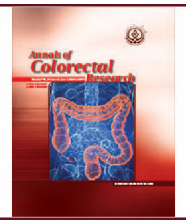
Original Article

Ann Colorectal Res 2021;9(2):58-62.

Annals of Colorectal Research
(Iranian Journal of Colorectal Research)



FDG PET/CT and Colonoscopy Combine Synergistically in Primary Colorectal Cancer Diagnosis

Doruk Seyfi*[1], *MD;* *Chuong Bui*[2], *MD; Walid Barto*[1], *MD; Assad Zahid*[1], *PhD Candidate; Christopher J Young*[3]*, *MD

[1]*Department of Colorectal Surgery, Nepean Hospital, Penrith, NSW, Australia*
[2]*Department of Nuclear Medicine and PET, Nepean Hospital, Penrith, NSW, Australia*
[3]*The University of Sydney, Central Clinical School, Sydney, New South Wales, Australia*

Corresponding authors:
Christopher J Young,
RPAH Medical Centre, Suite G07/100 Carillon Avenue, Newtown, NSW 2042, Australia. **Tel:** +61-2-95190064; **Fax:** +61-13-00078746
Email: cyoungnsw@aol.com

Received: 02-05-2021
Revised: 12-06-2021
Accepted: 23-06-2021

Abstract

Background: Colonoscopy is the standard for primary colorectal cancer (CRC) detection, but is invasive and imperfect. This study aimed to assess the accuracy of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) and colonoscopy in the diagnosis of primary CRC.
Methods: A retrospective analysis of all patients identified as undergoing an FDG PET/CT scan and a colonoscopy within six months of each other, with no intervening malignancy treatment, over 12 months in a single university teaching hospital.
Results: Two hundred and sixty-two patients had FDG PET/CT and colonoscopy within six months. 206 were excluded for prior treatment. 56 patients were included; 26 (46%) with confirmed primary CRC tumors and 30 (54%) without. Multivariate logistic regression analysis indicated that CRC diagnosis was more likely when colonoscopy was performed before the FDG PET/CT (OR: 21.9, CI 2.6-183) and when CRC was diagnosed on FDG PET/CT (OR 12.3, CI 3.0-51.0). The ROC-AUC for FDG PET/CT and colonoscopy was 0.81 (CI 0.70-0.93, P<0.001) and 0.96 (CI 0.90-1.0, P<0.001), respectively.
Conclusions: Colonoscopy is very good and FDG PET/CT is good as diagnostic tests for CRC primary diagnosis. Together, they facilitated diagnosis in all primary cases of CRC. PET/CT should be considered in patients with incomplete colonoscopy where there is suspicion for primary CRC.

Keywords: 18F-fluorodeoxyglucose, Positron emission tomography, Computed tomography, Colonoscopy, Colorectal cancer

Please cite this paper as:
Seyfi D, Bui C, Barto W, Zahid A, Young CJ. FDG PET/CT and Colonoscopy Combine Synergistically in Primary Colorectal Cancer Diagnosis. *Ann Colorectal Res*. 2021;9(2):58-62. doi: 10.30476/ACRR.2021.91044.1095.

Introduction

There are about 16,700 new bowel cancers per year in Australia, with a 1 in 13 individual lifetime risk of colorectal cancer (CRC) (1). Colonoscopy is the reference standard for primary colorectal cancer (CRC) detection but is invasive and imperfect (2). Apart from its associated risks of perforation and bleeding, a colonoscopy may miss some polyps, more so on the right side of the colon, and more so if there is incomplete colonic visualization or poor bowel preparation (2).

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) has a role in the detection of incidental colorectal lesions (ICL) and the staging and detection of recurrence of CRC, especially distant metastases (3). A meta-analysis by Treglia et al. in 2014 reported a 3.6% prevalence of focal ICL detected by PET/CT (4). Mui et al. more recently reported 20 of 170 (12%) focal ICL on PET/CT being diagnosed on colonoscopy as adenocarcinoma (5).

The use of FDG PET/CT for CRC and adenoma detection as a screening tool has a low yield but has reported good sensitivity but poor specificity, meaning it will not detect all lesions and will detect a good number of false positives (6). What is not so clear is the role of PET/CT as a diagnostic tool for the detection of CRC, and what is the role of PET/CT and colonoscopy in combination in the diagnosis and management of primary CRC (7-9).

This study aimed to assess the accuracy of FDG PET/CT and colonoscopy in the diagnosis of primary CRC, and to assess the benefits of the interaction or synergy of the two investigations.

Patients and Methods

Patients

This study was a retrospective analysis of all patients identified as undergoing an FDG PET/CT scan and a colonoscopy, in any order, within six months of each other, over 12 months in a single hospital, from August 2014 to August 2015. All patients were >18 years old. The six-month period was selected to ensure no significant histological or metabolic changes had occurred between the two diagnostic modalities. Patients were excluded if they had any intervening malignancy treatment between the PET/CT and colonoscopy (systemic, radiotherapy, or surgical) and if the PET/CT and colonoscopy were more than six months apart.

Ethics approval for this study was granted by the Human Research Ethics Committee, Nepean Blue Mountains Local Health District, Sydney.

FDG PET/CT Imaging and Colonoscopy

All FDG PET/CT scans were reviewed and reported by consultant nuclear medicine physicians and/or radiologists, who were blinded from the colonoscopy result if the PET/CT was performed after colonoscopy. Ahead of the PET/CT scan, the patient fasted for at least 6 hours and the fasting glucose was <10 mmol/liter, then 250 MBq FDG was injected intravenously and the scan was performed after 60 minutes for 15-20 minutes from vertex to mid femora. Colonoscopies were performed by gastroenterologists, gastroenterology advanced trainees, general surgeons, fellows, or surgical registrars.

Confirmation of CRC diagnosis

All patients had histological confirmation of their primary CRC and the case was discussed at a CRC multidisciplinary team (MDT) meeting.

Outcomes

The primary outcome was the accuracy of detection of a CRC primary lesion by FDG PET/CT and colonoscopy. Secondary outcomes were the association between variables and the diagnosis of

Table 1: Demographics of patients who had both an 18F-fluorodeoxyglucose positron emission tomography/computed tomography and a colonoscopy within six months of each other with no intervening malignancy treatment.

	n (%) – unless otherwise specified
Mean age, years (SD) range	67 (11) 35-83
Gender	
Male	35 (63)
Female	21 (38)
Mean, median time in days (SD) range, between colonoscopy and PET/CT (regardless of order)	46, 22 (50) 1-179
MDT clinicopathological diagnosis of colorectal cancer (CRC)	
Yes	26 (46)
No	30 (54)
CRC diagnosed by:	
Both colonoscopy and PET/CT	23 (41)
PET/CT diagnosis only	2 (4)
Colonoscopy diagnosis only	1 (2)
No CRC diagnosis	30 (54)
CRC diagnosis order	
Diagnosed at colonoscopy first	23 (41)
Diagnosed on PET/CT first	3 (5)
No CRC diagnosis	30 (54)
CRC site	
Cecum to transverse colon	11 (20)
Descending colon to rectum	15 (27)
No CRC diagnosis	30 (54)

SD, standard deviation; PET, positron emission tomography; CT, computerized tomography; MDT, multidisciplinary team; CRC, colorectal cancer.

primary CRC, and finally the interaction of PET/CT and colonoscopy in aiding the diagnosis of CRC.

Statistics

Data were expressed as mean ± standard deviation (SD) and range, with numbers and percentages being given for categorical data. The χ^2 and Fisher's exact tests were used to test for the significance of differences between groups. All variables associated with study outcomes (P<0.1) were included in multivariable logistic regression models to assess the association. P<0.05 was considered statistically significant. Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated for colonoscopy and PET/CT. Receiver operating characteristic (ROC) curves, their corresponding area under the curve (AUC), and 95% confidence interval (CI) were used to assess the performance of colonoscopy and PET/CT to diagnose primary CRC tumors. All analyses were conducted using SPSS version 24 (SPSS Inc., Chicago, IL, USA). This study was approved by the Nepean Hospital Ethics Research Committee.

Results

Two hundred and sixty-two patients had FDG PET/CT and colonoscopy within 6 months during the study period. 206 were excluded for prior treatment. 56 patients were included in the study; 26 (46%) with a confirmed primary CRC tumor and 30 (54%) without. Demographic details are shown in Table 1. The 2 of 26 (8%) CRC cases that were not detected on colonoscopy were both right-sided CRC in patients who had an incomplete colonoscopy.

Univariate analysis revealed five factors significantly associated with the diagnosis of CRC (Table 2). Two of these five factors were rejected from the multivariate model, and multivariate logistic regression analysis indicated that CRC diagnosis was more likely when colonoscopy was performed before the PET/CT (Odds Ratio (OR) 21.9, CI 2.6-183) and when CRC was diagnosed on PET/CT (OR 12.3, CI 3.0-51.0) (Table 2.).

Sensitivity, specificity, accuracy, PPV, and NPV for FDG PET/CT and colonoscopy are shown in Table 3. The ROC curves are shown in Figure 1. The ROC-AUC for FDG PET/CT and colonoscopy was 0.81 (CI 0.70-0.93, P<0.001) and 0.96 (CI 0.90-1.0, P<0.001), respectively.

Discussion

In this study, colonoscopy was shown to be a more accurate diagnostic tool than FDG PET/CT in the diagnosis of primary CRC tumors. However,

Table 2: Univariate and multivariate analysis of primary colorectal cancer diagnosis in patients who had both an 18F-fluorodeoxyglucose positron emission tomography/computed tomography and a colonoscopy within six months of each other with no intervening malignancy treatment.

	MDT clinicopathological diagnosis of colorectal cancer (%)		Univariate P value	Multivariate *p* value (OR [CI])
	No	Yes		
Age			0.592	
≤68 years	17 (30)	12 (21)		
>68 years	13 (23)	14 (25)		
Gender			0.584	
Male	20 (36)	15 (27)		
Female	10 (18)	11 (20)		
Colonoscopy or CT/PET first			<0.001	0.001 (21.9 [2.6-183])
Colonoscopy	16(29)	25 (45)		
PET/CT	14 (25)	1 (2)		
Time between colonoscopy and PET/CT			0.015	0.804 (4.5 [1.5-13.9])
<22 days	10 (18)	18 (32)		
≥22 days	20 (36)	8 (14)		
CRC diagnosed at colonoscopy			<0.001	
Yes	0 (0)	24 (43)		
No	30 (54)	2 (4)		
CRC diagnosed on PET/CT			<0.001	<0.001 (12.3 [3.0-51.0])
Yes	10 (18)	25 (45)		
No	20 (36)	1 (2)		
Lymph node disease on PET/CT			<0.001	
Yes	3 (5)	15 (27)		
No	27 (48)	11 (20)		
Metastatic disease on PET/CT			0.231	
Yes	2 (4)	5 (9)		
No	28 (50)	21 (38)		

MDT, multidisciplinary team; OR, odds ratio; CI, confidence interval; CRC, colorectal cancer; CT, computerized tomography; PET, positron emission tomography.

Table 3: Diagnostic value of 18F-fluorodeoxyglucose positron emission tomography/computed tomography and colonoscopy for detecting primary colorectal cancer in patients who had both investigations within six months of each other with no intervening malignancy treatment.

	Sensitivity	Specificity	Accuracy	PPV	NPV
FDG PET/CT	96.2%	66.7%	80.4%	71.4%	95.2%
Colonoscopy	92.3%	100%	96.4%	100%	93.8%

PPV, positive predictive value; NPV, negative predictive value. MDT, multidisciplinary team; CP, clinicopathological; FDG ^{18}F-fluorodeoxyglucose; PET/CT, positron emission tomography/computed tomography.

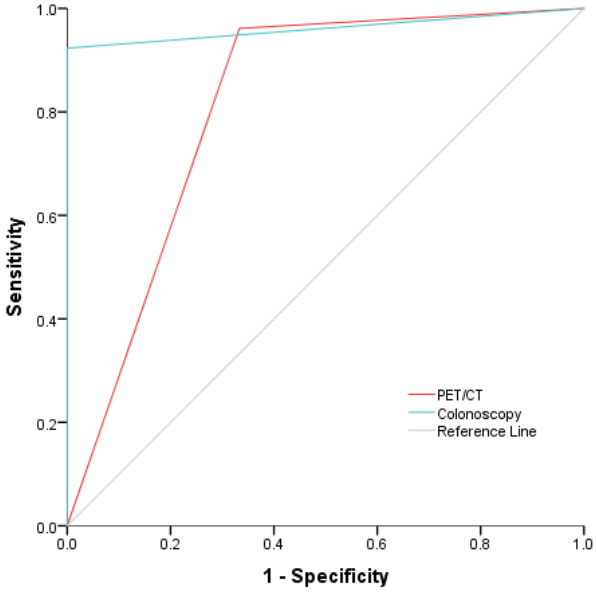


Figure 1: Receiver operating characteristic curves of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) and colonoscopy in diagnosing primary colorectal cancer lesions.

between them, the two modalities were able to detect all the CRCs in our cohort. The diagnosis of CRC was found to be significantly better in cases when the colonoscopy was performed before the PET/CT and in cases where the PET/CT was positive for a CRC. We interpret this as reflecting that the main role of diagnosis of CRC with PET/CT is in situations where suspicion for a primary CRC remains following a colonoscopy. This may be in cases of incomplete colonoscopy and poor bowel preparation.

Igarashi et al. in 2016 published a large cohort of patients undergoing both colonoscopy and PET/CT where PET/CT sensitivity was best for T2-4 CRCs but decreased for T1 CRCs, advanced adenomas, and low-grade adenomas (8). That would be in keeping with why the sensitivity of PET/CT was so good in our series given that our outcome was focused on diagnosing CRC and not adenomas. The reduced specificity of PET/CT would seem one of the major obstacles in it being used as a screening tool or a routine diagnostic tool for CRC. However, if the focus is on case-finding after an incomplete colonoscopy, it would appear that the high sensitivity of PET/CT for primary CRC tumors makes it ideal for reviewing the unassessed or poorly assessed large bowel. Kim et al. reported 100% sensitivity for the detection of proximal synchronous CRC using PET/CT in cases with obstructive CRC (10). Sekiguchi et al., however, reported quite poor sensitivity of PET/CT (6.9%) for advanced colorectal neoplasms (CRC and lesions with high-grade dysplasia) among 7505 asymptomatic individuals being screened (11). Interestingly, Hirakawa et al. reported in 2012 that the sensitivity of PET/CT was less for proximal colon tumors, which could limit its utility as a complementary investigation to colonoscopy (9).

The limitations of this study include that it was a retrospective study at a single hospital, and that the majority (74%) of our patients had a colonoscopy prior to the PET/CT, which may have improved the accuracy of PET/CT and biased the reading of PET/CT with the possible knowledge of the presence of a CRC. Our patients appear to be two quite separate cohorts, as those with colonoscopy first followed by PET/CT are more likely to have had a colonoscopy for symptoms, and those with PET/CT first were probably being investigated for some other malignancy and the CRC was an incidental finding.

We are not advocating by this study to routinely perform an FDG PET/CT and colonoscopy in all patients with suspected CRC. The study aimed to look at the utility of FDG PET/CT compared with colonoscopy when performed within six months of each other in diagnosing primary CRC lesions.

Based on cost alone, we would not recommend FDG PET/CT for routine CRC detection, as any lesion detected would still require a colonoscopy and its associated expense (9). However, in suspected cases where colonoscopy is incomplete, is not possible, or there is poor bowel preparation, we can see a clear role for proceeding with a PET/CT scan for the diagnosis of primary CRC tumors. This should not be conflated with the role of PET/CT in the staging of CRC or detection of recurrent CRC (3). The use of PET/CT has been found to have greater utility for CRC detection when used in combination with fecal occult blood tests, but has lesser utility for small lesions and adenomas (6).

At present, the Medicare Benefits Schedule (MBS) rebate that the Australian Government will pay for one FDG PET/CT is 953 AUD (MBS code 61541), for colonoscopy is 344.80 AUD (MBS code 32222), and for flexible sigmoidoscopy (defined as colonoscope passage up to but not beyond the hepatic flexure)is 114.85 AUD (MBS code 32084).

Conclusion

Colonoscopy is very good and FDG PET/CT is good

as diagnostic tests for the diagnosis of primary CRC. Together, they facilitated diagnosis in all primary cases of CRC in this study. Because of the superior accuracy of colonoscopy over PET/CT in the diagnosis of primary CRC, we recommend PET/CT should be considered for the diagnosis of CRC only following an incomplete colonoscopy where there is suspicion for a primary CRC.

Acknowledgments

No potential conflicts of interest were disclosed.

Conflicts of interests: None declared.

References

1. Australian Institute of Health and Welfare. Cancer compendium: information and trends by cancer type: Colorectal cancer in Australia. Available from: https://www.aihw.gov.au/reports/cancer/cancer-compendium-information-and-trends-by-cancer-type/report-contents/colorectal-cancer-in-australia (Accessed 22nd June 2019).
2. Dekker E, Rex DK. Advances in CRC prevention: screening and surveillance. Gastroenterology. 2018;154:1970-84.
3. Petersen H, Holdgaard PC, Madsen PH, Knudsen LM, Gad D, Gravergaard AE, et al. FDG PET/CT in cancer: comparison of actual use with literature-based recommendations. Eur J Nuc Med Mol Imaging. 2016;43:695-706.
4. Treglia G, Tarali S, Salsano M, Muoio B, Sadeghi R, Giovanelli L. Prevalence and malignancy risk of focal colorectal incidental uptake detected by (18)F-FDG-PET or PET/CT: a meta-analysis. Radiol Oncol. 2014;48:99-104.
5. Mui M, Akhurst T, Warrier SK, Lynch AC, Heriot AG. Detection of incidental colorectal pathology on positron emission tomography/computed tomography. ANZ J Surg. 2018;88:E122-6.
6. Minamimoto R, Senda M, Jinnouchi S, Terauchi T, Yoshida T, Inoue T. Detection of colorectal cancer and adenomas by FDG-PET cancer screening program: results based on a nationwide Japanese survey. Ann Nucl Med. 2014;28:212-9.
7. Liu T, Behr S, Khan S, Osterhoff R, Aparici CM. Focal colonic FDG activity with PET/CT: guidelines for recommendation of colonoscopy. World J Nucl Med. 2015;14:25-30.
8. Igarashi K, Hotta K, Imai K, Yamaguchi Y, Ito S, Kawata N, et al. Can positron emission tomography detect colorectal adenomas and cancers? J Gastroenterol Hepatol. 2017;32:602-8.
9. Hirakawa T, Kato J, Okumura Y, Hori K, Takahashi S, Suzuki H, et al. Detectability of colorectal neoplasia with fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT). J Gastroenterol. 2012;47:127-35.
10. Kim WS, Lee HS, Lee JM, Kwak MS, Hwang SW, Park SH, et al. Fluoro-2-deoxy-d-glucose positron emission tomography/computed tomography for the detection of proximal synchronous lesions in patients with obstructive colorectal cancer. J Gastroenterol Hepatol. 2017;32:401-8.
11. Sekiguchi M, Kakugawa Y, Terauchi T, Matsumoto M, Saito H, Muramatsu Y, et al. Sensitivity of 2-[18F]fluoro-2-deoxyglucose positron emission tomography for advanced colorectal neoplasms: a large-scale analysis of 7505 asymptomatic screening individuals. J Gastroenterol. 2016;51:1122-32.