

Incidental colonic focal FDG uptake on PET/CT: can the maximum standardized uptake value (SUV_{max}) guide us in the timing of colonoscopy?

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Abstract

Purpose In patients undergoing ¹⁸F-FDG PET/CT, incidental colonic focal lesions can be indicative of inflammatory, pre-malignant or malignant lesions. The maximum standardized uptake value (SUV_{max}) of these lesions, representing the FDG uptake intensity, might be helpful in differentiating malignant from benign lesions, and thereby be helpful in determining the urgency of colonoscopy. The aim of our study was to assess the incidence and underlying pathology of incidental PET-positive colonic lesions in a large cohort of patients, and to determine the usefulness of the SUV_{max} in differentiating benign from malignant pathology.

Methods The electronic records of all patients who underwent FDG PET/CT from January 2010 to March 2013 in our hospital were retrospectively reviewed. The main indications for PET/CT were: characterization of an indeterminate mass on radiological imaging, suspicion or staging of malignancy, and suspicion of inflammation. In patients with incidental focal FDG uptake in the large bowel, data regarding subsequent colonoscopy were retrieved, if performed within 120 days. The final diagnosis was defined using colonoscopy findings, combined with additional histopathological assessment of the lesion, if applicable.

Results Of 7,318 patients analysed, 359 (5 %) had 404 foci of unexpected colonic FDG uptake. In 242 of these 404 lesions (60 %), colonoscopy follow-up data were available. Final diagnoses were: adenocarcinoma in 25 (10 %), adenoma in 90 (37 %), and benign in 127 (53 %). The median [IQR] SUV_{max} was significantly higher in adenocarcinoma (16.6 [12 – 20.8]) than in benign lesions (8.2 [5.9 – 10.1]; $p < 0.0001$), non-advanced adenoma (8.3 [6.1 – 10.5]; $p < 0.0001$) and advanced adenoma (9.7 [7.2 – 12.6]; $p < 0.001$). The receiver operating characteristic curve of SUV_{max} for malignant versus nonmalignant lesions had an area under the curve of 0.868 (SD±0.038), the optimal cut-off value being 11.4 (sensitivity 80 %, specificity 82 %, positive predictive value 34 %, negative predictive value 98 %).

Conclusion In these patients with incidental colonic focal activity undergoing PET/CT (the largest series published to date), malignancies had significantly higher SUV_{max} values than all other types of lesions. However, SUV_{max} could not distinguish between benign lesions and adenomas. In conclusion, all incidental findings in the colon should be further evaluated and lesions with SUV_{max} ≥ 11.4 should be evaluated without delay.

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Introduction

PET or combined PET/CT using ¹⁸F-FDG has found widespread clinical application in the diagnosis and management of both malignant and benign diseases [1–5]. Incidental colonic focal lesions are observed in 1.3–3.4 % of patients who undergo FDG PET/CT for other reasons than expected colonic disease [6–11]. Unexpected increased FDG uptake in the large bowel is often nonspecific, yet it can also be indicative of inflammatory sites, or premalignant or malignant lesions [12–14]. Physiological FDG activity is commonly seen in the large bowel, but is usually of relatively low intensity [14] and typically follows a diffuse or linear pattern [12, 15]. Therefore it can hardly be mistaken for malignancy [14]. Yet, occasionally physiological bowel uptake of FDG may be focal [12, 14, 15], which hampers differentiation of a malignant change from a normal variant [14]. FDG PET/CT has been shown to assist differentiation of malignant from benign pulmonary nodules [7, 16]. In the large bowel, however, the capacity of PET/CT to differentiate of benign from malignant disease is to be less clear [15].

A few studies have demonstrated that 8.5–21 % of unexpected PET/CT foci in the colon correspond to malignant lesions upon further evaluation [6, 7]. There is a good correlation between the location of FDG uptake and the location of lesions observed on colonoscopy [12, 17]. Therefore, it is currently recommended that all incidentally detected colonic foci should be evaluated by colonoscopy [8, 18, 19].

As focal colonic FDG accumulation is not always related to pathological findings, the decision as to whether to perform further diagnostic evaluation can be difficult. A predictor of the risk of malignancy would therefore be helpful in determining the urgency of colonoscopy. The maximum standardized uptake value (SUV_{max}), representing the intensity of FDG uptake, is potentially helpful in differentiating malignant from benign FDG activity. Until now, few studies have evaluated the relationship between the SUV_{max} of incidental colonic PET-positive lesions and the corresponding colonoscopic findings. These small, mainly retrospective studies showed conflicting results [6, 8, 19–21]. One study showed a significant difference in SUV_{max} between false-positive lesions versus high-grade adenomas and malignancies [22], while five studies concluded that the SUV_{max} was not able to differentiate different groups of aetiology [6, 8, 19–21]. Therefore, we aimed to evaluate the SUV_{max} of incidentally detected PET-positive lesions in the colon on PET/CT in a large cohort of patients, and to correlate the SUV_{max} with the outcome of the corresponding colonoscopy.

Methods

The electronic records of all consecutive patients who had undergone FDG PET/CT during the period January 2010 to March 2013 in the St. Antonius Hospital, Nieuwegein, The Netherlands, were retrospectively reviewed. All patients with incidental focal FDG uptake in the large bowel mentioned in the PET/CT scan report were included. Diffuse, linear or segmental colonic FDG uptake was not taken into account, because this is usually physiological. Uptake was considered incidental in patients with a known gastrointestinal (GI) tract disorder in combination with focal FDG accumulation in areas not consistent with the known preexisting pathology, or in patients referred for PET/CT with a diagnosis of a non-GI tract disorder. The intensity of the FDG uptake was noted as the SUV_{max}, measured with the hybrid viewer software provided by the workstation manufacturer (Hermes Medical Solutions, Stockholm, Sweden). Only FDG activity greater than that of background liver uptake was considered abnormal. The body-low-dose CT component was used to determine the exact anatomical location of the focus. Electronic records were reviewed for findings on colonoscopy and histopathology, if available.

PET/CT protocol

Imaging was performed with a Philips Gemini TF-64 combined PET/CT device (Philips Medical Systems, Eindhoven, The Netherlands). All patients were prepared for the PET/CT scan in accordance with the EANM and SNMMI guidelines [23, 24]. The capillary blood glucose level of all patients was <10 mmol/L before injection of FDG. The interval between FDG injection (2.5 MBq/kg body weight) and the start of acquisition was 60±5 min. No oral or intravenous contrast medium was used. The emission scan took 3 min per bed position, with 50 % overlapping slices and typically nine or ten bed positions for adequate coverage from the head to the upper legs.

Correlation with colonoscopy

Data regarding subsequent colonoscopy were retrieved from the electronic records of all patients with an incidental finding of focal FDG uptake in the large bowel. Colonoscopy was considered diagnostic if performed within 120 days of the PET/CT scan. In patients with a longer interval between PET/CT and colonoscopy, the focal FDG uptake was considered as not further evaluated and the data were not included in the analysis. Colonoscopy reports were analysed for abnormalities correlating with the incidental finding on the PET/CT scan. When a biopsy or polypectomy of the location of the focus was recorded, the pathology report was subsequently evaluated. The final diagnosis was defined, using colonoscopy findings, combined with additional histological assessment

of the lesion, if available. Subsequently, the final diagnosis was placed into one of the following four categories: malignant lesions; advanced adenomas; non-advanced adenomas; and benign lesions (including hyperplastic polyps, inflammatory lesions and normal colonoscopic and/or histopathological findings). Advanced adenomas were defined as adenomas with a size of 1 cm or more, prominent villous features or high-grade dysplasia. Each area of FDG accumulation with negative colonoscopy or histopathological result was considered to represent a site of physiological uptake.

Outcome parameters

The assessed parameters were incidence, final diagnosis and intensity of FDG uptake in incidental colonic focal PET-positive lesions. The location was determined using the body low-dose CT scan. The final diagnosis was made on the basis of corresponding colonoscopic findings, combined with histopathological results, if available. The intensity of FDG uptake was measured in terms of SUV_{max} , an analogue scale ranging from zero (no uptake) to 40 (maximal uptake).

Statistical analysis

Statistical analysis was performed using SPSS Software for Windows (version 21.0; IBM SPSS statistics, IBM corporation, Chicago, IL, USA). Descriptive statistics were used to describe the incidence of unexpected focal colonic FDG accumulation. The Kruskal-Wallis test was used to compare the median SUV_{max} between groups in per-patient and per-focus analysis. Differences were considered significant when $p < 0.05$. An receiver operating characteristic (ROC) curve was plotted to define the optimal cut-off point to differentiate malignant from non-malignant lesions.

Results

Per-patient analysis

Between January 2010 and March 2013, 7,318 patients underwent PET/CT in the St. Antonius Hospital. Of these patients, unexpected colonic focal FDG uptake was mentioned in the PET/CT report of 359 (5 %), and of these 359 patients, 40 had two, and 2 had three separate incidental colonic findings on one PET/CT scan. Colonoscopy was performed in 203 of these 359 patients (57 %) within 120 days (median 25 days [interquartile range, IQR, 13 – 47]) of PET/CT. On colonoscopy, corresponding lesions were detected in 142 of the 203 patients (70 %; Fig. 1). Demographic data of the 203 patients with unexpected focal colonic FDG uptake and corresponding colonoscopy are shown in Table 1.

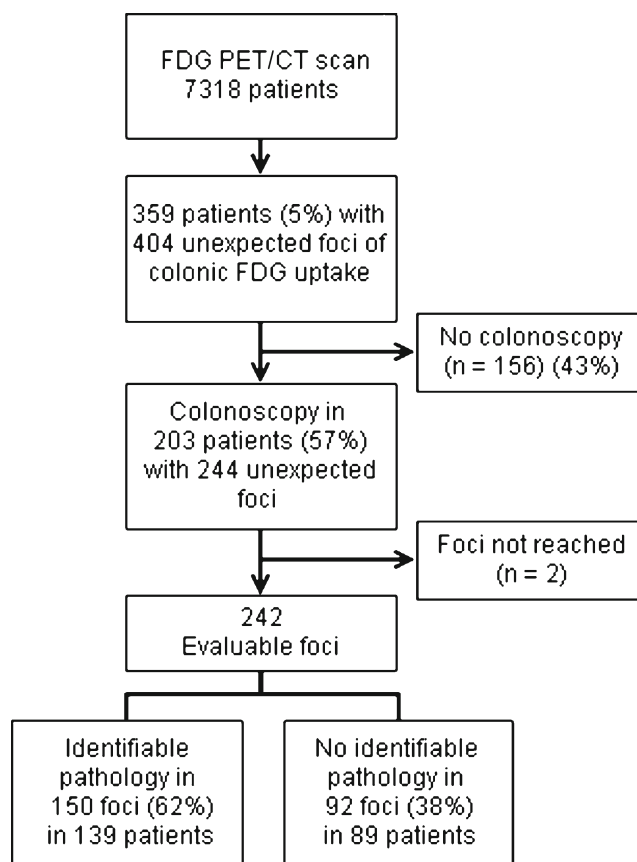


Fig. 1 Selection of patients undergoing FDG PET/CT between January 2010 and March 2013 in our hospital

Table 1 Baseline characteristics of 203 patients with unexpected focal colonic FDG uptake and confirmatory colonoscopic examinations

Characteristic	Value
Patients	
Sex (male/female), <i>n</i>	116/87
Age (years), mean \pm SD	66 \pm 11.9
Reason for PET/CT, <i>n</i> (%)	
Characterization of indeterminate nodule or mass on radiological imaging ^a	83 (41)
Staging of known carcinoma ^b	41 (20)
Detection of unknown primary tumour	32 (16)
Suspicion of inflammatory or infectious disease	28 (14)
Suspicion or activity analysis of interstitial lung disease	17 (8)
Melanoma	2 (1)
Blood glucose level before PET/CT (mmol/L), median (IQR)	5.5 (4.9 – 6.6)
Number of days between PET/CT and colonoscopy, median (IQR)	23 (13 – 47)

^a Thorax 74, abdomen 5, neck 4

^b Upper GI tract 14, lung 12, lymphoma 9, uro-/gynaecological 6

Of the 359 patients with incidental FDG-avid colonic foci, 156 did not undergo subsequent colonoscopic evaluation. The majority of these patients had advanced illnesses or terminal cancer, so that there were no consequences of a colonoscopy for (palliative) treatment. The reasons for lack of additional colonoscopy are presented in Table 2.

Per-focus analysis

A total of 404 incidentally detected FDG-avid foci in the colon were found, of which 244 (60 %) were followed up with colonoscopy. In two patients, the area of FDG uptake could not be evaluated because the colonoscope was unable to pass a distally located stenotic segment. Of the 242 evaluable sites with unexpected FDG accumulation, 92 (38 %) showed no mucosal abnormality. In the remaining 150 sites; colonic cancer was diagnosed in 25 (10 %), advanced adenomas in 64 (27 %), non-advanced adenomas in 26 (11 %), hyperplastic polyps in 25 (10 %) and inflammation in 10 (4 %). Of the adenomas (advanced and non-advanced), 45 were tubular adenomas, 6 were villous adenomas and 39 tubulovillous adenomas. At sites with no mucosal abnormality, hyperplastic polyps and inflammatory sites were considered benign lesions (Table 3).

The SUV_{max} of all evaluable areas of increased FDG uptake ranged from 3.1 to 28.4. The overall median SUV_{max} was 8.7 (IQR 6.3 – 11.4); the median SUV_{max} in benign lesions, non-advanced adenomas, advanced adenomas and malignant lesions were 8.2, 8.3, 9.7, and 16.6, respectively. There was a significant difference in median SUV_{max} between the benign and the malignant group ($p=0.0001$), between the non-advanced adenoma and the malignant group ($p=0.0001$) and between the advanced adenoma and the malignant group ($p=0.001$). There was also a significant difference between the advanced adenomas and the benign lesions ($p=0.03$). There was no significant difference in median SUV_{max}

Table 2 Reasons for lack of colonoscopic evaluation in 156 patients with incidental abnormal colonic FDG uptake

Reason	No. of patients (%)
Advanced or terminal illness	42 (27)
Marked as “probably physiological” in PET/CT report	22 (14)
Patient declined colonoscopy	20 (13)
Outpatient, lost to follow-up ^a	13 (9)
Different additional test ^b	11 (7)
Patient recently underwent a colonoscopy (<3 months)	7 (4)
Patient suddenly died before colonoscopy	2 (1)
Unknown	39 (25)

^a Patient from another hospital referred back for colonoscopy

^b CT scan or repeated PET/CT scan

Table 3 Aetiology and incidence of 242 unexpected colonic FDG-avid foci on PET/CT

Aetiology	No. (%) of foci
Colon carcinoma ^a	25 (10)
Advanced adenoma	64 (27)
Non-advanced adenoma	26 (11)
Hyperplastic polyp	25 (10)
Inflammation	10 (4)
No abnormality	92 (38)

^a Location of carcinomas: 2 in the caecum, 4 in the ascending colon, 2 in the transverse colon, 3 in the descending colon, 14 in the rectosigmoid

between the benign and the non-advanced adenomas, nor between the non-advanced and advanced adenomas (Table 4).

An ROC curve was plotted to evaluate the accuracy of the SUV_{max} in differentiating malignant from nonmalignant incidentally detected foci in the colon. The area under the curve was 0.868 (SD±0.038). The optimal cut-off SUV_{max} was 11.4 (sensitivity 80 %, specificity 82 %, positive predictive value 34 %, negative predictive value 98 %), in which lesions with $SUV_{max} \geq 11.4$ had a high risk of being malignant (Fig. 2).

Discussion

In 150 (62 %) of 242 evaluated sites with unexpected focal colonic FDG uptake, colonoscopy revealed an abnormal finding. Of the 150 positive lesions, a significant percentage were (pre)malignant: 25 (17 %) adenocarcinomas and 64 (43 %) advanced adenomas. This finding is in accordance with the findings of other studies [6, 17, 24, 25]. However, in 92 foci of

Table 4 Intensity of uptake in 242 unexpected colonic FDG-avid foci on PET/CT

Pathology	SUV_{max}	
	Median	Interquartile range
Benign ^a	8.2	5.9 – 10.1
Non-advanced adenoma	8.3	6.1 – 10.5
Advanced adenoma ^b	9.7	7.2 – 12.6
Colon carcinoma	16.6	12 – 20.8
Total	8.7	6.3 – 11.4

Significant differences in median SUV_{max} : benign vs. colon carcinoma group ($p=0.0001$), non-advanced adenoma vs. colon carcinoma group ($p=0.0001$), advanced adenoma vs. colon carcinoma group ($p=0.001$), advanced adenoma vs. benign group ($p=0.03$)

^a Benign: no abnormality on colonoscopy, normal histopathology, inflammatory sites and hyperplastic polyps

^b Advanced adenoma: adenoma with a size ≥ 1 cm, prominent villous features or high-grade dysplasia

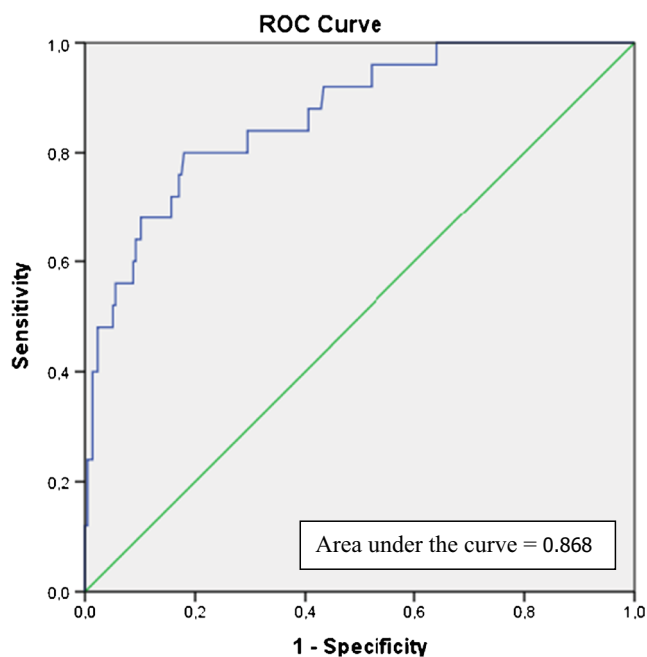


Fig. 2 ROC curve of malignant versus nonmalignant incidental FDG-avid lesions in the colon on PET/CT. The area under the curve is 0.868. The optimal SUV_{max} cut-off to differentiate malignant from nonmalignant incidentally detected foci in the colon is 11.4 (sensitivity 80 %, specificity 82 %, positive predictive value 34 %, negative predictive value 98 %)

increased FDG uptake, despite careful endoscopic examination, no visible lesions were found on colonoscopy, representing 38 % false-positive PET/CT lesions. A possible source of false-positive lesions on PET/CT FDG-PET is (transient) inflammation, physiological uptake [12–15] or uptake in the GI lymphoid tissue [18]. Other studies considering incidental focal FDG-enhanced lesions on PET/CT have shown conflicting false-positive percentages. Peng et al. [10] found a normal colon in 56 % of evaluated patients with focal colonic FDG uptake. Both Gutman et al. [6] and Treglia et al. [25] found that 23 % of unexpected colonic foci had no correlative colonic lesion on colonoscopy, while Putora et al. [8] and Farquharson et al. [11] found a negative colonoscopy result in 13.7 % and 16.7 % of patients with incidental focal colonic FDG uptake, respectively.

We found that malignant lesions had a significantly higher median SUV_{max} than all other types of lesions. Luboldt et al. [22] found that the mean SUV_{max} in high-grade adenomas and malignancies were significantly higher than the values in false-positive lesions. However, in five other previous studies evaluating the aetiology of incidental colonic FDG accumulation, no significant differences in median SUV_{max} were found between different groups of diagnoses [6, 8, 19–21]. We found a median SUV_{max} of 16.6 (IQR 12 – 20.8) for incidentally found colonic neoplasms, and lower median SUV_{max} for premalignant and benign lesions (ranging from 8.2 to 9.7). In previous studies a median or mean SUV_{max}

ranging from 5.7 to 17.3 were found for incidental carcinomas in the colon [6, 8, 19, 20–22].

Our results indicate that all incidental focal lesions showing FDG uptake with a $SUV_{max} \geq 11.4$ have a high risk of being malignant and should be examined by colonoscopy without delay. Luboldt et al. [22] suggested a SUV_{max} cut-off of ≥ 5 for differentiating malignant from nonmalignant lesions. This is a much lower cut-off value than we suggested. However, Luboldt et al. included only patients with known colorectal carcinoma. For that reason, the two studies should not be compared. In contrast, however, according to our results, the SUV_{max} is not able to differentiate benign lesions from non-advanced adenomas. These results indicate that all incidental findings in the colon (including those with $SUV_{max} < 11.4$) should be further evaluated. This is in accordance with the findings of many previous studies which have also shown that incidental focal colorectal uptake of FDG is associated with a high risk of neoplastic disease, and colonoscopy should be suggested in the PET/CT report [6, 8, 10, 11, 17, 19, 25].

Our study had some limitations. First, approximately 40 % of the patients with unexpected focally increased FDG uptake in the large bowel did not undergo further colonoscopic evaluation (Table 2). Therefore, we are unable to comment on the correlation of the colonoscopic findings of these lesions. However, both the median SUV_{max} and location of the incidental lesions without colonoscopic evaluation were comparable to those of the lesions followed-up by colonoscopy. The median (IQR) SUV_{max} was 7.8 (6.3 – 9.6) in the nonevaluated incidental foci, and 27 % and 50 % were located in the ileocaecal region and rectosigmoid, respectively. Of the lesions evaluated by colonoscopy, 23 % and 60 % were located in the ileocaecal region and rectosigmoid, respectively. Similar studies have shown comparable percentages on follow-up [6, 8, 11, 17]. Second, in 13 patients, the colonoscopy following the PET/CT scan was not performed to evaluate the unexpected PET/CT focus but for change in stools, rectal bleeding or follow-up of polyps. These patients were nevertheless included in the study if the colonoscopy was performed within 120 days of the PET/CT scan and the lesion correlated with the area of intense FDG uptake was properly described. Last, the baseline characteristics of 203 patients with incidental focal colonic activity and subsequent colonoscopy were retrieved. However, demographic data were not collected for all 7,318 patients who underwent PET/CT. Consequently, these two groups were not compared.

Conclusion

In conclusion, malignant colonic lesions had significantly higher SUV_{max} values on FDG PET/CT than all other types of lesions. The SUV_{max} may be helpful in differentiating malignant from nonmalignant lesions, with an optimal cut-off of ≥ 11.4 . However, SUV_{max} cannot differentiate benign

lesions from adenomas. Consequently, all incidental hotspots in the colon should be further evaluated by colonoscopy. SUV_{max} may help in determining the urgency of colonoscopy, but not in determining whether to perform a colonoscopy or not. SUV_{max} alone is therefore not sufficiently discriminative to differentiate malignant, premalignant and benign lesions. A prognostic score model including more additional factors (e.g. size of the focus, bowel wall thickening, pathological lymph node) could probably predict the presence and aetiology of pathological changes more precisely.

Conflicts of interest None.

Authors' contributions F. van Hoeij: Carried out the data collection, carried out the data analysis and drafted the manuscript.

R. Keijsers: Participated in the design of the study, participated in its coordination, contributed to acquisition and interpretation of data and was involved in drafting the manuscript of revising it critically for important intellectual content.

B. Loffeld: Contributed to collection of data.

G. Dun: Contributed to collection of data.

P. Stadhouders: Participated in the design of the study, contributed to collection of data.

B. Weusten: Participated in the design of the study, participated in its coordination, contributed to analysis, acquisition and interpretation of data and was involved in drafting the manuscript of revising it critically for important intellectual content.

All authors read and approved the final manuscript.

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