Management of Patients Following Detection of Unsuspected Colon Lesions by PET Imaging

MICHAEL LIN,[*,‡,§] JENN HIAN KOO,[*,‡,‖] and DAVID ABI–HANNA[*,‖]

*University of New South Wales, [§]Department of Nuclear Medicine and PET, and [‖]Gastroenterology and Liver Services, Liverpool Hospital, Liverpool, New South Wales; and [‡]South Western Sydney Colorectal Tumour Group, Liverpool, New South Wales, Austrailia

Positron emission tomography (PET) is a well-established and integral component of multimodality imaging in oncology. However, the expanded use of PET in oncological and also non-oncological imaging (such as in assessing inflammatory conditions) has identified more lesions or tumors at unsuspected locations, such as in the large bowel during examination of patients not known to have colorectal disease. We review the clinical significance of colon lesions that were discovered incidentally by PET imaging and management strategies for gastroenterologists.

Keywords: Polyp; Colon Cancer; Colorectal; Metastasis.

Positron emission tomography (PET) is now an integral part of multimodality imaging in oncology. During the last 2 decades there has been enormous growth in the literature demonstrating the benefits of PET in the management of many malignancies.[1] In colorectal cancer (CRC), PET is well-established in the assessment of recurrent disease and in patients before potential curative metastasectomy.[2] There is also emerging evidence in support of its use in staging CRC, especially in rectal cancer. The indications for PET are continually broadening, and there are active research interests in the use of PET in radiotherapy planning, early prognostication, and risk adaptive treatment planning.

With the expanding use of PET in oncology as well as non-oncological indications (eg, in the assessment of inflammatory conditions such as prosthetic infection and vasculitis), incidental findings are not uncommon and often pose a diagnostic and management dilemma to clinicians. These are findings that are detected at locations deemed unusual for metastatic disease from the index cancer and might represent benign lesions (such as inflammation or infection) or a second primary malignancy. A common site of such findings is in the large bowel during evaluation of non-CRC patients, and an opinion from a gastroenterologist is often sought. In this review our discussion will focus on the clinical significance and management of incidental colonic findings discovered on PET. Because the basic principles, patient preparation, and technical considerations of PET had been discussed in this journal recently,[3] the general principles of PET will only be outlined in brief.

Fluorodeoxyglucose Positron Emission Tomography and Positron Emission Tomography–Computed Tomography

PET detects pairs of gamma rays emitted in opposite directions from positron-emitting radioisotopes and localizes this process in vivo. Since 2001, combined PET and computed tomography (CT) scanners (PET-CT) provide functional and precise anatomic information in a single scan with significant improvement in diagnostic confidence and accuracy compared with PET and CT data viewed side-by-side, PET alone, or CT alone.[4–6] As a result, PET-CT has now replaced PET-alone systems.

Fluorodeoxyglucose (FDG) is a radiolabeled glucose analogue and is by far the most widely used radiopharmaceutical for PET. Malignant cells exhibit enhanced glycolytic metabolism, and this molecular process is depicted by mapping FDG uptake by using PET cameras. The degree of metabolic activity or FDG uptake by tissue can also be expressed semiquantitatively as standardized uptake value (SUV). However, FDG is not specific and can be taken up in benign conditions such as inflammation. Conversely, FDG PET can be falsely negative in certain malignancies such as mucinous CRC[2] or small lesions beyond the resolution of the PET camera.

Fluorodeoxyglucose Positron Emission Tomography and Large Bowel

Diffuse Colonic Fluorodeoxyglucose Uptake on Positron Emission Tomography

FDG colonic uptake on PET is common. The pattern of physiological uptake can be variable but is usually mild, diffuse, and linear. It has been attributed to various factors including physiological smooth muscle activation, reactive lymphocytes in the terminal ileum and cecum, and swallowed secretions.[7,8] In a study comprising patients with no known gastrointestinal tract disorder such as malignancy or inflammatory disease, F-18 radioactivity was found in patients' stools, providing direct evidence of intraluminal FDG excretion.[9] In the same study, patients with diarrhea and constipation also showed increased FDG uptake scores, which might be related to greater peristaltic movement. On the basis of these observations, various interventions to reduce physiological FDG colonic uptake by using antiperistaltic muscle relaxants[10] or a purgative such as senna glycoside solution[11] have been attempted. Unfortunately, these agents seem to increase FDG uptake and might be counterproductive. The use of oral iodine-based contrast solutions also

Abbreviations used in this paper: CRC, colorectal cancer; CT, computed tomography; FDG, fluorodeoxyglucose; OC, optical colonoscopy; PET, positron emission tomography; SUV, standardized uptake value.

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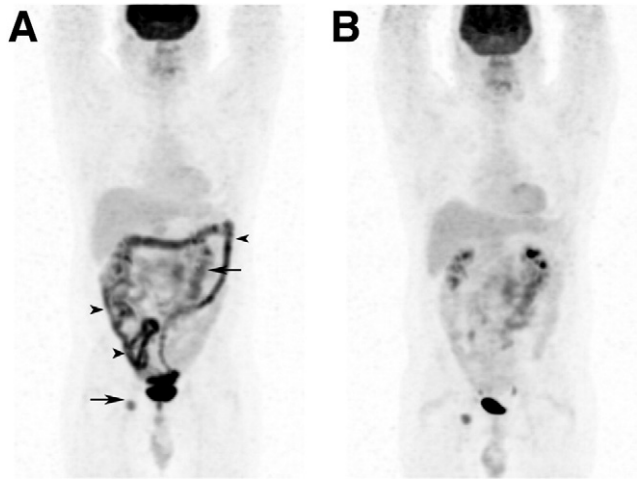

Figure 1. (*A*) Maximum intensity projection image of a 43-year-old man with newly diagnosed follicular grade 1 lymphoma, with abdominal and right inguinal lymphadenopathy (stage II), who underwent FDG PET scan for staging. He was known to have type 2 diabetes on metformin therapy. The scan demonstrated abnormal focal, moderately increased FDG uptake at the known sites of lymphoma (*arrows*) as well as moderate to intense diffuse FDG uptake throughout the bowel (*arrowheads*), most markedly in the large intestines. There was also physiological urinary tracer pooling in the bladder and physiological FDG accumulation in the brain, myocardium, and liver. (*B*) A repeat PET scan was performed 4 days later after 72 hours of withholding metformin, with resolution of reactive bowel uptake and better visualization of known sites of lymphoma. Physiological tracer uptake in the collecting system of the kidneys and intense urinary tracer pooling in the bladder were also noted.

appeared to increase FDG bowel uptake.[12] Use of water-based negative contrast material[13] or low-density barium sulfate preparations[14] as oral contrast agents does not seem to spuriously increase FDG accumulation in bowel and might be more suitable.

Recently, prominent diffuse bowel uptake has been found to be related to oral hypoglycemic therapy, in particular metformin.[15] The underlying mechanism was thought to be due to an increase in glucose use by the intestine from up-regulation of glucose transporters. In 1 series, the use of metformin with resultant prominent bowel FDG uptake was found to mask the presence of significant colonic pathology such as colon cancer.[16] One potential strategy suggested by the investigators to mitigate this was to cease metformin for 3 days before PET scanning (Figure 1). A recent study indicates that 2 days of discontinuation might be sufficient in reducing high intestinal uptake, whereas withholding for 1 or 1.5 days does not seem adequate.[17] Although transient discontinuation of metformin therapy appears effective in reducing intestinal FDG uptake, this has to be carefully balanced against potential hyperglycemia, which might impact on the quality of the PET images because of a competitive effect on tissue FDG accumulation. Whether this should be adopted as standard patient preparation before FDG PET is an area of continuing research.

Intense diffuse bowel uptake has also been observed in active colitis.[18] If this occurs in the right clinical setting, further investigations might be appropriate.

Segmental and Multifocal Colonic Fluorodeoxyglucose Uptake on Positron Emission Tomography

Segmental colonic FDG uptake has been described as a physiological pattern and more commonly seen in the rectosigmoid.[12] This pattern, however, can also represent bowel inflammation, especially if accompanied by bowel wall thickening with surrounding mesenteric fat stranding or diverticular disease on concurrent CT scan.[8] In the study by Tatlidil et al,[7] intense segmental uptake was observed in 5 of 6 patients with proctitis and colitis. Although investigation of segmental FDG uptake in asymptomatic patients might not be indicated, patients who exhibit symptoms suggestive of an inflammatory bowel condition would warrant further evaluation by colonoscopy.

A multifocal or multinodular pattern especially in the ascending colon might be seen in patients who have ingested oral contrast material.[12] In patients without recent oral contrast, this pattern might indicate significant pathology such as multiple dysplastic polyps, and evaluation with colonoscopy should be considered.[7]

Focal Colonic Fluorodeoxyglucose Uptake on Positron Emission Tomography

The prevalence of unexpected focal colonic FDG uptake on PET ranged between 0.6% and 3.7%.[19–24] Although various nonmalignant conditions such as constipation,[9] inflammation (eg, diverticulitis and post-irradiation inflammation),[19] and abscess formation[25] have been reported as causes for focal colonic uptake, the majority of cases are caused by a synchronous adenoma or carcinoma that is uncovered on further evaluation (Figure 2). Incidental detection of adenomatous polyps of the colon on FDG PET was first documented in 1998.[26] Since then, there have been several retrospective series dedicated to this topic by using PET alone[7,27–29] and combined PET-CT cameras.[18–25,30,31]

Location of Fluorodeoxyglucose Uptake and Pathology

One study evaluating the correlation between the location of FDG colonic uptake and malignant or premalignant pathology reported higher positive predictive value for uptake observed in the proximal colon.[20] In contrast, nonmalignant PET findings were found more frequently in the cecum, sigmoid, and rectum, with the majority of cases caused by stool (when correlated with concurrent CT scan), collapsed bowel loops, and inflammation.[22] In a recent study of 176 healthy subjects who underwent PET for screening and colonoscopy, the presence of hemorrhoids was also found to account for increased focal FDG accumulation in the rectum/anal region, with a maximum SUV ranging from 1.4–8.3.[32] However, because hemorrhoids are very common, they can coexist with other significant pathology, and further evaluation of focal FDG uptake to confirm the absence of premalignant lesions or malignancy might still be warranted.

Size and Grade of Dysplasia of Colonic Adenomas

The sensitivity of FDG PET in detecting premalignant adenomatous polyps correlated with their size.[27–29,31] In