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Original Article

# 18F FDG PET/CT in Follow-up of Cancer Colon

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## Abstract

**Background:**18 F-2-fuoro-2-deoxy-d-glucose (18F-FDG) positron emission tomography-computed tomography (PET-CT) is a method of imaging that measures metabolic activity in cancer cells. 18F-FDG PET-CT is important for detecting loco-regional recurrence, distant metastases, and assessment of the tumor response after chemotherapy and radiotherapy in patients with colorectal cancer.

**Objectives:** is to evaluate the diagnostic value of F-18 FDG PET/CT in detecting recurrence, and distant metastases in colorectal cancer (CRC) patients.

**Materials and Methods:** A retrospective analysis of 49 CRC patients were referred for follow-up by PET CT after treatment at Sohag Cancer Centre. Sociodemographic and follow-up data, such as recurrence , metastasis by PET CT, were retrieved and analyzed.

**Results:** We included 49 patients who have done PET CT. More than half of them (57.1%) were females, with a mean age of 50.63 ± 15.64. The vast majority (91.8%) of CRC pathological results were adenocarcinoma. To monitor the therapy response and detect recurrent disease as early as possible, PET/CT offered valuable information that significantly impacted disease management. Most patients (79.6%) received chemotherapy after surgery. The prevalence of distant LN affection was more prevalent in males (P-value = 0.045). Recurrence rate (P-value = 0.033), hepatic deposits (P-value = 0.032), and peritoneal deposits (P-value = 0.003) were significantly more prevalent in the mucinous type. Bone deposits (P-value <0.001) and free cases (P-value=0.040) were significantly more prevalent in the patients who received combined therapy.

**Conclusion:**FDG-PET-CT imaging is a valuable imaging method in assessing post-treatment colorectal cancer patients with probable tumor recurrence or distant metastases.

**Keywords:** Colorectal cancer , Positron Emission Tomography-Computed Tomography, Follow-up; Recurrence.
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## Introduction:

More than 1 million people worldwide get CRC each year, resulting in around 0.5million fatalities.its considered the most common detected malignancy. It represents a cancer entity that affects not only the elderly but also a growing number of young people. **(1)**

CRC ranks seventh among both genders, accounting for around 5% of all malignant tumors, following the Egypt Global Cancer Observatory figures, which explore Egypt's cancer burden. (2) PET/CT was presented at 2001, it is depend on glucose as the malignant cells, give energy at aerobic glycolysis, by using more glucose than the normal cells. That help detection of malignant tissues ,accumulating more in the malignant tissues more than other tissues . PET/CT can give anatomical plus metabolic data to respose definit medical inquiries. (3).

PET/CT image metabolism depending on the molecular data of the tissues with its PET portion and anatomy with its CT component. PET can picture metabolic variations in abnormal cells, distinguishing viable tumors from scar tissue at an early phase than other diagnostic modalities and in changes of tumor metabolic rate. Currently FDG-PET has an important role in staging disease before surgery, follow up of the disease, with rising of tumor marker (serum carcinoembryonic antigen) and in detecting residual masses after treatment. (4)

Dietary, familial, and environmental variables are all risk factors for CRC, which result in the slow accumulation of inherited mutations and epigenetic changes in promoting tumor formation with decades . Further than 80% of CRCs advance from adenomatous polyps, while fewer than 1% of adenomatous polyps smaller than 1 cm turn malignant. (5)

Improvements to recognize developing CRC have refine patient groups who will have value of general or targeted therapy. **(6)**

Staging is required for providing patients with possibly curative therapy options. The most common staging method for CRC is contrast-enhanced chest, abdomen, and pelvis CT, it gives only anatomical images for determining stage of the tumor , and minor affected LNs may be ignored. (7)

(FDG-PET/CT) performs well more than other types of imaging, as contrast-enhanced multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) It may additionally identify tumor changes resulting from therapies earlier than CT. (8)

To personalize treatment and achieve the best possible therapeutic result, several studies have looked into the use of it in assessing follow up after therapy in CRC (9).

The biological result of treatment, as observed on PET/CT imaging, is considered a more significant predictor than morphological changes. **(10)**

**Materials and Methods:**

49 CRC patients with elevated tumor markers (either only CEA, CA 19-9, or both) refered for PET/CT imaging detect recurrent CRC, from January 2022 - December 2024 at Sohag Cancer Centre following the approval from Sohag University Hospital's ethical committee standard procedure guidelines under IRB registeration number ; **Soh-Med-24-8-02PD**.

**Our research include** any patient proved to be CRC by histo-pathology .

**Data collection**

We retrieved the patients' sociodemographic data (age and gender), pathological biopsy results, and the progression findings over the follow-up period using PET/CT. The findings were analyzed. The lesion site, characteristics and avidity were analyzed for each patient and included within the patients' sample.

**Preparation of the patient for PET CT imaging:**

All patients should be fasted for 4-6 hours. blood glucose sample reading shouldn,t be more than 200 mg/dl before radiotracer administration of adose 0.1 mCi/kg of 18F-FDG. patients should be well hydrated and asked to empty their bladders immediately before imaging. After the 18F FDG injection, image acquisition began 45- 60 minutes later ,no motion during the acquisition time. Protocol of imaging from the vertex to the midthighs with the arms kept above the head by GE Discovery PET CT .

During the analysis of PET/CT images which was carried out by two experienced physicians ((one nuclear medicine physician and one radiologist) .A bnormal uptake was considered if it was exist

outside the physiological locations or had more uptake than the normal liver .

In pateints with high tumor markers and abnormal PET/CT are categorized as True positive group, confirmed to be positive for malignancy by histology or follow-up. Lesions were truly negative if the tumor markers were negative and PET/CT results were confirmed that by histology or by decreasing CEA levels to normal values without imaging denoting recurrence during the follow-up. False-positive patients with doubtful lesions with confirmed negative histology for malignancy or cured with time of follow-up imaging are categorized as falsly negative group . patients in the category of false negative when their tumor markers, or PET/CT images were negative but the reference standard approve malignancy.

**Statistical analysis**

Following the collection, revision, coding, and data entry into IBM SPSS version 20, the measurable data were expressed as mean, standard deviations, $\chi 2$ test compared the two groups' qualitative data groups. The acceptable margin of error at 5%, and the confidence interval was set at 95%.

**Results**

In a retrospective analysis of 49 CRC were referred for follow-up by PET CT after treatment, more than half (57.1%) were females. Their ages between 22 to 80 years, with a mean age of 50.63 ± 15.64 years in Table (1)

**Table (1): Sociodemographic data of the patients (n=49).**

| Parameters | |
|---|---|
| **Age** | |
| **Mean ± SD** | **50.63 ± 15.64** |
| **Range** | **22-80** |
| **Sex** | |
| **Male** | **21 (42.9%)** |
| **Female** | **28 (57.1%)** |

The vast majority of 45 patients with CRC pathological results (91.8%) were non-mucinous adenocarcinoma. Most patients (91.8%) underwent surgical resection. Most patients (79.6%) received chemotherapy after surgery, and 20.4% received combined therapy (chemotherapy and radiotherapy) **Table (2).**

**Table (2): classification according to pathology and type of treatment .**

| Parameter | (%) |
|---|---|
| **Pathology** | |
| **Non Mucinous adenocarcinoma** | **45 (91.8%)** |
| **Mucinous** | **4 (8.2%)** |
| **Surgical intervention** | |
| **Yes** | **45 (91.8%)** |
| **No** | **4 (8.2%)** |
| **Chemo/Radio** | |
| **Chemotherapy** | **39 (79.6%)** |
| **Combined** | **10 (20.4%)** |

Recurrence in adenocarcinoma in 20 patients out of 45 patients (44.4% ), all cases with mucinous pathology have a recurrence, with a P-value of 0.033.

As regard hepatic deposits (75%) and peritoneal deposits (100%) were significantly more prevalent in the mucinous type (P-value=0.033), (P-value <0.001), (P-value=0.032), and (P-value=0.003),in that order. The table indicates a statistically significant increase in the number of false negatives (p-value<0.001) in the mucinous group in comparison to the non-mucinous adenocarcinoma group **Table (3).**

**Table (3): Association between pathological outcomes of follow-up patients by PET CT with CRC after adjuvant chemotherapy.**

| Parameter | Presence or absence | Adenocarcinoma (n=45) | Mucinous (n=4) | Test value | P-value |
|---|---|---|---|---|---|
| Recurrence | Yes<br>No | 20 (44.4%)<br>25 (55.6%) | 4 (100%)<br>0 (0%) | 4.537* | 0.033 S |
| Local spread | Yes<br>No | 18 (40%)<br>27 (60%) | 1 (25%)<br>3 (75%) | 0.348 | 0.555 NS |
| Hepatic deposits | Yes<br>No | 11 (24.4%)<br>34 (75.6%) | 3 (75%)<br>1 (25%) | 4.601* | 0.032 S |
| Pulmonary deposits | Yes<br>No | 12 (26.7%)<br>33 (73.3%) | 2 (50%)<br>2 (50%) | 0.980 | 0.322 NS |
| Bone deposits | Yes<br>No | 2 (4.4%)<br>43 (95.6%) | 1 (25%)<br>3 (75%) | 2.701 | 0.1 NS |
| Peritoneal deposits | Yes<br>No | 12 (26.7%)<br>33 (73.3%) | 4 (100%)<br>0 (0%) | 8.983* | 0.003 S |
| Local Lymph nodes | Yes<br>No | 12 (26.7%)<br>33 (73.3%) | 1 (25%)<br>3 (75%) | 0.063 | 0.801 NS |
| Distant Lymph nodes | Yes<br>No | 6 (13.3%)<br>39 (86.7%) | 2 (50%)<br>2 (50%) | 3.615 | 0.057 NS |
| Free | Yes<br>No | 3 (6.7%)<br>42 (93.3%) | 0 (0%)<br>4 (100%) | 0.284 | 0.594 NS |
| False positive | Yes<br>No | 2 (4.4%)<br>43 (95.6%) | 0 (0%)<br>4 (100%) | 0.511 | 0.474 NS |
| False-negative | Yes<br>No | 0 (0%)<br>45 (100%) | 2 (50%)<br>2 (50%) | 18.933 | 0.000 HS |

*Chi-square test NS: non-significant as P-value >0.05 S: Significant P<0.05
HS: Highly significant P<0.01

This analysis found that bone deposits (30%), and free cases (20%) were significantly more prevalent in the patients who received combined therapy (P-value <0.001), (P-value <0.001), and (P-value=0.040), respectively **Table (4).**

**Table (4): Relation between treatment and findings of follow-up PET CT patients with CRC after adjuvant chemotherapy.**

| Parameter | Presence or absence | Combined (n=10) | Chemo (n=39) | Test value | P-value |
|---|---|---|---|---|---|
| Recurrence | Yes<br>No | 5 (50%)<br>5 (50%) | 19(48.7%)<br>20 (51.3%) | 0.005 | 0.942 NS |
| Local spread | Yes<br>No | 3 (30%)<br>7 (70%) | 16 (41%)<br>23 (59%) | 0.408 | 0.523 NS |
| Hepatic deposits | Yes<br>No | 3 (30%)<br>7 (70%) | 11 (28.2%)<br>28 (71.8%) | 0.13 | 0.911 NS |
| Pulmonary deposits | Yes<br>No | 3 (30%)<br>7 (70%) | 11 (28.2%)<br>28 (71.8%) | 0.13 | 0.911 NS |
| Bone deposits | Yes<br>No | 3 (30%)<br>7 (70%) | 0 (0%)<br>39 (100%) | 12.463* | <0.001 HS |
| Peritoneal deposits | Yes<br>No | 4 (40%)<br>6 (60%) | 12 (30.8%)<br>27 (69.2%) | 0.308 | 0.579 NS |
| Local lymph nodes | Yes<br>No | 3 (30%)<br>7 (70%) | 10 (25.6%)<br>29 (74.4%) | 0.219 | 0.640 NS |
| Distant lymph nodes | Yes<br>No | 3 (30%)<br>7 (70%) | 5 (12.8%)<br>34 (87.2%) | 1.720 | 0.190 NS |
| Free | Yes<br>No | 2 (20%)<br>8 (80%) | 1 (2.5%)<br>38 (97.5%) | 4.210 | 0.040 S |
| False positive | Yes<br>No | 0 (0%)<br>10(100%) | 2 (5.1%)<br>37 (94.9%) | 0.5 | 0.5 NS |
| False-negative | Yes<br>No | 0 (0%)<br>10 (100%) | 2 (5.1%)<br>37 (94.9%) | 0.5 | 0.5 NS |

*Chi-square test NS: non-significant as P-value >0.05 S: Significant P<0.05

HS: Highly significant P<0.01

The sensitivity of PET was very high 91.7%, high specificity also 92%, positivly predictive value (PPV) 91.7% and negativly predictive value (NPV) 92%. an insignificant difference between PET and standard diagnosis of recurrence after CRC is noted , as shown in Table 5.

**Table (5): Chi-square statistical study of follow-up PET CT in cases with CRC and sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of follow-up PET CT to detect recurrence versus histology:**

| Follow-up PET CT | Histology and follow-up positive | Histology and follow-up negative | Chi-square test | |
|---|---|---|---|---|
| | N=24 | N=25 | Total =49 | p-value |
| Positive | 22 (91.7%) TP | 2 (8%) FN | 24 | $X^2$=0.002* |
| Negative | 2 (8.3%) FP | 23 (92%) TN | 25 | 0.9 NS |
| Sensitivity=91.7% | Specificity=92% | PPV=91.7% | NPV=92% | |

*Chi-square test NS: non-significant as P-value >0.05 S: Significant P<0.05
TP: True positive; FP: false positive; FN: false negative; TN: true negative; PPV: positive predictive value; NPV: negative predictive value.

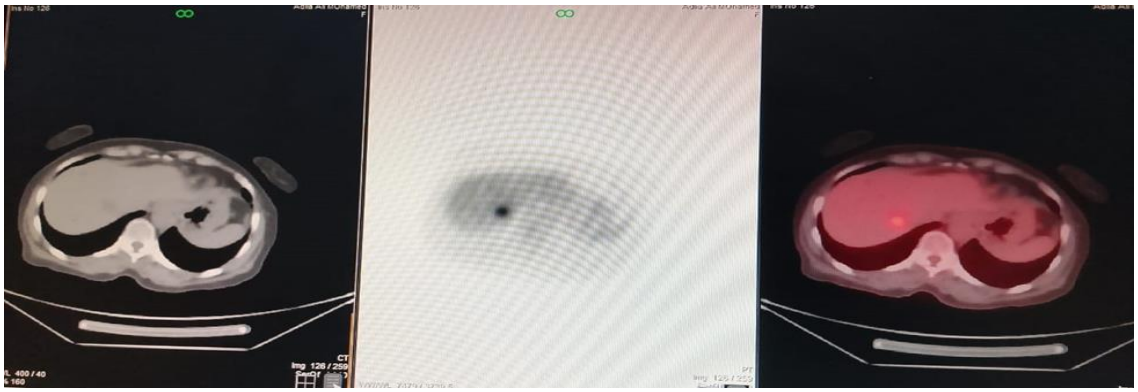

**Figure 1**: 69 years female patient with cancer colon, PET CT revealed FDG avid hepatic focal lesion +/-25mm with SUV max 4.12

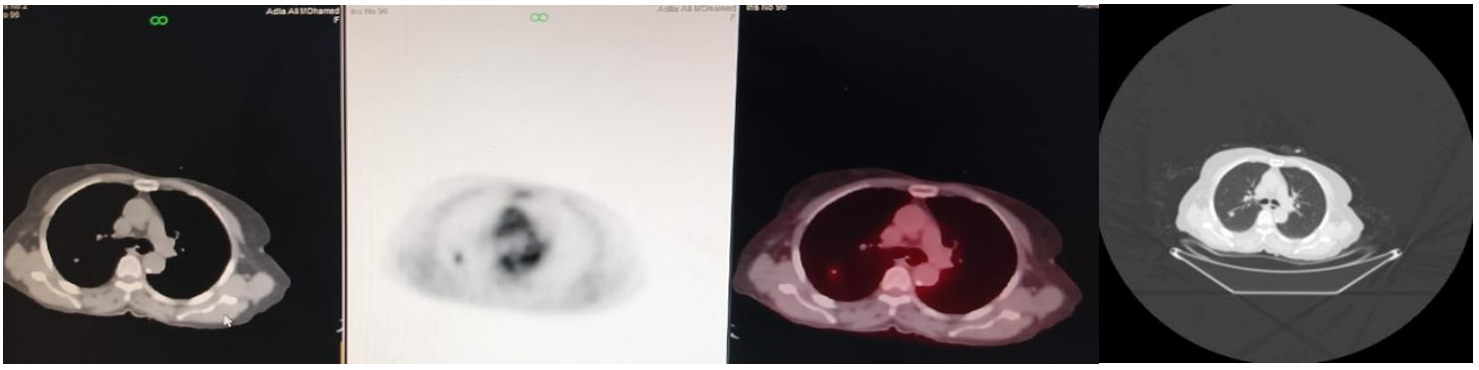

**Figure 2** :male patient, 62 years old with cancer colon, PET CT revealed pulmonary nodule of average 12mm with SUV max 4 with (lung window).

## Discussion

CRC is considered the third prominent cause of cancer global; it is responsible for a high percentage of tumour-related deaths, and recurrence occurs in roughly one-third of patients within the first two years following surgery PET/CT has been established to have a vital role in the early detection

of post-therapeutic recurrence in patients with colon cancer due to its direct investigation of malignant cellular metabolic rate. [11]

Most (91.8%) of CRC pathological results were adenocarcinoma. Most patients (91.8%) underwent surgical resection, and most (79.6%) received chemotherapy after surgery. This was in line with **Zhang et al. [12]** who reported that 87.9% of CRC pathological results were non mucinous adenocarcinoma .

We found that distant LNs affection was more dominant in males (p-value=0.045). Nodal metabolic activity measurement with FDG PET not rely just on it,s size to detect if being there cancer or not. On FDG PET scans, nodes that are small in size may contain tumors, whereas bigger nodes can be reactive. For this reason, PET is more delicate and precise than CT alone for detecting LN metastases. [13]

However, PET has size restrictions since falsly negative results can occur in small LNs, and falsly positives might occur due to inflammation. Furthermore, some lesions not have significant FDG uptake. We found that recurrence rate, metastases, hepatic deposits, and peritoneal deposits were significantly more prevalent in the mucinous type (P-value=0.033), (P-value <0.001), (P-value=0.032), and (P-value=0.003), respectively. **Elia et al.** [14] reported that metastases were significantly more common in the mucinous type. Furthermore, the pathology of mucinous colorectal adenocarcinomas are more often detected in progressive phases with inferior chemotherapeutic reactions than non-mucinous counterparts. **[15]**

**Hugen et al.**[16]hypothesized that a reduced prognosis with mucinous type found solely in cancer rectum , not colon origin.besides , a meta-analysis of 44 researches , including more than 220,000 patients, revealed worse prediction in individuals with mucinous type.

However, it is essential to note that signet-ring cell type, a different sort of adenocarcinoma that exhibits rich intracellular mucin to the point where the nucleus is displaced, shares molecular structures with mucinous type, such as the incidence of MSI-H, CpG island methylator phenotype-high (CIMP-H), and numerous BRAF alterations. **[17]**

We found that metastases (P-value <0.001), bone deposits (P-value <0.001), and free cases (P-value=0.040) were significantly more prevalent in the patients who received combined therapy. This implies that the chemotherapy has better results over the follow-up period. **Chiewvit et al.** [18] demonstrated that 18F-FDG PET/CT is a practical technique for post-operative assessment of lesions that probably recurrence colorectal malignancies with within normal CEA level, as earlier described that supported by the analysis, recurrences or metastases can be identified from changes postoperativly or benign lesions characteristics .

This study found that the mucinous group had a higher PET-CT falsly negative rate than the Non mucinous adenocarcinoma patients , with a p-value of less than 0.001. The results aligned with **Whiteford et al.[19]** who discovered that the furthermost frequent aetiology of false-negative images was mucinous carcinoma and that two-quarters of falsly-negative cases were caused by mucinous type. In complete accordance with the results, they reported that mucinous adenocarcinoma exhibits significantly lower FDG-PET sensitivity than non-mucinous carcinomas and that mucinous colorectal carcinoma exhibits fewer uptakes on FDG-PET analysis than non-mucinous type.

Compared to patients who just got chemotherapy, we found that cases who had combined therapy had a statistically greater falsly positive rates (p-value = 0.033). The results align with those of **Hetta et al.** [20], who discovered 60 individuals, of whom 21 had truly positive cases, 37 had truly negative patients, one had falsly positive case, and one had falsly negative instances. After second biopsy, the falsly-positive patient was found to be negative (colitis) despite having a positivly long segment improving mural thickening of the rectum at the anastomotic site with increased FDG uptake (abnormal SUVmax). at follow-up, performed after six months without therapy, discovered a regressive sequence concerning the mural thickening .

this study can help identify subgroups of CRC patients at a higher risk of recurrence and metastasis, guiding clinicians in tailoring more aggressive monitoring or additional therapies for

these patients. Findings can provide insights into the effectiveness of different adjuvant chemotherapy regimens, potentially influencing treatment guidelines and clinical practice. Understanding the recurrence and metastasis rates can also shed light on the long-term quality of life with overall survival of CRC cases , emphasizing the necessity for supportive care measures. Healthcare systems can use the study's findings to assign resources more efficiently , confirming that high-risk patients obtain suitable follow-up andattention.

**Future directions**

Prospective research should be conducted to validate the findings and eliminate the biases present in retrospective assessments. This could help to corroborate the connections and causal relationships discovered. Investigate the molecular and genetic mechanisms behind recurrence and metastasis in CRC. Studies on genetic alterations, tumour microenvironments, and immune response could provide further information about the mechanisms that drive these processes. Long-term follow-up studies should be implemented to track the late effects of adjuvant chemotherapy, allowing for a more complete understanding of its impact on patient outcomes over time. The use of modern imaging and monitoring tools, such as liquid biopsies, in the early detection of recurrence and metastasis, with the potential to improve early intervention options, should be investigated.

We should encourage collaborative research among oncologists, radiologists, pathologists, and data scientists_to create complete models for predicting and managing unfavourable outcomes. By addressing these consequences and future research approaches, your study can substantially contribute to the field, ultimately improving patient outcomes and furthering our understanding of cancer recurrence and metastasis after adjuvant treatment.

## Conclusion

Regarding F18 FDG PET CT findings, this study included more female CRC patients, but the male gender was associated with more distal LN affection. The mucinous CRC type was associated with worse outcomes than adenocarcinoma, Chemotherapy showed better outcomes than the combined approach. Further prospective research with a larger sample size and extended follow-up periods is required. Therfor PET CT is considered avaluable imaging technique in detecting early recurrence and metastases in patients with CRC post treatment**.**

**Conflict of Interest**

No conflict of interest

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