FDG PET/CT in follow UP patients with colorectal carcinoma after adjuvant chemotherapy

Remon Zaher Elia, Rafik Abdelazem Elbastawessy*, Hanaa Abdelkader Abdelmgeguid and Ahmed Mohamed Bassiouny

Abstract

Background: 18F-2-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography-computed tomography (PET-CT) is a method of imaging that assesses and measures metabolic avidity in cancer cells, acting as a proxy for underlying cellular activity and vitality and so providing anatomic and metabolic information. 18F-FDG PET-CT is beneficial for detecting local recurrence, distant metastases, and monitoring tumor viability after chemotherapy and radiotherapy in patients with colorectal cancer. Strict adherence to set protocols, technological processes, and good patient preparation are essential to produce the greatest results. The goal of the trial was to see how useful PET/CT was in following up on patients who had resected colorectal cancer and had completed adjuvant chemotherapy rounds.

Results: In this study, PET/CT early detected hepatic deposits, pulmonary masses, bone deposits, and sizable LNs. PET/CT provided useful information and had a considerable impact on disease management, enabling the detection of recurrent disease as early as possible with high accuracy in assessment of therapeutic response. It detected viable residual tumor cells in operative bed scar, small metabolically active LNs, hepatic focal lesions, peritoneal deposits, pulmonary secondaries, and bone deposits avoiding unnecessary surgeries.

Conclusion: Because of its high accuracy in detection and capacity to identify recurrent illness, FDG-PET-CT imaging is effective in evaluating post-therapeutic colorectal cancer patients with suspected tumor recurrence or distant metastases.

Keywords: FDG PET/CT, Colorectal carcinoma, Adjuvant chemotherapy

Background

Colorectal cancer (CRC) is the third most prevalent malignant tumor in both men and women in the developed world, as well as the second leading cause of cancer-related mortality [1].

Despite breakthroughs in surgical treatment and the introduction of combination therapeutic modalities, 5-year survival rates seldom reach 60%, ranging from 90% in localised illness to 11% in patients with distant organ metastasis. Because of the high risk of recurrence or metachronous metastasis in patients with colorectal cancer, non-invasive restaging and therapeutic monitoring are becoming increasingly popular. Patients’ prognosis have been shown to improve when recurrences are detected early [2].

A non-invasive technique to restaging for suspected locally recurring colorectal cancer, detecting probable metastatic disease, and assessing therapy efficacy is becoming increasingly important. CT and MRI have become standard in such examinations, while PET and PET/CT have been proved to be highly successful for...
specific uses in this population over the last two decades [3].

18 F-fluorodeoxy glucose positron emission tomography/computed tomography (FDG-PET/CT) can detect tumor changes caused by chemotherapy and targeted therapy earlier than CT and better than other imaging modalities like contrast-enhanced multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) in distinguishing benign post-treatment changes from local recurrence and detecting undetected metastases [4].

Many studies have investigated the use of 18 F-FDG PET/CT in the evaluation of therapy response in colorectal cancer, with the goal of treatment individualization to get the best possible therapeutic outcome [5].

In comparison to anatomical changes, the biological effect of therapy, as seen on PET/CT imaging, was thought to be a greater predictive indicator [6].

The goal of this study is to evaluate the role of PET/CT in follow up patients with resected colorectal carcinoma and finished cycles of adjuvant chemotherapy.

**Methods**

This is a prospective study was carried out at Egyptian Military and Ain Shams University Hospitals within a period of 24 months. The study includes 30 patients who are histopathologically confirmed colorectal carcinoma, curative resection of the primary tumor and on follow up after finishing adjuvant chemotherapy.

The inclusion criteria of the study were no age prediction and both genders. While patients with previous history of another type of malignancy, strong history of atopic disorders and renal function impairment (with serum creatinine > 2 mg/dl) were excluded from the study.

Ethical permission was obtained from the radiodiagnosis and nuclear medicine committee of Ain Shams University and Military hospitals. The study group was informed about the nature and the purpose of the study. Confidentiality was ensured.

**Table 1** Demographic data of the studied patients

| Total no. = 30 |
|----------------|
| Age           |
| Mean ± SD     | 58.03 ± 12.34 |
| Range         | 36–77 |
| Gender        |
| Female        | 20 (66.7%) |
| Male          | 10 (33.3%) |

**Table 2** Pathological results and treatment of the studied patients

| Total no. = 30 |
|----------------|
| Pathology      |
| Adenocarcinoma | 26 (86.7%) |
| Mucinous       | 4 (13.3%)  |
| Treatment      |
| Surgery        |
| No             | 0 (0.0%) |
| Yes            | 30 (100.0%) |
| Chemo/radio    |
| Chemo          | 24 (80.0%) |
| Combined       | 6 (20.0%) |

**Table 3** Relation of gender of the studied patients with PET-CT findings in follow up patients with colorectal carcinoma after adjuvant chemotherapy

|                  | Female No. = 20 | Male No. = 10 | Test value | P-value | Sig. |
|------------------|-----------------|---------------|------------|---------|------|
| Recurrence       | 15 (75.0%)      | 3 (30.0%)     | 5.625*     | 0.018   | S    |
| Local spread     | 15 (75.0%)      | 3 (30.0%)     | 5.625*     | 0.018   | S    |
| Metastases       | 10 (50.0%)      | 7 (70.0%)     | 1.086*     | 0.297   | NS   |
| Hepatic deposits | 6 (30.0%)       | 6 (60.0%)     | 2.500*     | 0.114   | NS   |
| Pulmonary deposits| 4 (20.0%)      | 4 (40.0%)     | 1.364*     | 0.243   | NS   |
| Local LNs        | 16 (80.0%)      | 2 (20.0%)     | 10.000*    | 0.002   | HS   |
| Distant LNs      | 8 (40.0%)       | 3 (30.0%)     | 0.287*     | 0.592   | NS   |
| Bone deposits    | 3 (15.0%)       | 3 (30.0%)     | 0.938*     | 0.333   | NS   |
| Peritoneal deposits| 4 (20.0%)    | 0 (0.0%)      | 2.308*     | 0.129   | NS   |
| False +ve        | 2 (10.0%)       | 1 (10.0%)     | 0.000*     | 1.000   | NS   |
| False -ve        | 2 (10.0%)       | 1 (10.0%)     | 0.000*     | 1.000   | NS   |

*Chi-square test
All included patients were subjected to full history taking with emphasis on the clinical data of the patients, routine laboratory investigations, the 18 F-FDG PET/CT examinations were performed on colorectal cancer patients during their follow up period after finishing adjuvant chemotherapy, and before FDG administration, all patients had a blood glucose level of less than 200 mg/dL (11.1 mmol/L).

**Study procedures**

296–444 MBq of FDG was administered intravenously 50–60 min before undergoing PET and CT scanning. PET emission images for 5–7 bed positions were collected using a weight-based technique with 3 min of acquisition time per bed position. Three hours later, a delayed imaging of the ROI or suspected lesion location was performed. CT, PET, and combined PET/CT transverse, sagittal, and coronal sections were produced with a section thickness of 5 mm using an iterative technique and CT-based attenuation correction. In order to interpret the images, visual assessment and semi-quantitative analysis were used. The highest standardised uptake value (SUVmax) was retrieved at the area that most clearly showed the hyper-intensive radioactivity.

### Table 4 Relation of pathological results of the studied patients with PET-CT findings in follow up patients with colorectal carcinoma after adjuvant chemotherapy

| Pathology          | Test value | P-value | Sig. |
|--------------------|------------|---------|------|
| **Adenocarcinoma** |            |         |      |
| No. = 26           |            |         |      |
| Recurrence         | Positive   | 0.192*  | 0.661| NS   |
|                    |            | 16 (61.5%)| 2 (50.0%)| NS   |
| Local spread       | Positive   | 0.192*  | 0.661| NS   |
|                    |            | 16 (61.5%)| 2 (50.0%)| NS   |
| Metastases         | Positive   | 6.036*  | 0.014| S    |
|                    |            | 17 (65.4%)| 0 (0.0%)| NS   |
| Hepatic deposits   | Positive   | 3.077*  | 0.079| NS   |
|                    |            | 12 (46.2%)| 0 (0.0%)| NS   |
| Pulmonary deposits | Positive   | 1.678*  | 0.195| NS   |
|                    |            | 8 (30.8%)| 0 (0.0%)| NS   |
| **Mucinous**       |            |         |      |
| No. = 4            |            |         |      |
| Recurrence         | Positive   | 0.192*  | 0.661| NS   |
|                    |            | 16 (61.5%)| 2 (50.0%)| NS   |
| Local spread       | Positive   | 0.192*  | 0.661| NS   |
|                    |            | 16 (61.5%)| 2 (50.0%)| NS   |
| Metastases         | Positive   | 6.036*  | 0.014| S    |
|                    |            | 17 (65.4%)| 0 (0.0%)| NS   |
| Hepatic deposits   | Positive   | 3.077*  | 0.079| NS   |
|                    |            | 12 (46.2%)| 0 (0.0%)| NS   |
| Pulmonary deposits | Positive   | 1.678*  | 0.195| NS   |
|                    |            | 8 (30.8%)| 0 (0.0%)| NS   |

*Chi-square test

### Table 5 Relation of treatment of the studied patients with PET-CT findings in follow up patients with colorectal carcinoma after adjuvant chemotherapy

| Chemo/radio       | Test value | P-value | Sig. |
|-------------------|------------|---------|------|
| **Chemo Combined**|            |         |      |
| No. = 24          |            |         |      |
| Recurrence         | Positive   | 0.139*  | 0.709| NS   |
|                    |            | 14 (58.3%)| 4 (66.7%)| NS   |
| Local spread       | Positive   | 0.139*  | 0.709| NS   |
|                    |            | 14 (58.3%)| 4 (66.7%)| NS   |
| Metastases         | Positive   | 1.663*  | 0.197| NS   |
|                    |            | 15 (62.5%)| 2 (33.3%)| NS   |
| Hepatic deposits   | Positive   | 0.139*  | 0.709| NS   |
|                    |            | 10 (41.7%)| 2 (33.3%)| NS   |
| Pulmonary deposits | Positive   | 0.384*  | 0.536| NS   |
|                    |            | 7 (29.2%)| 1 (16.7%)| NS   |
| **Chemo**          |            |         |      |
| No. = 6            |            |         |      |
| Recurrence         | Positive   | 0.313*  | 0.576| NS   |
|                    |            | 15 (62.5%)| 3 (50.0%)| NS   |
| Local LNs          | Positive   | 1.292*  | 0.256| NS   |
|                    |            | 10 (41.7%)| 1 (16.7%)| NS   |
| Distant LNs        | Positive   | 0.052*  | 0.819| NS   |
|                    |            | 5 (20.8%)| 1 (16.7%)| NS   |
| Bone deposits      | Positive   | 1.154*  | 0.283| NS   |
|                    |            | 6 (23.1%)| 0 (0.0%)| NS   |
| Peritoneal deposits| Positive   | 0.710*  | 0.399| NS   |
|                    |            | 4 (15.4%)| 0 (0.0%)| NS   |
| False + ve         | Positive   | 0.513*  | 0.474| NS   |
|                    |            | 3 (11.5%)| 0 (0.0%)| NS   |
| False – ve         | Positive   | 21.667*| 0.000| HS   |
|                    |            | 0 (0.0%)| 3 (75.0%)| NS   |

*Chi-square test

PET emission images for 5–7 bed positions were collected using a weight-based technique with 3 min of acquisition time per bed position. Three hours later, a delayed imaging of the ROI or suspected lesion location was performed. CT, PET, and combined PET/CT transverse, sagittal, and coronal sections were produced with a section thickness of 5 mm using an iterative technique and CT-based attenuation correction. In order to interpret the images, visual assessment and semi-quantitative analysis were used. The highest standardised uptake value (SUVmax = SUVmax, delayed-SUVmax, early) was retrieved at the area that most clearly showed the hyper-intensive radioactivity.

(See figure on next page.)

**Fig. 1** a NCCT axial image showed no significant abnormality at the operative bed, while b PET-CT fused image revealed 2 focal areas of abnormal FDG overactivity related to the anastomotic site (arrows) (SUVmax measures 4.4). c NCCT axial image showed right lobe segment VII hypodense focal lesion, while d PET-CT fused image confirmed right hepatic lobe FDG avid, hyper metabolically active focal lesion (SUVmax measures 14.0). e NCCT axial images showed rounded shape enlarged left external iliac lymph node compressing the adjacent segment of left ureter & subsequent hydroureter and hydronephrosis, while f Fused PET-CT images revealed and confirmed left external iliac avid metabolically hyperactive LN (SUVmax measures 13.0).
Fig. 1 (See legend on previous page.)
Statistical analysis
Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20 and the following were done: Quantitative data was provided as mean, standard deviations, and ranges, whereas quantitative data were presented as mean, standard deviations and ranges. The comparison between two groups with qualitative data were done by using $\chi^2$ test. The confidence interval was set at 95%, while the acceptable margin of error was set at 5%.

Results
This prospective study was conducted in Egyptian Military and Ain Shams University Hospitals on 30 patients with age ranged from 36 to 77 years with mean $\pm$ SD of 58.03 $\pm$ 12.34; they were 20 females (66.7%) and 10 males (33.3%) (Tables 1, 2, 3).

The previous table shows that there was statistically significant increase in the percentage of recurrence, local spread and local lymph nodes in females than males with $p$-value $= 0.018$, 0.018 and 0.002 respectively while no statistically significant relation found between gender of the studied patients and the other findings (Table 4).

The previous table shows that there was statistically significant increase in the percentage of patients with metastases in adenocarcinoma group than mucinous group with $p$-value $= 0.014$; also the table shows that there was statistically significant increase in the false negative rate in mucinous group than adenocarcinoma group with $p$-value $< 0.001$ while no statistically significant relation found between pathological results and the other findings (Table 5).

The previous table shows that there was statistically significant increase in the false positive rate in patients with combined treatment than those with chemotherapy only with $p$-value $= 0.033$ while no statistically significant relation found between treatment of the studied patients and the other findings.

Sample of study cases
Figures 1, 2 and 3.

Discussion
Colorectal cancer is the third leading cause of cancer worldwide, accounting for a substantial number of tumor-related deaths. Recurrence occurs in roughly one-third of patients during the first two years after surgery. Due to its direct examination of malignant cellular metabolism, PET/CT has been shown to have a crucial role in early diagnosis of post-therapeutic recurrence in patients with cancer colon. It plays an important role in detecting metabolically active small LNs, local operative bed recurrence, small metastasis, early osseous deposits, and post-therapeutic evaluation of viable and non-viable malignant lesions (post chemotherapy and radiotherapy).

This study was conducted on 30 patients with age ranged from 36 to 77 years old with mean $\pm$ SD of 58.03 $\pm$ 12.34; they were 20 females (66.7%) and 10 males (33.3%).

Based on lesions analysis, the final diagnosis of local recurrence/spread in post-therapeutic cancer colon was visible in 18 cases (60.0 percent) of the patient group. The study almost agreed with Mittal et al. [7], who found recurrences in 71 percent of post-operative CRC patients using PET/CT, but these findings differ from those of Hetta et al. [8] analyzed 60 instances and discovered that 22 cases (36.7 percent of the total evaluated cases) developed a local recurrence and 38 cases did not (63.3 percent percentage of the total studied cases). The study looked at the sensitivity, specificity, and accuracy of PET/CT in detecting local recurrence in colorectal cancer patients who had completed their treatment. The accuracy is 96.7 percent, with a sensitivity of 95.45 percent, a specificity of 97.36 percent, and a sensitivity of 95.45 percent.

In this study, the number of patients with local nodal involvement were 18 cases (60%). While 12 patients did not develop nodal metastatic deposits (40%). The findings are consistent with those of O'Connor et al. [9], who found that on PET-CT, enlarged and non-enlarged FDG avid lymph nodes can be seen in the mesentery, indicating the existence of regional lymph node metastases; this is shown when patients with CRC are restaged. The study agreed because the research found...
Fig. 2 (See legend on previous page.)
that PET/CT was quite sensitive in detecting regional lymph nodes; however, this contradicts Kim et al. [10], who found that nodal 18F-FDG uptake findings were highly specific for LN metastatic status, but had a low sensitivity; this study’s low sensitivity was attributed to the fact that the subsequent study excluded patients who had received neoadjuvant treatment, and they stated that if these advanced rectal cancer patients who had received neoadjuvant chemotherapy were included in the current study, the LN detectability of 18F-FDG PET/CT would be improved because the majority of these patients had shown high nodal 18F-FDG uptake.

The end diagnosis of distant metastases in posttherapeutic cancer colon was visible in 17 individuals (56.7%) of the patient group based on lesions investigation. Patients with hepatic metastatic deposits accounted for 12 instances (40%); those with pulmonary nodular deposits accounted for 8 cases (26.7%); those with osseous deposits accounted for 6 cases (20%); and those with peritoneal deposits accounted for four cases (40%).

PET/CT was therefore useful in detecting hepatic and extrahepatic metastases.

The findings are consistent with those of Kijima et al. [11], who found that FDG-PET and PET/CT have high accuracy for the detection and staging of liver lesions in CRC patients, with a combined sensitivity and specificity of 93 percent, and Zhang et al. [12], who found that PET/CT had better sensitivity and specificity (87–100 percent and 90–98 percent, respectively) for the detection and staging of liver lesions in CRC patients.

In this study, females had a statistically significant higher rate of PET-CT detection of recurrence, local spread, and local lymph nodes than males, with p-values of 0.018, 0.018, and 0.002, respectively, whereas there was no statistically significant relation between gender of the studied patients and the other findings, which could be due to small sample size.

In this study, there was statistically significant increase in the PET-CT false negative rate in mucinous group than adenocarcinoma group with p-value < 0.001 while no statistically significant relation found between pathological results and the other findings.

The findings were consistent with those of Whiteford et al. [13] and Borasio et al. [14], who found that mucinous adenocarcinoma was responsible for two-quarters of false-negative cases and that mucinous carcinoma was the most common cause of false-negative scans. They stated that mucinous colorectal carcinoma has lower uptakes on FDG-PET imaging than non-mucinous carcinoma and that FDG-PET sensitivity for mucinous adenocarcinoma is much lower than non-mucinous carcinomas, which is completely consistent with the findings. PET/CT was also unable to identify vitality in subcentimetric hepatic focal lesions and pulmonary nodules, as well as the evaluation of mucinous tumor deposits, particularly in hypocellular lesions with extensive mucin, according to Lee et al. [15]. The use of a delayed regional scan has recently been found to be more effective in detecting these metastases.

In investigation, patients who had combined treatment had a statistically significant higher false positive rate than those who received only chemotherapy (p-value = 0.033), but no statistically significant relation was established between the treatment of the investigated patients and the other findings.

The findings are consistent with those of Hetta et al. [8], who found that there were 60 patients in all, with 21 true positive cases, 37 true negative cases, one false-positive case, and one false-negative case. The false-positive case had positive long segment enhancing rectal mural thickening around the anastomotic site with high FDG uptake (high SUVmax), but it was later proven to be a negative case (colitis) after the second biopsy; the follow-up examination, done 6 months later with no treatment or further management, shows regressive course regarding the mural thickening and metabolic act. The false-negative case had low SUV-max at the collapsed rectosigmoid colon site and presacral soft tissue sheet; the known false-negative results of colorectal mucinous adenocarcinoma

![Fig. 3](see figure on next page.)

**Fig. 3** a NCCT of the abdomen showing soft tissue density related to the operative bed inseparable from the left ilio-psoas muscle complex. b Fused PET-CT image revealed and confirmed operative bed FDG avid metabolically overactivity denoting recurrence, infiltrating the left ilio-psoas muscle (SUVmax measures 13). c NCCT of the abdomen showing thickened left peri-renal fascia. d Fused PET-CT image confirmed FDG avid metabolic overactivity (SUVmax measures 10). The arrow refers to left ureteric double-J catheter. e NCCT of the abdomen showing nodular soft tissue density at the left anterior abdominal wall (arrow). f Fused PET-CT image confirmed FDG avid metabolic overactivity (arrow) (SUVmax measures 9). g NCCT of the abdomen showing right hepatic lobe segment-IV ill-defined hypodense focal lesion ± 3.5 cm in diameter, h Fused PET-CT image confirmed right hepatic lobe segment-IV FDG avid hypermetabolic active focal lesion eliciting (SUVmax 12.5). I NCCT lung window axial image shows right para hilar speculated soft tissue density mass lesion ± 3 cm surrounded by reticular densities and atelectatic bands (arrow) j Fused PET–CT image confirmed right para-hilar FDG avid hypermetabolic active deposit (SUVmax measures 16.5) (arrow). k NCCT lung window axial image shows small peripheral nodule (+ 7 mm) at the right lower lung lobe (arrow). l Fused PET–CT image revealed FDG-avid small nodule of low grade activity at the left upper lung lobe (SUVmax measures 2.7) (arrow).
were concerning for a biopsy, which revealed positive tumor recurrence, and follow-up studies after chemotherapy showed uptake and size regression.

In investigation, the percentage of PET-CT metastases detected in the adenocarcinoma group was statistically significantly higher than in the mucinous group (65.4 percent, p-value = 0.014).

These findings matched those of Mittal et al. [7], who studied 73 patients (55 males, 18 females; age range 25 to 80 years) with histopathologically established CRC who received FDG PET/CT imaging for the identification of recurrence and/or metastasis after initial treatment. In 51 patients, rising CEA levels were found. PET/CT scans were positive in 13 patients (3 with liver lesions, 5 with lymph node involvement, 2 with bone metastases, 1 with local recurrence in the urinary bladder wall, 1 with lymph node and liver metastases, and 1 with lymph node and bone metastases), resulting in a change in management.

Going along with the findings of Chen et al. [16], who comprised 56 and 158 patients with a history of colorectal cancer who came with increasing CEA levels and conventional imaging modalities suggested an ambiguous reason for the elevated CEA level. PET/CT had a sensitivity of 98.1 percent and a specificity of 75 percent.

Chiewvit et al. [17] have shown that 18F-FDG PET/CT is a viable approach in postoperative evaluation of patients with suspected recurring colorectal malignant lesions and a normal CEA level, as previously reported and corroborated by the investigation. Local recurrences or metastases can be distinguished from postoperative alterations or benign disease features by 18F-FDG PET/CT.

As previously mentioned, PET/CT has been demonstrated to be useful in detecting post-therapeutic cancer colon recurrence and distant metastasis. PET/CT scans revealed greater information and better lesion characterization.

Conclusion

Because of its high accuracy in detection and capacity to identify recurrent disease, FDG-PET-CT imaging is effective in evaluating post-therapeutic colorectal cancer patients with suspected tumor recurrence or distant metastases.

Abbreviations

18F-FDG: 18F-2-fluoro-2-deoxy-D-glucose; CRC: Colorectal cancer; FDG-PET/CT: 18F-FDG positron emission tomography/computed tomography; MDCT: Multidetector computed tomography; PET-CT: Positron emission tomography-computed tomography; ROI: Region of interest; SPSS: Statistical package for social science.

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Authors’ contributions

All authors of this research paper have directly participated in the planning, execution, or analysis of this study. All authors of this paper have read and approved the final version submitted. The contents of this manuscript have not been copyrighted or published previously. The contents of this manuscript are not now under consideration for publication elsewhere. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere, while acceptance by the Journal is under consideration.

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Availability of data and materials

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Faculty of Medicine Ain Shams University, Research Ethics Committee. Each patient was provided a written informed consent for analysis of anonymized data.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study. Patients who where less than 16-year-old, deceased, or unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their parents or legal guardians.

Competing interests

The authors declare that they have no competing interests.

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