# The ability of positron emission tomography/computed tomography to detect synchronous colonic cancers in patients with obstructive colorectal cancer

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**Abstract.** Positron emission tomography/computed tomography (PET/CT) is frequently used to detect colorectal cancer. The present retrospective study assessed the ability of PET/CT to identify synchronous colonic lesions in 72 patients with obstructive colorectal cancer. All patients had undergone surgical resection without undergoing preoperative total colonoscopy (TCS) at the Digestive Disease Center (April 2007 to September 2016), and subsequently underwent TCS of the proximal colon within 2 years post-surgery. A total of 11 patients exhibited 18F-fluorodeoxyglucose uptake during PET/CT of the proximal colon (4 invasive cancers, 3 advanced adenomas and 4 false-positive results), and 61 patients had no uptake in the proximal colon. Among these 61 patients, postoperative TCS revealed 2 invasive cancers and 4 advanced adenomas. The sensitivity of PET/CT for detecting synchronous invasive cancers was 66.6% (4/6), with a specificity of 89.4% (59/66), a positive predictive value of 36.4% (4/11), a negative predictive value of 96.7% (59/61), and an accuracy of 87.5% (63/72). Negative PET/CT results indicated a low probability of synchronous lesions in the proximal colon. Thus, PET/CT may be a useful tool for detecting synchronous colonic cancers in patients with obstructive colon cancer.

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## Introduction

Positron emission tomography/computed tomography (PET/CT) is sequential CT and PET scans that are performed during a single procedure using a hybrid PET/CT scanner. This modality combines the advantages of PET's high contrast resolution and CT's high spatial resolution. Furthermore, intravenous contrast agents are not required for PET/CT, because glucose metabolism is visualized using fluorodeoxyglucose (FDG) uptake, which is quantified and evaluated based on the standardized uptake value (SUV). As glucose metabolism is enhanced in colon cancer cells (1), PET/CT is useful for detecting primary colon cancer, metastatic lesions, and recurrent lesions (1,2).

Synchronous colon cancers are defined as two or more distinct primary tumors that are separated by normal mucosa, which excludes direct extension or metastasis of another lesion (3). Synchronous tumors are discovered within one year after surgery (4), and occur in 2-5% of patients with colorectal cancer (5,6). Although total colonoscopy (TCS) is considered the most sensitive and specific method for identifying colorectal lesions (7,8), it cannot be performed for patients with an obstructive colorectal cancer. Thus, the American Society of Clinical Oncology and the American Cancer Society recommend follow-up TCS within 6 months after resection for patients with an obstructive cancer (9,10). Patients who cannot undergo preoperative TCS may be evaluated for proximal lesions using barium enema, CT colonography, intraoperative palpation, or intraoperative colonoscopy. However, magnetic resonance imaging and CT are not ideal for detecting small lesions, and the inability of barium or air to pass through the obstruction may limit the use of CT colonography or barium enema. Furthermore, the use of barium can increase the risk of barium inspissation, which may delay adequate cleansing of the colon before surgery (11), and ≥40% of lesions around the splenic flexure can be missed during intraoperative palpation (12). Moreover, intraoperative colonoscopy can be limited by the patient's physical position and expansion of the intestinal tract by air from the endoscope. As PET/CT is less invasive, compared to the previously mentioned modalities, the present study aimed to evaluate the ability of PET/CT to detect proximal synchronous colonic cancers in patients with obstructive colorectal cancer.

## Materials and methods

*Patients*. The present study's retrospective protocol was approved by the Ethics Committee of Showa University Northern Yokohama Hospital (1310-14). Between January 2007 and September 2016, 2,796 patients with colorectal cancer underwent surgical resection at the Showa University Northern Yokohama Hospital. Among these individuals, 417 patients with obstructive colorectal cancer could not undergo preoperative TCS. The exclusion criteria were patients who underwent right hemicolectomy and ileocecal resection (complete resection of the proximal colon), and patients who had familial adenomatous polyposis, ulcerative colitis, or Crohn's disease. A total of 275 eligible patients required evaluation of the proximal colon, and 180 of these patients also underwent TCS within 2 years after surgery. These 180 patients included 72 patients who underwent both preoperative PET/CT and postoperative TCS, and 108 patients who underwent only postoperative TCS (Fig. 1).

*Methods*. For the present study, we defined 'advanced adenoma' as adenomas with a diameter of >10 mm and high-grade dysplasia adenoma/mucosal cancer. 'Advanced lesions' were defined as invasive cancers and advanced adenomas. 'Obstructive colorectal cancer' was defined as cases in which the colonoscope could not reach the cecum because of cancer-related obstruction or stenosis.

The PET/CT was performed after the patients completed a fast of ≥4 h, and their blood glucose levels were measured before the FDG administration to ensure that they were within the normal range. All patients received 185 MBq of FDG, and the uptake period was defined as 60 min. The PET/CT was performed using a Siemens Biograph 16 (Siemens Healthcare, Berlin, Germany), with the following imaging parameters: slice thickness of 1.5 mm, total scale time of 30 sec, tube current-time of 50 mAs, and tube potential of 120 kV. The SUV was defined as the concentration of FDG in the tissue or lesion of interest, and was calculated as SUV = concentration [MBq/g] / (injected dose [MBq] / patient's body weight [g]). The SUVmax was defined as the maximum SUV value in a region of interest (13), and we defined malignancy as focal FDG uptake above the level of the surrounding tissue with an SUV of >3.5 (1).

## Results

*The association between FDG uptake and proximal colonic lesions*. All 72 patients who underwent preoperative PET/CT plus postoperative TCS within 2 years exhibited FDG uptake in the main tumor, and the mean SUVmax in the main tumor was 15.0 (range: 9.3-24.7). The association between FDG uptake and proximal colonic lesions detected using postoperative TCS is shown in Table I. The sensitivity of PET/CT for detecting synchronous colon lesions was 53.8% (7/13), with a specificity of 93.2% (55/59), a positive predictive value of 63.6% (7/11), a negative predictive value of 90.2% (55/61), and an accuracy of 86.1% (62/72). The sensitivity of PET/CT for detecting synchronous invasive cancers was 66.6% (4/6), with a specificity of 89.4% (59/66), a positive predictive value of 36.4% (4/11), a negative predictive value of 96.7% (59/61), and an accuracy of 87.5% (63/72).
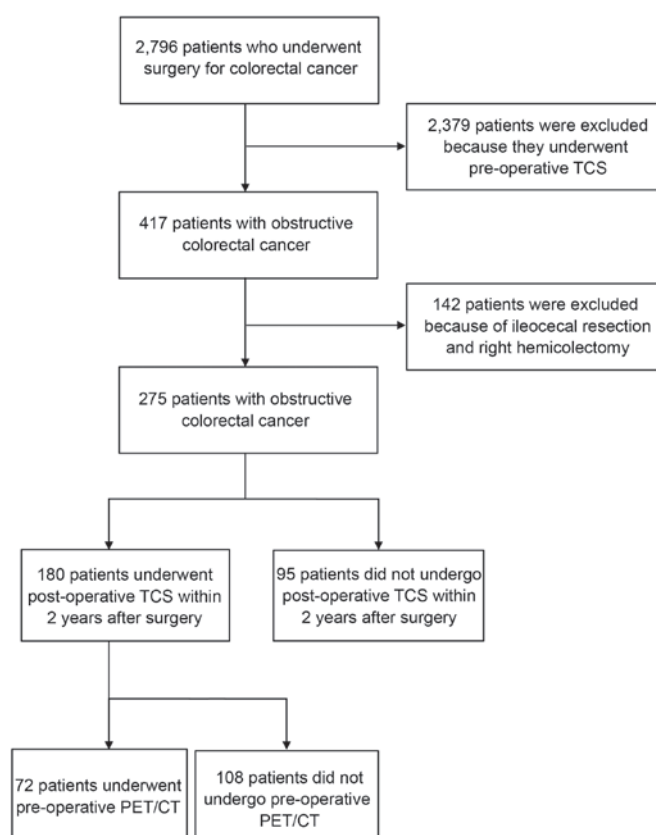


Figure 1. Flowchart for patient selection. TCS, total colonoscopy; PET-CT, positron emission tomography/computed tomography.

*Clinical characteristics of the 11 patients with FDG uptake during the PET/CT scan of the oral side of the colon*. Eleven patients exhibited FDG uptake in the colon, and these patients had three advanced adenomas (a 20-mm Is mucosal adenoma, a 28-mm IIa mucosal adenoma, and an 18-mm Is mucosal adenoma), four invasive cancers (a 45-mm pT3 tumor, a 22-mm pT2 tumor, a 70-mm pT3 tumor, and a 23-mm pT3 tumor), and four false-positive results (Table II). The patients with the 22-mm pT2, 70-mm pT3, and 23-mm pT3 tumors were treated using a single-stage operation, and the patient with the 45-mm pT3 tumor was treated using a two-stage operation. The first stage involved resection of the rectosigmoid colon cancer, although the patient had severe left ventricular dysfunction and the pT3 tumor in the splenic flexure was not palpated during the surgery. After the cancer in the splenic flexure was diagnosed using postoperative TCS, it was resected during a second surgery. Three patients with an advanced adenoma underwent endoscopic mucosal resection after the original surgery.

One of the four patients with false-positive results exhibited FDG uptake in the terminal ileum, and sigmoidectomy and ileum resection were performed because the ileum was adhered to the primary sigmoid colon cancer. This patient had previously experienced cecum perforation, and the pathological diagnosis was granuloma. The other three patients with false-positive results underwent further evaluation, and no >5-mm polyps were detected near the site of the FDG uptake.

*Clinical strategy for obstructive colorectal cancer*. The remaining 61 patients did not exhibit FDG uptake in the

Table I. Associations between FDG uptake and oral-sided colonic lesions detected using postoperative TCS.

| | Patient underwent pre-op PET/CT | | | |
| Colonic lesion detected | Positive findings | Negative findings | No pre-op PET/CT performed | Total |
|---|---|---|---|---|
| Proximal advanced lesions[a] (+) | 7 | 6 | 13 | 26 |
| Advanced adenoma[b] | 3 | 4 | 9 | 16 |
| Invasive cancer | 4 | 2 | 4 | 10 |
| Proximal advanced lesions (-) | 4 | 55 | 95 | 154 |
| Total no. of lesions | 11 | 61 | 108 | 180 |

[a]Advanced lesion: Advanced adenoma and invasive cancer; [b]Advanced adenoma: Adenomas that were ≥10 mm and mucosal cancers. FDG, fluorodeoxyglucose; TCS, total colonoscopy; PET-CT, positron emission tomography/computed tomography.

Table II. Clinical characteristics of the 11 patients with FDG uptake during the PET/CT scan of the oral side of the colon.

| | | Primary colorectal cancer | | | Proximal colorectal lesions | | | | |
| Case | Age/sex | Location | Depth | Size (mm) | Location/histology | Depth | Size (mm) | Intraoperative palpation | Treatment |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 73/M | RS | T3 | 60 | D/cancer | T3 | 45 | Not palpable | Two-stage op |
| 2 | 85/M | S | T3 | 42 | S/cancer | T2 | 22 | Palpable | One-stage op |
| 3 | 75/M | S | T4 | 40 | S/cancer | T3 | 70 | Palpable | One-stage op |
| 4 | 65/F | D | T3 | 50 | D/cancer | T3 | 23 | Palpable | One-stage op |
| 5 | 53/M | S | T3 | 52 | T/cancer | Tis | 20 | Palpable | Op + endoscopic resection |
| 6 | 89/M | R | T3 | 95 | C/cancer | Tis | 28 | Palpable | One-stage op |
| 7 | 61/M | Ra | T4 | 62 | S/cancer | Tis | 18 | Palpable | One-stage op |
| 8 | 63/M | RS | T3 | 61 | C/granuloma | - | - | Palpable | One-stage op |
| 9 | 70/M | Ra | T3 | 64 | C/hyper | - | 3 | Not palpable | - |
| 10 | 67/F | S | T3 | 40 | A/hyper | - | 4 | Not palpable | - |
| 11 | 71/M | S | T3 | 46 | A | - | - | Not palpable | - |

FDG, fluorodeoxyglucose; M, male; F, female; C, cecum; A, ascending colon; T, transverse colon; D, descending colon; S, sigmoid colon; RS, rectosigmoid colon; Ra, upper rectum; Hyper, hyperplastic polyp; PET-CT, positron emission tomography/computed tomography; Tis, carcinoma *in situ*; T2, tumor invades muscularis propria; T3, tumor invades through the muscularis propria into pericolorectal tissues; T4, tumor penetrates the surface of the visceral peritoneum.

proximal colon. Postoperative TCS subsequently revealed four advanced adenomas (a 12-mm IIa adenoma, a 6-mm IIa mucosal cancer, a 20-mm IIa adenoma, and a 20-mm Ip adenoma) and two invasive cancers (a 7-mm Is pT1b tumor and a 12-mm IIa pT1b tumor). One hundred and eight patients did not undergo preoperative PET/CT, and postoperative TCS subsequently revealed nine advanced adenomas and four invasive cancers. There was no significant difference in the incidences of proximal colonic lesions when we compared the groups with and without positive findings during the preoperative PET/CT (Fisher's exact test).

## Discussion

Synchronous colon cancers occur in 2-5% of patients with colorectal cancer (5,6). Thus, as patients with obstructive cancers cannot be evaluated using preoperative TCS, other

methods are needed to assess the proximal colon, such as CT colonography and self-expandable metallic stents. For example, a self-expanding metal stent can be placed endoscopically to facilitate preoperative TCS and provide a bridge to surgery in patients with obstructive tumors, as a Japanese study revealed that it provided a high technical success rate and a low complication rate among patients with colorectal cancer (14). However, the European Society of Gastrointestinal Endoscopy clinical guidelines do not recommend colonic self-expanding metal stent placement as a bridge to elective surgery (15), and we believe it is better to avoid stent use until the long-term oncological and safety outcomes are confirmed. In addition, endoscopic observation of the proximal colon after stenting can cause stent migration or perforation. Therefore, stenting does not always make preoperative TCS possible. In contrast, CT colonography can be used to detect synchronous proximal colon cancers in

patients with obstructive lesions (16), although the procedure requires adequate bowel preparation, fecal tagging, and colonic distension using air or CO2. Nevertheless, PET/CT can detect colonic lesions even if the colon proximal to the obstruction is not adequately prepared (17).

As PET/CT provides a high detection rate for colorectal cancer, the present study evaluated its ability to detect cancers in patients with obstructive colon cancer. Compared to barium enema or intraoperative colonoscopy, PET is a less invasive screening technique that uses FDG (a commonly used PET tracer), which is a glucose analogue with no risks of side effects or pharmacological allergies. However, PET is associated with several disadvantages, such as FDG uptake being affected by cell density. Therefore, it is difficult for PET to identify malignant tumors with low cell density, such as bronchioloalveolar carcinoma or gastric signet ring cell carcinoma (18,19). Hyperglycemia can also cause false-negative results for FDG uptake in the body (20). Another disadvantage of PET is that its spatial resolution is inferior to that of CT, and an improved diagnostic ability is achieved using the combination of PET and CT (21).

Previous studies have indicated that PET has a high sensitivity (90%) and specificity (66%) for identifying primary colorectal tumors (2), and FDG-PET provides a sensitivity of 90% for detecting metastatic liver lesions, with a specificity of 100% (1). Another common use of PET is screening for colorectal cancer (22), and Friedland *et al* (23) have reported that PET detected 100% of malignant lesions with a diameter of ≥2 cm, but only 17% of lesions with a diameter of <2 cm, and that PET had lower sensitivity for detecting flat adenomatous lesions than for protruding lesions (23). Another study revealed that 90% of adenomatous polyps with a diameter of ≥13 mm were detected incidentally during FDG-PET (24). In particular, villous adenomas tend to have elevated FDG uptake (25), and the lesion's size and its morphological or pathological type can affect the ability to identify colorectal lesions. The large intestine is a well-known site of physiological FDG uptake, and intestinal FDG uptake also poses a practical problem during PET, as it can disguise FDG uptake by adenomatous lesions (26).

In the present study, false-negative PET/CT results were observed for four advanced adenomas (a 6-mm IIa mucosal cancer, a 12-mm IIa adenoma, a 20-mm IIa adenoma, and a 20-mm Ip adenoma) and two invasive cancers (a 7-mm Is pT1b tumor and a 12-mm IIa pT1b tumor). These mucosal and invasive cancers were relatively small, and their FDG uptake was likely affected by their grade of differentiation and number of tumor cells. However, the negative predictive value was high for both synchronous advanced lesions (90.2%, 55/61) and invasive cancers (96.7%, 59/61), which suggests that negative PET results indicate a low probability of proximal invasive colon cancer. Postoperative endoscopy can be used to treat proximal mucosal cancer or advanced adenoma, which are both movable during intraoperative palpation because they are not firmly adherent to the muscularis propria. Based on these results, we have developed a clinical strategy for treating obstructive colon cancer (Fig. 2). In this strategy, patients with negative PET results can undergo postoperative TCS, while patients with positive PET results should undergo preoperative TCS using
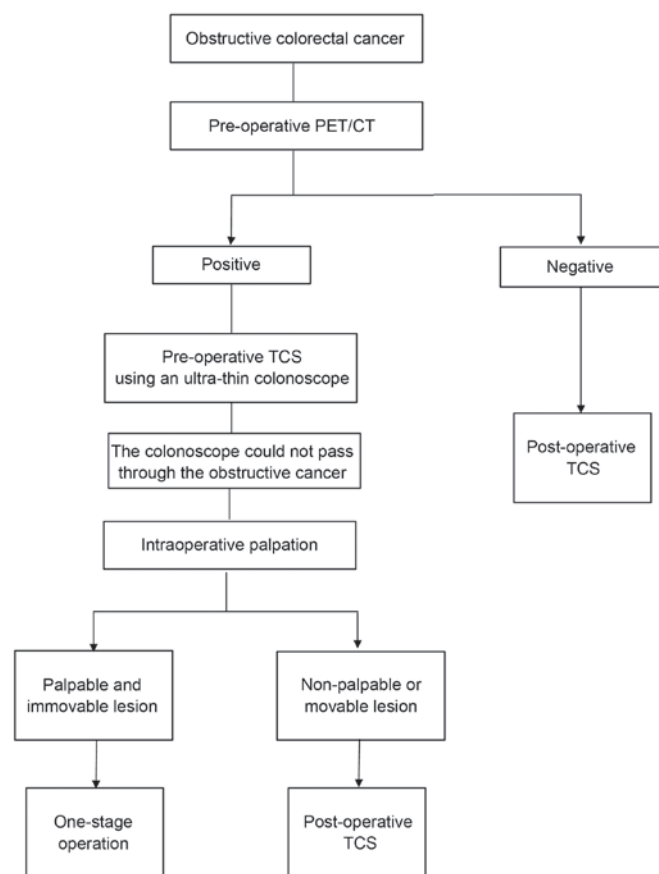


Figure 2. Clinical strategy for obstructive colorectal cancer. TCS, total colonoscopy; PET-CT, positron emission tomography/computed tomography.

an ultra-thin colonoscope. If the ultra-thin colonoscope cannot pass through a cancer-related obstruction, intraoperative palpation is needed. Patients with negative palpation results, or lesions that are movable and palpable, can undergo postoperative TCS. Lesions that have positive PET results and are not movable during palpation may be suitable for a single-stage surgery. As intraoperative palpation is difficult during laparoscopic surgery, it may be necessary to perform hand-assisted laparoscopic surgery to facilitate the palpation. Moreover, we misdiagnosed a case of colon cancer in the splenic flexure, which suggests that splenic flexure uptake during PET/CT requires careful attention during the surgery.

The present study has several limitations. First, the retrospective design is associated with known limitations and risks of bias. Second, the TCS was not performed within 1 year after surgery, which is a requirement for diagnosing synchronous colon lesions. Third, the patients did not undergo colonoscopy using an ultra-thin colonoscope (outer diameter: 6.8 mm). Nevertheless, relative to CT colonography and self-expanding metal stent placement, PET/CT is less invasive and more useful for detecting proximal colon cancers.

Based on the high negative predictive value, negative PET/CT results indicate a low probability of synchronous colon cancer in the proximal colon. Therefore, PET/CT may be a useful tool for detecting synchronous colonic cancers in patients with obstructive colon cancer.

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