefulness of the ^{18}F FDG PET-CT scan, a molecular imaging method in the management of PCa patients in Bangladesh, and that is also in a cost-effective way.

CONCLUSION

Prostate cancer patients with biochemical recurrence with raised Gleason scores at diagnosis are most likely to benefit from ^{18}F FDG PET-CT scans, as they can detect the presence of disease in follow-up cases. Aggressive and dedifferentiated prostate cancer results in increased glucose metabolism, which enables the tumors to be detected by ^{18}F FDG PET-CT scan. So ^{18}F FDG PET-CT imaging has the potential to improve knowledge about the glucose metabolism in prostate cancer and can serve as a good prognostic tool as such while doing so in a cost-effective way.

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