# $^{18}$F-FDG PET-CT in Re-staging Post-operative Renal Cell Carcinoma: A Five-year Experience in INMAS Dhaka

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## ABSTRACT

***Background:*** Renal cell carcinoma (RCC) includes a wide variety of histopathologic subtypes. About 25–30% patients present with metastatic disease initially and 20%-40% patients later develop distant metastases. Accurate re-staging of disease as early as possible is crucial for optimum therapeutic decision and alters outcome of patients. F-18 FDG PET-CT plays a vital role in effective postoperative surveillance and restaging with high sensitivity, specificity, and accuracy.

***Materials & Methods:*** This prospective observational study included 67post-operative patients with renal cell carcinoma who were referred to Institute of Nuclear Medicine and allied sciences, Dhaka for an $^{18}$F FDG PET scan during the period of July, 2019 to July, 2024. PET-CT was performed with 'Philips 128 slice ingenuity TF PET CT' machine 60 minutes after intravenous administration of radiopharmaceutical. Semi-quantitative estimation of FDG uptake was performed by calculating SUVmax value, corrected for dose administered and body weight (g/ml).

***Results:*** 16 out of 22 patients with suspected metastases in other imaging modalities were positive in $^{18}$F FDG PET-scan. 22 new metabolically active distant metastatic foci without previous evidence were detected. 8 new locoregional recurrences were found. In total,35 patients had distant metastases in 114 foci among which lymph node (41 foci, comprising of 34 %) & lung (27 foci, comprising of 22.5 %) were the commonest sites. The other metastatic foci were present in adrenal glands (12 foci), peritoneum (7 foci), pleura (4 foci), bones (12 foci), soft tissue (8 foci), muscle (4 foci), liver (3 foci), brain (1 foci) & opposite kidney (1 foci).

***Conclusion:*** Our study was done to find the impact of $^{18}$F FDG PET-CT in restaging of post-operative cases due to RCC.

***Keywords:*** Renal cell carcinoma, re-staging, $^{18}$F FDG PET-CT, local recurrence, metastases.

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## INTRODUCTION

Renal cell carcinoma (RCC) includes a wide variety of histopathologic subtypes and accounts for about 3% of all cancers worldwide (1, 2). In 2020, there were an estimated 431,288 new cases of RCC globally (3). Though more common in western world, it is not rare in Asian countries like ours. Overall, 5-year survival rate of RCC is 68.4% (4). Localized cases are surgically treated &usually have favorable outcomes whereas about 25–30% patients present with metastatic disease initially and 20%-40% patients later develop distant metastases.

Unlike most of the malignancies, impact of 18F-fluorodeoxyglucose positron emission tomography–computed tomography scan ($^{18}$F FDG PET-CT) is limited in evaluation of primary lesion, mainly due to renal excretion of FDG, which decreases contrast between renal mass and normal tissue and thus obscuring or masking the lesions sometimes yielding false negative results and decreasing overall sensitivity of the modality, 60% vs 91.7% in case of conventional CT (5).In other hand, in case of metastatic RCC it has better specificity (83%-100%) and sensitivity (80%-100%) as compared with CT scan or PET scan alone, particularly for detection of involved lymph nodes& locoregional recurrence (4, 6, 7, 8).CT scan uses the 1 cm size criteria and interpretation of the renal fossa in postoperative state is difficult due to postoperative changes. PET-CT, being a metabolic scan, is independent from these factors. Moreover, CT scan from vertex to mid-thigh is done in a single setting during the procedure. Therefore, PET/CT can identify locoregional recurrence or distant metastases earlier and better than CT scan (7). PET-CT is similarly useful in renal impairment where a contrast CT or MRI cannot be performed. Acting as an imaging biomarker, it can provide useful information about patient's survival.

Current guidelines do not recommend FDG PET-CT as the initial diagnostic imaging modality of choice in RCC. However, multiple studies revealed this scan to be better than conventional imaging for detecting local recurrence and distant metastases (6) thus yielding better patient management. Our study was done to find the impact of FDG PET-CT in re-staging and thus management of patient with RCC.

## PATIENTS AND METHODS

This prospective observational study included 67 post-operative (nephrectomy/ partial nephrectomy) patients with renal cell carcinoma who were referred to Institute of Nuclear Medicine and allied sciences, Dhaka for an $^{18}$F FDG PET scan from July, 2019 to July, 2024. Informed consent was obtained from the patients or their accompanied persons. Meticulous review of medical history was done regarding evidence of previous known metastases, locoregional recurrence based on available histopathology, CT scan, USG, bone scan, tumor markers, etc. Proper treatment history was sought about chemo-radio and immunotherapy. All the patients were advised standard preparations for PET-CT. Proper history was taken regarding pregnancy & lactation. Patients were counseled about radiation hazards. Dose of F-18 FDG was calculated according to patient weight. PET-CT was performed with 'Philips 128 slice ingenuity TF PET CT' machine 60 minutes after intravenous administration of radiopharmaceutical. Images were reconstructed using List mode TF HD algorithm and slices were reformatted into trans-axial, coronal and sagittal views. Semi-quantitative estimation of FDG uptake was performed by calculating SUVmax value, corrected for dose administered and body weight (g/ml).

## RESULT

Among the 67 patients 55 were male (80%) and the rest 13 (20%) female with age ranging from 31 to 78 year (mean age 58 year). All cases were post-operative. Histopathology revealed 49 (72%) clear cell carcinomas, 7 (10%) papillary carcinomas, 4 (5%) transitional cell carcinomas, 3 (4%) sarcomoid carcinoma, 1 (1.5%) chromophobe type & 4 (5%) reports shows renal cell carcinoma without other histopathologic specification.

4 cases had known locoregional recurrence while 16 had known metastases. All of them received chemo, radio and/or immunotherapy. 22 patients had evidence of suspected metastases in other imaging modalities among which 8 were ametabolic in $^{18}$F FDG PET-scan.35 (52%) patients out 67 had distant metastases. New metabolically active foci were found beyond renal bed without previous evidence in 11 patients (16%). 8 (12%) patients revealed locoregional recurrence without prior evidence. Lymph nodes (41 foci, comprising of 34 %) & lungs (27 foci, comprising of 22.5 %) were the commonest distant metastatic sites among 114 foci. The other metastatic foci were present in adrenal glands (12foci), peritoneum (7 foci), pleura (4 foci), bones (12 foci), soft tissue (8 foci), muscle (4 foci), liver (3 foci), brain (1 foci) & opposite kidney (1 foci).

One patient had diffuse FDG uptake along the incision site with multiple discharging sinuses and was later diagnosed as tuberculosis by histopathology.

**Table 1: Comparison of findings between CT scan and PET-CT among the study population**

| Patient groups | Patients with metabolically active lesion in FDG PET-CT | Patients without metabolically active lesion in FDG PET-CT | Total |
|---|---|---|---|
| Patients with suspected metastases in CT scan (22) | 14 | 8 | 22 |
| Patients without any CT evidence of suspected metastases (45) | 19 | 26 | 45 |
| Total | 33 | 34 | 67 |

## DISCUSSION

Renal cell carcinoma is usually detected incidentally and about one-fourth of the patients are found to be metastatic at initial presentation. About 20%-40% patients later develop distant metastases (6).

Conventional CT-scan provides anatomical detail while PET offers metabolic status of any suspected lesions. MRI is considered better for detecting brain metastasis; however, it is not routinely one and is suggested only in symptomatic patients. (7). PET plays vital role in detecting neoplastic potential in an otherwise normal CT finding, e.g. a lymph node less than 10 mm in diameter. In case of metastatic RCC, PET has better specificity (83%-100%) and sensitivity (80%-100%) in comparison to CT (4, 6, 7, 8).In other hand, PET-CT has a sensitivity of 86% and a specificity of 96% for disease assessment, compared to 81% and 41% for CT alone.

PET-CT examination offers complete anatomic as well as metabolic evaluation in a single scan. Moreover, scanning from vertex to mid-thigh allows better detection of local recurrence as well as distant metastasis. Knowledge of both anatomic and metabolic characteristics of renal lesions on PET-CT is necessary to help minimize unnecessary biopsies and ensure the ideal treatment of doubtful lesions. (9, 10,11)

In our study, 16 patients out of 67 had distant metastases in initial diagnoses which comprises about 23% and another 4 had local recurrence. These patients came for post-therapy (Radio/chemo/immune therapy) evaluation. Among these 16 cases 6 revealed no residual mass or any metabolically active foci throughout the scanned area in PET-CT while the rest (~70%) had one or more metabolically active foci in renal bed or distant sites.

22 patients presented with evidence of suspected metastases in other imaging modalities, e.g. CT and MRI. 16 of them (72%) showed metabolically active foci in corresponding CT abnormalities suggesting metastases.

In 11 patients (16%) new distant metastatic foci were detected in total 22 foci without any prior CT abnormality or known metastases. 8 new cases of locoregional recurrences (11%) without previous evidence were also found.

Nakatani et al. evaluated the surveillance role of FDG PET in 23 postoperative patients with RCC (12). FDG PET was demonstrated to have 81% sensitivity, 71% specificity, and 79% diagnostic accuracy. PET was able to accurately detect local recurrence and metastases to the peritoneum, bone, muscle, and adrenal gland in all cases. In six cases (21%), additional information was obtained from scans, ultimately affecting the course of therapeutic management in three cases (11%). In our study, PET-CT provided undetected foci in 16% cases which is closer to the result of the stated above.

Kumar et al. assessed FDG PET-CT scans of 63 patients with suspected recurrent RCC after nephrectomy, confirmed with histological examination and/or clinical follow-up and conventional imaging modalities (13). The results of the scans were 63 true positive studies, 30 true negative studies, 7 false negative studies, and 3 false positive studies. 109 lesions were detected by FDG PET/CT in the 63 true positive scans. FDG PET-CT was demonstrated to have 90% sensitivity, 91% specificity, and 90% accuracy in the study. Bertagna et al. retrospectively evaluated 68 patients with renal carcinoma who had postoperative FDG PET-CT following partial or radical nephrectomy (4). FDG PET-CT was reported to have 82% sensitivity, 100% specificity, 100% positive predictive value, 66.7% negative predictive value, and 86.6% accuracy. In another study reported by Fuccio et al., the usefulness of FDG PET-CT was assessed in the restaging of 69 RCC patients with clinical or radiological suspicion of metastases after nephrectomy (6, 18). Validation of FDG PET-CT results was established by biopsy, other imaging modalities, and/or clinical and radiological follow-up of 12 months. Forty patients had true positive, 2 patients false positive, 23 patients true negative, and 4 patients false negative. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were 90, 92, 91, 95, and 85%, respectively. On a lesion basis, FDG PET-CT detected 114 areas of abnormal uptake in 42 positive patients of which 112 resulted to be true positive.

Aide et al. stated that PET is more efficient than CT in diagnosing distant metastasis in RCC, particularly lymph node metastases as CT commonly uses the size criteria of

1cm (15). In our study, we found metabolic activity multiple subcentimetric lymph nodes.

In our study PET-CT complied with 72% of suspected lesions in CT scan, detected unknown metastatic foci in 16% cases and local recurrence in 11% cases. The result guided the oncologists for a better management of patients thus affecting outcome and overall survival. Our limitation was the inability to confirm histopathology of each metabolically active foci which is not feasible in our socio-economic context.

## CONCLUSION

F-18 FDG PET-CT plays a vital role in effective postoperative surveillance and restaging, though limited use is observed in evaluating primary lesions due to renal excretion of FDG, which can mask lesions and decrease sensitivity. However, it has better specificity and sensitivity in metastatic RCC, particularly for detecting involved lymph nodes and locoregional recurrence. PET/CT is independent of postoperative changes and can identify recurrence or distant metastases earlier than CT scans. It is also useful in renal impairment where contrast CT or MRI cannot be performed.

Conflict of Interest: The authors has no conflict of interest regarding this study.

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