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Clinical Impact of Preoperative ^{18}F-FDG PET/CT in Localized Colon Cancer: A Prospective Study with Long-Term Follow-Up

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Abstract

The present investigation evaluated the potential added value of preoperative ^{18}F-FDG PET/CT over conventional primary staging procedures in patients diagnosed with presumed non-metastatic colonic cancer (CC). In addition, the study assessed the prognostic implications of ^{18}F-FDG uptake in the primary tumor, with an average follow-up of 15 years. Patients newly diagnosed with apparently localized CC were prospectively recruited and underwent ^{18}F-FDG PET/CT scanning before surgery. SUVmax, SUVpeak, TLG, and MTV were quantified for each colonic lesion and analyzed for their prognostic potential. A total of 48 patients participated in the study. Histopathological examination of surgical specimens identified 103 colonic lesions, comprising 58 invasive adenocarcinomas, 4 in situ adenocarcinomas, 3 high-grade dysplastic adenomas, and 38 low-grade dysplastic adenomas. Per-lesion diagnostic performance for primary colonic tumor detection yielded sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 78%, 97%, 98%, and 73% for conventional workup, versus 94%, 87%, 92%, and 89% for ^{18}F-FDG PET/CT. A statistically significant difference was observed solely in sensitivity between the two approaches. PET imaging revealed 10 additional pathological colonic lesions in 7 patients. SUVmax, SUVpeak, and TLG values differed significantly between invasive adenocarcinomas, in situ adenocarcinomas, and high-grade dysplasia lesions when compared with low-grade dysplasia. A significant distinction was also noted between pT1-pT2 and pT3-pT4 adenocarcinomas. On a patient-based basis, nodal staging performance showed sensitivity, specificity, PPV, and NPV of 22%, 84%, 44%, and 65% for contrast-enhanced CT (CECT) and 33%, 90%, 67%, and 70% for ^{18}F-FDG PET/CT, without reaching statistical significance. Furthermore, PET/CT revealed occult metastatic disease and one synchronous primary lung cancer in four patients. In total, ^{18}F-FDG PET/CT supplied supplementary diagnostic information in 11 of the 48 patients (23%). Uptake intensity of ^{18}F-FDG in the primary tumor did not predict nodal involvement or distant metastases. Stratification of disease-free survival according to median values of SUVmax, SUVpeak, TLG, and MTV revealed no significant differences. In summary, preoperative ^{18}F-FDG PET/CT serves as a valuable tool for detecting colonic lesions missed by conventional assessments, especially when colonoscopy cannot be completed. It reliably identifies distant metastases but shows limited accuracy in N staging. Largely due to the modest cohort size, the quantitative evaluation of 18F-FDG uptake in the primary lesion demonstrated no association with recurrence or disease-free survival and therefore provided no substantial prognostic information.

Keywords: Colon, Carcinoma, Presurgical, Surgery, Staging, 18F-FDG

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Introduction

Colorectal cancer (CRC) constitutes a major worldwide public health challenge, representing approximately 10% of all malignancies globally. It ranks as the fourth most

common cause of cancer mortality, accounting for roughly 600,000 deaths per year [1, 2].

Early-stage CRC (Stages I and II) is typically confined to the bowel wall and is associated with a relatively favorable outcome [3, 4]. Management of localized disease centers on surgical excision of the tumor, with the operative strategy and resection margins guided by the lesion's anatomical site and dimensions [5]. In specific circumstances [6], postoperative adjuvant chemotherapy is used to reduce the risk of relapse. Prognosis for patients with localized CRC remains generally positive and is determined chiefly by the initial disease stage [7, 8]. Five-year survival rates approach 90% in localized cases but decline to 70.4% with regional lymph node involvement and decrease sharply to 12.5% in the presence of distant metastases [8, 9].

Precise primary staging is fundamental for tailoring therapeutic strategies and providing reliable prognostic information. Contemporary clinical staging integrates clinical examination, conventional radiological modalities, including computed tomography (CT) and magnetic resonance imaging (MRI), endoscopic techniques such as colonoscopy and endoscopic ultrasonography, and histopathological analysis of endoscopically acquired or surgically resected tissue samples [3, 4].

Despite its proven high sensitivity for both primary tumor detection and distant metastasis identification, the routine integration of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) exerts only a moderate impact on clinical decision-making [10-14] and is not endorsed by current international guidelines for initial preoperative staging of CRC [3]. The technique displays reduced sensitivity for locoregional lymph node metastases, primarily because involved nodes often lie adjacent to the intensely avid primary tumor, hindering reliable differentiation [10, 15, 16]. Conversely, ^{18}F-FDG PET/CT provides superior performance in detecting distant metastatic sites when conventional imaging yields ambiguous or negative results. It demonstrates enhanced precision in identifying extrahepatic disease, including periportal and para-aortic lymph node involvement and peritoneal dissemination [13, 17]. In addition, the modality can detect synchronous colonic neoplasms in patients with incomplete colonoscopy [10].

Metabolic indices derived from ^{18}F-FDG PET/CT, notably the maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG), have been explored as candidate prognostic biomarkers. Elevated SUVmax at diagnosis is commonly correlated with adverse clinical outcomes. In numerous tumor entities, patients with lesions exhibiting high SUVmax values have significantly shorter overall survival than those with lower uptake [18-22]. Nevertheless, research specifically addressing the utility of quantitative ^{18}F-FDG uptake parameters for survival prediction in CRC remains scarce and has produced conflicting findings [23-25].

To expand the existing evidence base, this prospective study systematically investigated the incremental value of preoperative 18F-FDG PET/CT over standard staging methods in patients with presumed non-metastatic colon cancer (CC) undergoing curative-intent surgery. The study further examined the long-term prognostic significance of ^{18}F-FDG uptake intensity measured in the primary colonic tumor.

Materials and Methods

Patient population

This work constitutes a secondary analysis within a single-institution prospective trial examining long-term outcomes in patients with sentinel lymph node micrometastases originating from colonic cancer (CC). Enrollment adhered to predefined eligibility requirements: (i) newly diagnosed CC requiring staging; (ii) preoperative conventional imaging with contrast-enhanced (CE) thoraco-abdomino-pelvic CT confirming localized disease and excluding any uncertain distant spread; and (iii) planned laparoscopic resection. Among eligible participants, the present evaluation was restricted to those who also underwent preoperative 18F-FDG PET/CT.

Patients were excluded if they were pregnant, required emergency intervention for colonic obstruction or perforation, presented with visceral metastases detected on standard imaging before surgery, or had a documented history of another malignancy with a disease-free period shorter than 5 years before the current CC diagnosis.

Family cancer history was documented for every individual. Serum carcinoembryonic antigen (CEA) concentration was quantified preoperatively. Replication error phenotype (RER) status was also determined. In instances of incomplete initial colonoscopy, a thorough endoscopic evaluation was completed within 6 months postoperatively.

The operating surgeon received the ^{18}F-FDG PET/CT results before the procedure, and the operative plan was formulated using information from both conventional staging and PET/CT. Because no surgical plan was established before the PET/CT examination, the potential effect of PET/CT on altering the surgical strategy could not be quantified. All abdominal regions showing extra-colonic ^{18}F-FDG activity were systematically inspected intraoperatively via thorough manual exploration, liver ultrasonography, peritoneal sampling, and cytological examination of peritoneal fluid where appropriate. Primary tumors underwent detailed histopathological assessment by a specialized pathologist and were staged according to the 7th TNM edition of the UICC.

In line with institutional regulations, all enrolled patients granted written informed consent permitting the anonymous utilization of their clinical data for research or epidemiological analyses. The protocol was reviewed and approved by the Institutional Review Board and Ethics Committee (CPP Est IV, PRI 2006—HUS N°3737).

^{18}F-FDG PET/CT

All patients received preoperative ^{18}F-FDG PET imaging on a hybrid PET/CT system (Discovery ST, General Electric, Milwaukee, WI, USA). To maintain blood glucose below 6.6 mmol/L, participants fasted for 6 hours before receiving an intravenous dose of 4.5 MBq/kg ^{18}F-FDG. Premedication consisted of 5 mg diazepam and 80 mg phloroglucinol. Whole-body (WB) PET/CT scanning was initiated 60 minutes after tracer injection. This included a low-dose CT acquisition without contrast enhancement (oral and intravenous contrast; 140 kV, 80 mA s, 0.8 s/rotation) acquired during free breathing, followed by a 2D PET emission scan covering 7 bed positions (15 cm per field, 4 minutes per field, 3.27 mm slice thickness). When feasible and with patient agreement, a delayed acquisition was obtained around 120 minutes post-injection, targeting the abdomino-pelvic region (one to three bed positions) to evaluate all focal colonic activities noted on the early scan. PET reconstruction was performed both with and without attenuation correction derived from CT data, using an ordered-subset expectation-maximization (OSEM) algorithm (2 iterations, 30 subsets, 128 × 128 matrix).

Images (CT, corrected PET, and fused PET/CT) were reviewed on a dedicated Xeleris workstation (GE Medical Systems, Milwaukee, WI, USA). Two nuclear medicine specialists, knowledgeable of the overall clinical context but blinded to the exact colonic tumor site, performed independent visual analysis. Scans were categorized as positive or negative. Positive uptake was characterized by discrete focal hypermetabolism distinctly greater than adjacent background and normal physiologic patterns. Any focal bowel activity present on the initial PET/CT but resolving on delayed imaging was not interpreted as malignant. Consensus reading resolved any inter-observer disagreement. The co-registered CT images were examined for corresponding structural changes, including wall thickening or adjacent mesenteric fat stranding.

For each PET/CT-positive lesion, SUVmax, SUVpeak, TLG, and MTV were measured on both early whole-body and delayed acquisitions. Measurements used a spherical volume of interest (VOI) that fully encompassed the focal area of increased activity. The MTV calculation employed a fixed threshold of 40% of SUVmax.

The average time interval between PET/CT imaging and surgical resection was 5 days. The conventional diagnostic workup was completed no more than 2 months before surgery.

Gold standard

The definitive diagnosis was based on postoperative histopathological evaluation. For PET-detected abnormalities outside the abdomen, supplementary data from conventional imaging—either preoperative or obtained during subsequent surveillance—were used when tissue confirmation was not feasible.

Statistical analysis

Continuous data are reported as mean ± standard deviation (SD). Group comparisons were conducted with the two-tailed nonparametric Mann–Whitney U test. Relationships between continuous variables were examined using Spearman's rank correlation. Receiver operating characteristic (ROC) analysis identified an optimal SUVmax cutoff that distinguished patients with a good clinical course from those who succumbed during follow-up. The potential prognostic value of SUVmax, SUVpeak, TLG, and MTV was investigated via univariate methods. Survival probabilities were estimated with Kaplan–Meier curves, and differences were tested using the log-rank statistic. Statistical significance was defined as $P < 0.05$. All analyses were performed with GraphPad Prism software version 6.0 (GraphPad Software, Boston, MA 02110, USA).

Results and Discussion

Patient population

Forty-eight patients, consisting of 23 women and 25 men, were prospectively recruited after undergoing preoperative ^{18}F-FDG PET/CT and included in the final analysis **(Table 1)**.

Table 1. Demographic and clinical features of the enrolled cohort.

Variable	Findings
Number of patients	48
Sex distribution	Male: 25 (52%), Female: 23 (48%)
Age (years)	67 ± 16
Diabetes mellitus	7/48 (14.6%)
Colonoscopy findings	Complete colonoscopy: 42/48 (88%), Incomplete colonoscopy: 5/48 (10%), Not feasible: 1/48 (2%)
Contrast-enhanced CT (CECT)	Performed in 48/48 patients (100%)
^{18}F-FDG PET/CT examination	Whole-body standard acquisition: 48/48 (100%). Additional delayed imaging: 36/48 (75%)
Histopathological findings (103 lesions)	Low-grade dysplasia: 38 (37%), High-grade dysplasia: 3 (2.9%), pTis carcinoma: 4 (3.9%), pT1 carcinoma: 10 (9.7%), pT2 carcinoma: 5 (4.9%), pT3 carcinoma: 40 (38.8%), pT4 carcinoma: 3 (2.9%)
Anatomical distribution of premalignant and malignant lesions	Caecum: 14 (21.5%), Right colon: 17 (26.2%), Transverse colon: 5 (7.7%), Left colon: 8 (12.3%), Sigmoid colon: 21 (32.3%)
Pathological T category (62 malignant lesions)	pTis: 4 (6.5%), pT1: 10 (16.1%), pT2: 5 (8%), pT3: 40 (64.5%), pT4: 3 (4.8%)
Largest lesion diameter (65 lesions, cm)	Mean size: 4.77 ± 2.02, Range: 1–11
Tumor histological type	Adenocarcinoma: 48/48 (100%), Mucinous subtype: 5/48 (10.4%)
Adenocarcinoma differentiation grade	Well differentiated: 40 (83.3%), Moderately differentiated: 2 (4.2%), Poorly differentiated: 6 (12.5%)
Microsatellite instability status (patients)	8/48 (16.7%)
Angioinvasion (patients)	6/48 (12.5%)
Lymph node involvement (N+) (patients)	18/48 (37.5%)

Participants had a mean age of 66 ± 13 years, with ages ranging from 29 to 88 years. A family history of CRC was noted in three cases, one of which involved familial polyposis. Reasons for initial diagnosis of CC were anemia (n = 12), rectal bleeding (n = 12), positive screening result (n = 8), abdominal discomfort (n = 6), symptoms of obstruction (n = 4), diarrhea (n = 2), fever (n = 1), incidental finding on routine colonoscopy (n = 1), *Enterococcus faecalis* bacteremia (n = 1), and evaluation for deep venous thrombosis (n = 1). Surgical pathology identified 103 colonic lesions in total: 58 invasive adenocarcinomas (including 5 mucinous variants), 4 in situ adenocarcinomas, 3 adenomas exhibiting high-grade dysplasia, and 38 adenomas with low-grade dysplasia **(Table 2)**.

Table 2. Lesion-by-lesion comparison of preoperative conventional assessment and ^{18}F-FDG PET/CT against postoperative histopathological confirmation in 48 patients. Low-grade dysplastic adenomas are excluded from analysis.

Histopathological diagnosis after surgical resection	Number of lesions identified at final pathology	Conventional preoperative workup (colonoscopy and CECT)	^{18}F-FDG PET/CT
Adenoma with low-grade dysplasia	38	1	5
Adenoma with high-grade dysplasia	3	0	3
Carcinoma in situ	4	2	4
Invasive carcinoma (overall)	**58**	**49**	**54**

└─ pT1 stage	10	6	6
└─ pT2 stage	5	3	5
└─ pT3 stage	40	37	40
└─ pT4 stage	3	3	3
Neoplastic and premalignant lesions*	**65**	**51**	**61**

In all subsequent evaluations, adenomas with low-grade dysplasia were categorized as benign. In contrast, lesions showing high-grade dysplasia (precancerous) were combined with invasive and in situ adenocarcinomas.

Primary tumor assessment

Every patient in the cohort received contrast-enhanced CT (CECT) covering the thorax, abdomen, and pelvis. Colonoscopy was performed in 47 individuals (1 declined the procedure), and complete visualization was achieved in 42. Incomplete endoscopic access resulted from tumoral narrowing situated either beyond or proximal to the main lesion in three and two patients, respectively **(Table 3)**.

Table 3. Preoperative conventional evaluation and ^{18}F-FDG PET/CT findings in five patients with incomplete colonoscopy and one patient lacking endoscopic examination.

Endoscopic limitation (blockage site)	Cause of incomplete endoscopic examination	Tumor location and pathological T stage	Colon segment containing colon cancer (CC) visualized by endoscopy (+/−)	Standard preoperative workup (+/−)	^{18}F-FDG PET/CT detection (+/−)	Incremental diagnostic value of PET/CT (yes/no)
LC	Looping	Sigmoid colon (S), pT3	+	+	+	No
S	Looping	Caecum (C), pT3	−	+	+	No
S	Tumor obstruction	Sigmoid colon (S), pT3	+	+	+	No
S	Tumor obstruction	Left colon (LC), pT2	−	−	+	Yes
S	Tumor obstruction	Caecum (C), pT2	−	−	+	Yes
LC	Tumor obstruction	Sigmoid colon (S), pT3	+	+	+	No
LC	Tumor obstruction	Left colon (LC), pT3	+	+	+	No
S	Tumor obstruction	Sigmoid colon (S), pT4	+	+	+	No
Endoscopy not performed	Patient refusal	Left colon (LC), pT1	/	−	+	Yes

Abbreviations: S = sigmoid, LC = left colon, C = caecum, CC = colorectal cancer.

For the patients with obstructed colonoscopy and the individual without endoscopic evaluation, colonic cancer diagnosis was established through virtual colonoscopy performed via CT. Taken together, the standard diagnostic pathway (colonoscopy plus CECT) detected 49 of the 58 invasive adenocarcinomas, 2 of the 4 in situ adenocarcinomas, and none of the high-grade dysplasia lesions. When benchmarked against the complete postoperative pathological assessment (103 lesions), the conventional workup demonstrated sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of 78%, 97%, 98%, and 73%, respectively, for colonic lesion detection.

The average time lapse between ^{18}F-FDG PET/CT and conventional imaging was 29.8 ± 12.9 days (range 7–53 days), and between PET/CT and surgical resection was 5 ± 4 days (range 1–23 days). Dual-time-point imaging, consisting of an initial whole-body scan followed by a delayed abdominopelvic acquisition, was performed in 36 of the 48 patients. Evaluation of the colon was unreliable in two patients with diabetes on metformin therapy due to widespread intestinal ^{18}F-FDG activity; PET/CT missed two T1 carcinomas in these individuals. Compared with the histopathological gold standard, ^{18}F-FDG PET/CT accurately detected 54 invasive adenocarcinomas (encompassing all five mucinous

types), all 4 in situ adenocarcinomas, and all 3 high-grade dysplastic adenomas. All tumors previously identified by colonoscopy displayed increased pathologic ^{18}F-FDG avidity **(Figure 1)**.

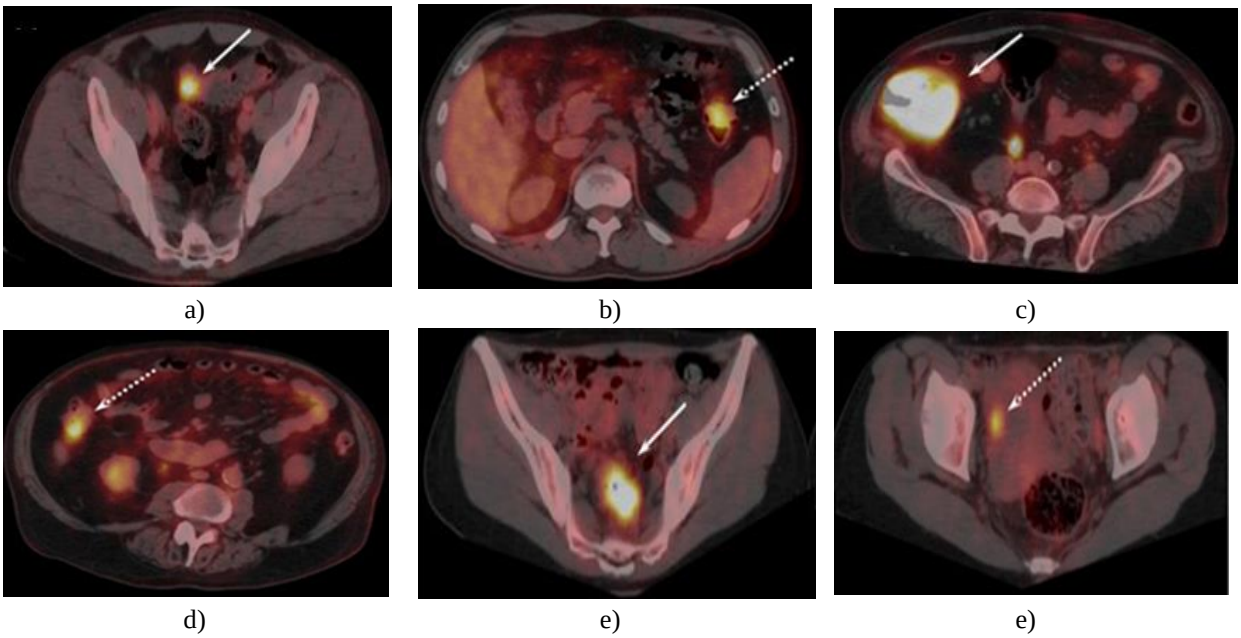

Figure 1. Preoperative ^{18}F-FDG PET/CT scans from three patients initially considered to have localized CC, revealing extra lesions or distant spread missed by routine staging (dotted arrows)

A 57-year-old male patient with a pT3 sigmoid cancer (a) and a synchronous T2 carcinoma in the left colon (b). A 74-year-old male patient showing an 11 cm pT3 caecal mass (c) along with a high-grade dysplastic adenoma in the right colon (d). A 46-year-old female patient with sigmoid stenosis preventing complete colonoscopy (pT3) (e) and an unsuspected metastasis to the right ovary (f).

On the other hand, false-positive results occurred in 5 of 38 low-grade dysplastic adenomas, whereas false-negative findings were observed in 4 pT1 adenocarcinomas. In six patients, transient focal colonic uptake was observed on the early scan but largely disappeared on delayed images. No structural correlates were identified during surgery in any of these cases, and follow-up colonoscopy in five patients confirmed benign processes (true negatives). Accordingly, ^{18}F-FDG PET/CT achieved sensitivities of 94%, 87%, 92%, and 89% and specificities of 87%, 92%, 89%, and 94% for colonic lesion identification. The PET/CT sensitivity advantage over conventional methods reached statistical significance (P = 0.02). Differences in specificity (P = 0.2), PPV (P = 0.22), and NPV (P = 0.07) did not attain significance. PET/CT identified 10 additional pathologic lesions in 7 patients (3 high-grade dysplastic adenomas, 2 in situ adenocarcinomas, and 5 invasive carcinomas) that were not recognized by standard evaluation. Details regarding the supplementary benefit of ^{18}F-FDG PET/CT in cases where the two modalities disagree are presented in **Table 4**.

Table 4. Cases of disagreement between conventional workup and ^{18}F-FDG PET/CT in the assessment of colonic lesions involving 12 patients and 12 lesions. The additional diagnostic contribution of 18F-FDG PET/CT is highlighted.

Tumor location	Tumor size (mm)	Standard workup result	^{18}F-FDG PET/CT result	Additional value provided by PET/CT
Transverse colon (T), pT1	40	TP	TP	Identification of two additional adenomas with high-grade dysplasia

Right colon (RC), high-grade dysplasia (HG)	25	–	TP	
Right colon (RC), high-grade dysplasia (HG)	30	–	TP	
Sigmoid colon (S), pT1	50	TP	TP	Identification of one additional adenoma with high-grade dysplasia
Transverse colon (T), high-grade dysplasia (HG)	12	–	TP	
Sigmoid colon (S), carcinoma in situ (is)	10	FN	TP	Detection of one synchronous carcinoma in situ not identified during colonoscopy
Caecum (C), pT3	60	TP	TP	
Sigmoid colon (S), pT3	30	FN	TP	Detection of one synchronous invasive adenocarcinoma and one additional carcinoma in situ
Caecum (CG), carcinoma in situ (is)	15	FN	TP	
Sigmoid colon (S), pT3	55	TP	TP	Detection of two additional synchronous invasive adenocarcinomas beyond a sigmoid tumor stenosis
Left colon (LC), pT2	25	FN	TP	
Caecum (C), pT2	30	FN	TP	
Sigmoid colon (S), pT3	70	FN	TP	Detection of one synchronous invasive adenocarcinoma not identified during colonoscopy
Caecum (CG), carcinoma in situ (is)	60	TP	TP	
Sigmoid colon (S), pT3	45	TP	TP	Detection of one synchronous invasive adenocarcinoma not identified during colonoscopy
Sigmoid colon (S), pT3	25	FN	TP	
Sigmoid colon (S), carcinoma in situ (is)	15	FN	FN	
Caecum (CG), carcinoma in situ (is)	15	FN	FN	
Sigmoid colon (S), low-grade dysplasia (LG)	35	TP	TP	No additional benefit (perioperative detection of a caecal carcinoma in situ)
Caecum (C), carcinoma in situ (is)	25	FN	FN	
Caecum (C), pT3	55	TP	TP	
Sigmoid colon (S), pT1	10	FN	FN	No additional benefit (perioperative detection of a sigmoid invasive adenocarcinoma)
Caecum (C), pT2	50	TP	TP	
Transverse colon (T), pT3	45	TP	n/a	No additional benefit (diffuse intestinal uptake associated with metformin use)
Caecum (C), pT3	30	TP	n/a	No additional benefit (diffuse intestinal uptake associated with metformin use)
Left colon (LC), pT3	70	TP	TP	No additional benefit (false-positive results)
Not applicable	–	–	FP	

Abbreviations: S = sigmoid, LC = left colon, T = transverse colon, RC = right colon, C = caecum, is = in situ, HG = high-grade dysplasia.

Quantitative measurements of SUVmax, SUVpeak, TLG, and MTV obtained from all identified invasive adenocarcinomas, in situ adenocarcinomas, and adenomas showing either low- or high-grade dysplasia

are summarized in **Table 5**. The parameters SUVmax, SUVpeak, and TLG exhibited statistically significant differences when comparing the combined group of invasive adenocarcinomas, in situ adenocarcinomas, and high-grade dysplasia lesions against low-grade dysplasia (P = 0.002, P = 0.003, P = 0.006, respectively). Significant distinctions were also present between early (pT1-pT2) and more advanced (pT3-pT4) adenocarcinomas for these uptake values (P = 0.009, P = 0.004, P < 0.005, and P < 0.005, respectively). Nevertheless, the PET-derived indices did not permit reliable separation of low-grade from high-grade dysplastic adenomas. No notable associations were identified between any of the metabolic parameters (SUVmax, SUVpeak, TLG, MTV) and other histopathological characteristics, including depth of invasion (pT), presence of vascular invasion, histological grade, mucinous histology, lymph node status, distant metastasis, or RER phenotype. A moderate positive correlation was observed between maximum tumor diameter and SUVmax (R = 0.54, P = 0.005), SUVpeak (R = 0.54), TLG (R = 0.66), and MTV (R = 0.59).

Table 5. Average SUVmax, SUVpeak, TLG, and MTV values stratified according to histopathological classification.

	SUVmax	SUVpeak	TLG	MTV
LG dysplasia	6.02 ± 0.66	4.48 ± 0.71	25.93 ± 12.48	7.42 ± 3.89
HG dysplasia	6.41 ± 0.94	4.13 ± 0.39	13.25 ± 9.57	3.85 ± 3.53
In situ carcinoma	5.64 ± 1.5	4.2 ± 1.4	47.2 ± 53.1	15.47 ± 19.49
T1 carcinoma	10.99 ± 1.84	8.46 ± 2.56	66.97 ± 65.37	9.19 ± 8.38
T2 carcinoma	14.52 ± 10.27	10.55 ± 7.34	62.1 ± 52.93	6.77 ± 3.75
T3 carcinoma	19.41 ± 10.03	15.34 ± 7.32	269.08 ± 245.22	22.86 ± 17.58
T4 carcinoma	13.19 ± 0.98	10.82 ± 0.5	189.3 ± 68	24.36 ± 7.82

Abbreviations: LG = low-grade, HG = high-grade.

Nodal involvement and distant metastases assessment

Histopathology confirmed regional lymph node metastases in 18 patients (38% of the cohort). Patient-based evaluation showed that CECT achieved a sensitivity of 22% and ^{18}F-FDG PET/CT a sensitivity of 33% (P = 0.2) for nodal disease detection. Specificities were 84% and 90% (P = 0.7), positive predictive values were 44% and 67% (P = 0.08), and negative predictive values were 65% and 70% (P = 0.7), respectively. Metabolically active pericolic nodal metastases were visible on both early and delayed PET/CT scans. In a single case, a 9 mm peritumoral lymph node metastasis became apparent only on the delayed acquisition. Restricting analysis to the 11 lymph nodes larger than 10 mm yielded 2 true-positive, 5 true-negative, 3 false-positive, and 1 false-negative results for 18F-FDG PET/CT, yielding an NPV of 83%. Inflammatory adenitis caused by tumor-associated intestinal fistulas accounted for two of the three false-positive interpretations.

^{18}F-FDG PET/CT identified an ovarian secondary deposit in one patient and combined peritoneal, hepatic, and pulmonary involvement in another patient, with histological confirmation obtained during surgery in both instances. In a different patient, the modality incidentally detected a previously unrecognized primary lung cancer. In one additional case, a hepatic lesion suspected on PET/CT was later validated by follow-up conventional imaging six months after the operation. In contrast, PET/CT missed a small solitary hepatic metastasis identified intraoperatively in one patient and failed to detect millimetric peritoneal seeding in two further patients. In keeping with the study's inclusion criteria, preoperative CECT revealed no evidence of distant metastasis. Intensity of ^{18}F-FDG uptake in the primary tumor did not predict the likelihood of nodal or distant metastatic disease. No significant differences in SUVmax, SUVpeak, TLG, or MTV were evident between patients with and without lymph node involvement or visceral metastases.

Survival analysis

After a mean postoperative observation period of 183 months (range 164–195 months), one patient who died due to surgical complications was excluded from survival evaluations. Fourteen patients succumbed to unrelated causes, and five patients died as a result of progressive colonic cancer. No link was identified

between initial SUVmax levels and patient mortality. Disease recurrence occurred in six patients at a mean of 19 months following surgery (range 4–48 months), primarily involving hepatic metastases in five cases and peritoneal carcinomatosis in one case. The ability of SUVmax to anticipate recurrence was examined through ROC curve analysis. Since no effective cutoff value reached significance, the metabolic parameters were categorized using their median values: 14.2 for SUVmax, 11.2 for SUVpeak, 117.5 for TLG, and 13.1 for MTV. None of these ^{18}F-FDG uptake indices derived from the primary tumor proved useful for predicting clinical outcome. Stratification of patients by median SUVmax, SUVpeak, TLG, and MTV did not show significant differences in disease-free survival. Likewise, these parameters did not differ meaningfully between survivors and those who died during follow-up. The limited statistical power of these findings is likely due to the small number of patients who experienced disease progression. The sole independent prognostic factor for disease-free survival was nodal (N) stage. Lymph node metastasis was associated with significantly worse outcomes. Kaplan–Meier survival curves showed 97% progression-free survival in patients without nodal involvement, compared with 67% in those with nodal metastases ($P = 0.0023$).

This prospective investigation evaluates the diagnostic and prognostic usefulness of preoperative ^{18}F-FDG PET/CT scanning among patients with resectable colorectal cancer (CC). The present findings support the role of 18F-FDG PET/CT in uncovering synchronous primary intestinal tumors and distant metastases that remained undetected during routine preoperative staging. Nevertheless, the modality showed shortcomings in reliably identifying regional nodal involvement and in delivering meaningful prognostic data derived from quantitative measures of ^{18}F-FDG avidity within the primary lesion.

Aligning with prior research [26, 27], 18F-FDG PET/CT provided additional diagnostic benefit beyond conventional presurgical evaluation for identifying colonic lesions (sensitivity: 94% versus 78%). The technique facilitated preoperative recognition of otherwise undetected synchronous colon cancers in 7 out of 48 (14.6%) patients. These included 2 cases featuring incomplete or impossible colonoscopy, 2 of 4 synchronous in situ carcinomas, and all 3 adenomas exhibiting high-grade dysplasia. However, the clinical relevance of these detections remains debated and warrants further elucidation. In individuals with incomplete endoscopic assessment, guidelines recommend peri- or postoperative colonoscopy to detect lesions obscured by obstructing tumors. Under these circumstances, ^{18}F-FDG PET/CT can enable earlier identification and simultaneous surgical management of synchronous colonic neoplasms during a single operation, providing substantial clinical benefit. Such information is particularly important for patients scheduled for laparoscopic resection, as tactile examination and thorough visual inspection of the bowel are not feasible in this setting. It is also noteworthy that CT colonography is the preferred alternative when colonoscopy cannot be performed [3]. Future comparative trials comparing CT colonography with 18F-FDG PET/CT would help clarify the supplementary value of the latter approach.

Accurate preoperative detection of lymphatic metastases remains difficult. Previous studies and a comprehensive meta-analysis [20, 28, 29] have shown that while ^{18}F-FDG PET/CT is effective for T and M staging, it has limited sensitivity for lymph node metastases. This reduced performance largely stems from the intense metabolic activity of the adjacent primary tumor, which can conceal ^{18}F-FDG uptake in nearby nodes. Physiological tracer accumulation in the bowel and urinary bladder may further confound evaluation of regional lymphatic territories in the pelvis and peritumoral areas [16]. The utilization of an older PET/CT system without time-of-flight or analog detector technology also likely contributed to the modest nodal detection rate in this cohort. Importantly, 18F-FDG PET/CT demonstrated a strong negative predictive value, enabling reclassification of patients with indeterminate CECT results. Among the 11 regional lymph nodes exceeding 10 mm and considered equivocal on CECT, the negative predictive value reached 83%. Two of the three false-positive findings on ^{18}F-FDG PET/CT were attributable to inflammatory changes associated with an intestinal fistula.

Although dual-time-point imaging was not universally applied (largely due to patient refusal), it helped distinguish physiological from neoplastic colonic activity in 6 of 36 patients (17%). It improved the overall negative predictive value of ^{18}F-FDG PET/CT. Incorporating dual-time-point protocols into routine practice may enhance specificity when evaluating colonic foci, particularly those showing isolated uptake without a visible structural correlate. This strategy could

restrict the need for invasive follow-up procedures to cases with sustained metabolic abnormalities, thereby limiting unnecessary endoscopic examinations.

^{18}F-FDG PET/CT successfully detected occult metastases to the ovaries, peritoneum, and liver, along with one primary lung carcinoma, across four patients. In keeping with earlier observations [30], a 1-mm liver metastasis became apparent only on delayed-phase imaging. In contrast, both ^{18}F-FDG PET/CT and CECT missed small peritoneal deposits measuring only a few millimeters in two patients, underscoring the limited sensitivity of contemporary imaging methods for detecting minute peritoneal disease. Delayed acquisitions conferred no additional diagnostic advantage for identifying peritoneal carcinomatosis.

Research examining the prognostic relevance of quantitative ^{18}F-FDG uptake in primary colon tumors remains scarce. In one such study, Shi *et al*. [23] suggested that SUVmax could serve as a predictor of survival. Their analysis involved 107 patients with colon cancer who underwent surgery and were monitored for 5 years, with 30 deaths recorded. This sample permitted the determination of a significant SUVmax threshold at 11.85. Conversely, Lee *et al*. [24] reported no association between SUVmax and either recurrence or progression-free survival (PFS) in a retrospective series of 163 patients followed for 4 years, including 25 recurrences. These discrepant outcomes raise uncertainty about the reliability of metabolic parameters as prognostic tools. A subsequent retrospective investigation of 91 CRC patients assessed the supplementary role of preoperative ^{18}F-FDG PET/CT and correlated metabolic indices, pericolic fat stranding, histopathological findings, and overall survival [25]. In multivariate modeling, tumor differentiation, MTV, TLG, and lymphovascular invasion emerged as independent predictors of overall survival. Preoperative PET/CT further supported CC care by identifying additional metastatic sites and improving distinction between T3 and T4 stages. Despite a mean observation period of 15 years, the current study could not reliably predict disease progression. This limitation is attributable chiefly to the smaller cohort (48 patients) relative to earlier publications. Most tumors were localized and underwent curative resection, resulting in infrequent recurrences. The consequent paucity of events rendered the PFS evaluation inconclusive and highlighted the necessity for substantially larger cohorts.

In contrast to findings reported in studies of other tumor types [18-20, 23], no ^{18}F-FDG PET/CT parameter demonstrated prognostic significance here for survival, nodal status, or metastatic spread. Such results likely reflect the restricted sample size and the generally favorable outlook for patients diagnosed with localized disease, where metastatic progression and cancer-specific mortality rates are low. Even the prolonged 15-year mean follow-up after surgery could not overcome the low event rate, consistent with meta-analytic evidence that most relapses occur within 2 years of resection [31]. Interestingly, non-surviving patients in this series exhibited a substantially elevated rate of metastases compared with survivors. This pattern implies that, while PET/CT itself may not carry intrinsic prognostic weight, its ability to uncover occult metastatic disease—well recognized for its negative impact on outcome—remains clinically relevant. Recent evidence has also identified ^{18}F-FDG uptake in bone marrow and spleen as potential imaging biomarkers reflective of systemic inflammation [32].

Additionally, ^{18}F-FDG PET/MRI, a relatively new hybrid technique implemented in specialized centers, has demonstrated strong diagnostic performance for lesion and metastasis detection in colon cancer, as summarised in a recent meta-analysis [33]. Novel tracers such as 68Ga-DOTA-FAPI-04 show further potential for superior diagnostic precision, notably higher specificity, in evaluating primary tumors and metastases across diverse cancers. These agents appear especially effective for liver metastases, peritoneal carcinomatosis, and brain lesions [34].

One major constraint of this work arises from the age of the dataset, collected roughly 15 years ago with an early-generation PET/CT scanner, which restricted overall diagnostic capability. Moreover, substantial advances in CC treatment since that period may have influenced patient management and prognosis. Contemporary studies employing modern imaging systems are therefore warranted. The average 30-day interval (range 7–53 days) between ^{18}F-FDG PET/CT and conventional imaging may also represent a minor limitation.

Conclusion

Among patients with non-metastatic CC, preoperative 18F-FDG PET/CT successfully detects synchronous colonic lesions that are often missed by routine diagnostic approaches. It likewise identifies distant

metastases effectively, yet its performance for N staging is only moderate. Due largely to the limited cohort size, the quantitative assessment of 18F-FDG uptake in the primary tumor showed no association with recurrence or disease-free survival in this population. It thus provided no meaningful prognostic stratification for individual patients.

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