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Incidental Uptake in Gastrointestinal Tract on 18F-FDG-PET/CT: Is It Worth to Investigate? A Study with 371 Patients

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Keywords
Colorectal polyps · Gastrointestinal cancer · Endoscopy · Incidental gastrointestinal lesions · Positron emission tomography/computed · Tomography

Abstract

Background and Study Aims: Positron emission tomography/computed tomography (PET/CT) with 2-[18F]FDG (FDG) has been increasingly used to detect or monitor neoplasms. Gastrointestinal tract (GIT) is one of the most common sites of FDG uptake, leading to increasing requests for endoscopic examinations. We aimed to evaluate the nature and significance of unexpected PET/CT-FDG findings in the GIT. ***Patients and Methods:*** We retrospectively analyzed 371 consecutive patients with incidental GIT findings on PET/CT-FDG between June 2016 and October 2021 who were subsequently referred to endoscopic examinations. Demographic data, PET/CT-FDG results, endoscopic findings, and histological analysis were analyzed. ***Results:*** Of 194 colonic incidental uptakes, 102 (52.6%) corresponded to at least premalignant lesions, being 57 (29.4%) advanced adenomas and 23 (11.9%) adenocarcinomas. Of 193 upper GIT incidental uptakes, there were 11 (13.8%) esophageal and 14 (14.4%) gastric malignant/premalignant lesions. The maximum standardized uptake value (SUVmax) significantly varied according to the nature of the lesion, being higher in malignant lesions (in the esophagus, stomach, and colon). However, an optimal SUVmax cutoff was only found for stomach (SUVmax 8.2; sensitivity of 79% and specificity of 76%). There was a significant association between the site of uptake and the nature of the lesion – left colon and gastric body uptake were associated with neoplastic origin whereas rectum and lower esophagus were associated with inflammatory or no endoscopic changes. ***Conclusions:*** Any incidental uptake in the lower GIT should be investigated provided that patients are suitable for further treatment. However, in the upper GIT the characteristics of uptake on ^{18}F-FDG-PET/CT may allow to select those who need endoscopic examination.

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Achados incidentais ao nível do trato gastrointestinal em 18F-FDG-PET/CT: valerá a pena investigar? Um estudo com 371 doentes

Palavras Chave
Colonoscopia · Cancro gastrointestinal · Endoscopia · Lesões gastrointestinais incidentais · Tomografia computadorizada de emissão de positrões (PET-TC)

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Resumo

Introdução: A tomografia por emissão de positrões/tomografia computadorizada (PET/CT) com 2-[18F]FDG (FDG) tem sido cada vez mais utilizada para detetar ou monitorizar neoplasias. O trato gastrointestinal (TGI) é um dos locais mais comuns de captação de FDG, levando a um aumento na solicitação de exames endoscópicos. O nosso objetivo foi avaliar a natureza e o significado destes achados inesperados ao nível do TGI em PET/CT-FDG. ***Métodos:*** Foram analisados retrospetivamente 371 doentes consecutivos com achados incidentais no TGI em PET/CT-FDG entre 06/2016 e 10/2021, posteriormente encaminhados para exames endoscópicos. Dados demográficos, resultados da PET/CT-FDG, achados endoscópicos e análise histológica foram avaliados. ***Resultados:*** Das 194 captações incidentais cólicas, 102 (52,6%) eram pelo menos pré-malignas. 57 (29,4%) adenomas avançados e 23 (11,9%) adenocarcinomas. Das 193 captações incidentais do TGI superior, 11 (13,8%) do esófago e 14 (14,4%) do estômago eram malignas/pré-malignas. O SUVmax variou significativamente com a natureza da lesão, sendo maior nas lesões malignas, tanto no esófago, estômago ou cólon. No entanto, um valor de corte ideal de SUVmax só foi encontrado para o estômago de 8,2, com sensibilidade de 79% e especificidade de 76%. Houve uma associação significativa entre o local de captação e a natureza da lesão, o cólon esquerdo e o corpo gástrico apresentaram mais lesões pré-malignas/malignas, enquanto o reto e o esófago inferior apresentaram mais lesões inflamatórias/sem alterações. ***Conclusões:*** Qualquer captação incidental no TGI inferior, se os pacientes forem adequados para tratamento adicional, deve ser investigada. No entanto, no TGI superior, as características de captação na 18F-FDG-PET/CT podem permitir selecionar aqueles que necessitam de exame endoscópico.

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Introduction

Positron emission tomography (PET) employing fluorodeoxyglucose (FDG) has become an increasingly used diagnostic tool in oncology for tumor staging or posttreatment patient monitoring. Additionally, PET-FDG has also expanded beyond oncological applications into non-oncological contexts [1–4]. Among PET radiolabeled tracers, 18 Fluorine-fluorodeoxyglucose (18F-FDG-PET/CT) stands out as the most frequently employed. Operating as a glucose analog, 18F-FDG serves as an indicator of glucose metabolism [5]. Conditions characterized by heightened metabolic activity, such as cancer or inflammation, exhibit increased FDG uptake, resulting in anomalous accumulation [2, 6]. However, the nonspecific nature of 18F-FDG-PET/CT uptake poses challenges, as physiological or benign conditions may manifest with patterns resembling pathological accumulation, potentially leading to misinterpretations and resource utilization [7, 8]. Specifically concerning lesions within the gastrointestinal tract (GIT), 18F-FDG-PET/CT demonstrates high sensitivity but lacks specificity [9]. The uptake of 18F-FDG within the GIT exhibits considerable variability, ranging from mild to intense, and may manifest with either focal or diffuse distribution patterns. While diffuse uptake is often attributed to physiological or inflammatory origins, focal uptake more commonly indicates a pathological condition [10, 11]. Incidental or unexpected 18F-FDG uptake is relatively prevalent [12], yet the clinical significance of such occurrences in patients with malignancies remains incompletely defined [9]. Previous investigations have addressed this topic; however, many were constrained by small sample sizes [1, 9] or focused solely on colorectal uptake [13, 14]. This study aimed to conduct a retrospective evaluation of the nature and clinical significance of unexpected 18F-FDG-PET/CT findings within the GIT among patients subsequently referred for endoscopic examination.

Materials and Methods

Patients

This retrospective study was conducted from June 2016 to October 2021 and included all patients who underwent 18F-FDG-PET/CT at our facility and exhibited incidental uptake within the GIT leading to endoscopic examination within a 12-month period. Lesions identified as physiological by nuclear physicians were also included in the analysis. When applicable, endoscopic reports were supplemented with histological examination findings.

The clinical indications for 18F-FDG-PET/CT were established by the assistant physicians overseeing patient care. These indications encompassed both diagnostic evaluations and follow-up assessments for a spectrum of malignancies, such as Hodgkin and Non-Hodgkin lymphoma, breast carcinoma, lung carcinoma, uterine and cervical carcinoma, esophageal adenocarcinoma, head and neck malignancies, melanomas, multiple myelomas, colon carcinoma, among others.

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We defined incidental uptake as an unexpected detection of FDG accumulation in the GIT, when the ^{18}F-FDG-PET/CT scan was not the intended to target any pathology of the GIT. We defined the right colon as cecum/ascending colon/transverse colon and left colon as descending and sigmoid colon.

Patients with incomplete endoscopic examinations (that did not reach the location of the uptake – 3 patients) or that were not submitted to endoscopic examination in the 12 month-period (12 patients) were excluded from this analysis. All the data were collected through assessment of clinical records, which included nuclear medicine report regarding 18F-FDG-PET/CT scans, gastroenterologist endoscopic examinations, and histopathological reports. The studied was carried out in accordance with Declaration of Helsinki and was approved by the Ethics Committee of our institution.

PET/CT Scan and Report

Patients were asked to fast for a minimum of 4 h prior to ^{18}F-FDG injection, and not to ingest any food with sugar in the day before. They were also asked to avoid physical exercise in the day prior to the exam.

On the day of the examination, each patient received an intravenous injection of 3.7 MBq/kg of 18F-FDG. Blood glucose levels were required to be <200 mg/dL, and diabetic patients were instructed to abstain from insulin usage. Patients were advised to rest for 1 h prior to the examination to minimize muscular activity and were encouraged to void to reduce bladder activity.

Imaging was performed 60 min after injection of ^{18}F-FDG. Patients were in supine position, with both arms crossed above the head. A topogram was acquired to ensure body coverage from the apex of the skull to the mid-thigh, followed by the acquisition of low-dose CT attenuation correction maps (3–5 mSv). PET acquisition entailed 3 min of data acquisition for each bed position. Image fusion was executed utilizing an iterative algorithm.

We defined unexpected FDG uptake as any instance where the nuclear medicine physician visually deemed the GIT uptake abnormal, based on either its pattern or quantity, with consequent documentation on the report. In some 18F-FDG-PET/CT reports, the nuclear medicine physician provided a qualitative assessment indicating whether the uptake was suggestive of inflammatory nature or suspicious for malignancy. This assessment was based on the physician's experience, involving visual analysis of the images, correlation with the uptake on the CT component of the study as well as the nature of the uptake, focal or diffuse. These data were gathered to evaluate the physician's capability to discern whether the uptake warranted further investigation. Additionally, the uptake pattern (focal or diffuse) and maximum standardized uptake value (SUVmax) were also recorded.

Endoscopy Findings

All procedures were carried out by an accredited gastroenterologist. All endoscopic examinations were retrospectively reviewed via medical records. Colonoscopies adhered to institutional bowel preparation protocols. Lesions considered were those correlating with the sites of uptake as indicated in the 18F-FDG-PET/CT report; if multiple lesions were present, only the most advanced was considered. Esophagogastric and colorectal lesions were categorized by appearance into likely cancerous, premalignant, nonneoplastic, inflammatory, or showing no changes. In cases of multiple lesions, only those at the site of uptake were analyzed.

Histopathological Findings

Biopsy or resection, when considered appropriate, was conducted in all patients exhibiting suspicious malignant or premalignant lesions. Histological sampling was selectively conducted solely in cases demonstrating abnormal findings; therefore, if the endoscopic examination yielded normal results, no histological samples were acquired.

Histopathological analysis of the biopsies was carried out utilizing the latest classification provided by the World Health Organization and by dedicated GI tract pathologists. Premalignant lesions were stratified based on the assessment of low- or high-grade dysplasia.

Patients who had serrated sessile lesions and adenomas with low- or high-grade dysplasia, and with malignant lesions, were labelled has having pre-malignant/malignant findings, while all other findings were considered benign. In the colon, adenomas (tubular or tubulovillous) were considered advanced if ≥1 cm and/or with high-grade dysplasia. In regard with serrated sessile lesions, only those with at least 1 cm or with dysplasia were considered advanced.

Statistical Analysis

The χ^2 test was used to identify association between location of the uptake and pre-malignant/malignant findings, and between these and the nuclear medicine physician's qualitative assessment. To evaluate differences between SUVmax of benign and premalignant/malignant findings, the Mann-Whitney U test was used. In addition, receiver-operating characteristic (ROC) analysis was used to identify cut-off values for SUVmax, to accurately differentiate benign from premalignant/malignant findings. Sensitivity and specificity with a 95% confidence interval were also obtained. SPSS Statistics for Windows, version 27.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

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Table 1. Characterization of the patients included

	N	%
Gender		
Male	206	55.5
Female	165	44.5
Median age, years (range)	63 (13–90)	
Mean time between PET/CT-FDG and endoscopy (days)	61	
Referral specialty		
Hematology	120	32.6
Oncology	87	23.8
Dermatology	32	8.8
Pulmonology	30	8.0
Motive for PET/CT FDG		
Surveillance	149	40.1
Staging	82	22.2
Assessment after treatment	72	19.3
Suspicion of progression	60	16.3
Relapse suspicion	8	2.1
Total	371	100
SUVmax range of incidental findings	[2.0 - 50.6]	

Table 2. Upper GIT uptake distribution

Location	*N*	%
Proximal esophagus	5	2.6
Medial esophagus	10	5.2
Distal esophagus/GEJ	65	33.7
Total esophagus	80	41.5
Stomach – fundus	19	9.8
Stomach – body	27	14.0
Stomach – antrum	17	8.8
Stomach – not specified	34	17.6
Total stomach	97	50.2
Duodenum	15	7.8
Anastomosis	1	0.5
Total	193	100

Results

A total of 371 consecutive patients with incidental GIT uptakes who underwent endoscopic examination within 12 months following 18F-FDG-PET/CT examination were included in the study. The mean interval between 18F-FDG-PET/CT and endoscopic examination was 61 days.

The majority of patients were referred by hematology (32.6%) and oncology (23.8%) departments, with most undergoing 18F-FDG-PET/CT examination for neoplasm surveillance (40.1%) or staging (22.2%), as detailed in Table 1. Analysis included 387 incidental uptakes from 371 patients, comprising 206 males and 165 females, aged 13–90 years (mean 63). Among these, 193 uptakes were located in the upper GIT, prompting investigation via upper endoscopy, while 194 were identified in the lower GIT, requiring sigmoidoscopy or colonoscopy examination.

Upper GIT

There were 193 incidental uptakes in the upper GIT among 187 patients, comprising 101 (54.0%) males and 86 (46.0%) females, aged between 13 and 90 years, with a median age of 63. The distribution of these uptakes within the upper GIT is detailed in Table 2.

Esophagus

In the esophagus, 13.8% (11/80) of incidental 18F-FDG-PET/CT uptakes corresponded to malignancies. Of these, 2 patients presented with adenocarcinoma (both located at the distal esophagus/gastroesophageal junction [GEJ]), while nine exhibited squamous cell carcinoma, predominantly situated in the proximal and mid esophagus (four each), with one located at the distal esophagus. However, the majority of incidental uptakes corresponded to inflammatory conditions (Fig. 1), with most patients displaying reflux esophagitis or no abnormalities during endoscopy.

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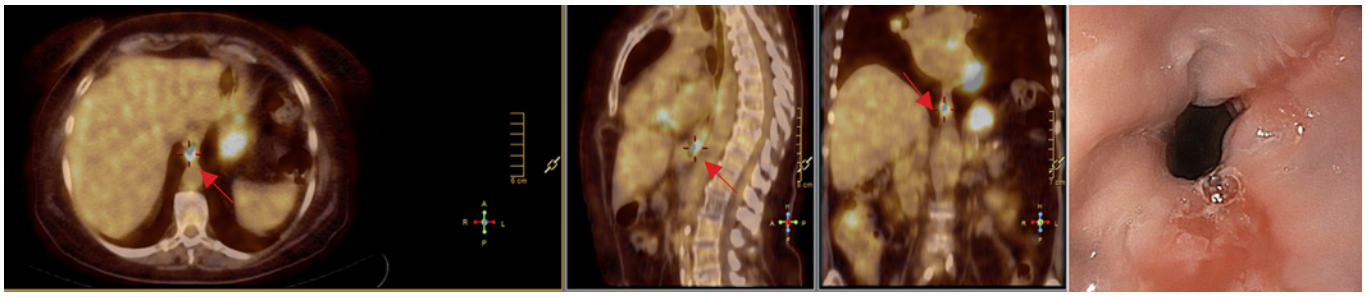

Fig. 1. Sixty-two-year-old woman was submitted to 18Fluorine-FDG PET/computer tomography in the context of surveillance of a melanoma. There was incidental FDG uptake in the lower esophagus. The patient underwent upper endoscopy, which showed a reflux esophagitis. Fused PET/CT image showing FDG uptake (standardized uptake value, SUVmax 9.8) in the lower esophagus (arrow) in axial, coronal and sagittal planes. Upper endoscopy image showed the Los Angeles grade C esophagitis.

Regarding uptake patterns, 15 cases (18.8%) demonstrated diffuse uptake, 47 cases (58.7%) exhibited focal uptake, while in 18 cases (22.5%) uptake pattern was not specified in the report. Among the malignancies, focal uptake was observed in 6 cases (54.5%), diffuse uptake in 3 cases (27.3%), while uptake specification was lacking in 2 cases (18.2%).

There was a significant association between the location of the incidental ^{18}F-FDG-PET/CT uptake and malignant findings. Specifically, uptakes detected in the mid-esophagus exhibited a higher propensity for malignancy, whereas those located in the distal esophagus/GEJ were more frequently benign (likelihood ratio = 8.619, $p = 0.012$).

The nuclear medicine physician provided a qualitative assessment in 40 patients, suggesting a benign nature in 26 cases (65.0%) and suspicion for malignancy in 14 cases (35.0%). There was an association between the qualitative analysis by the nuclear medicine specialist and the lesion's nature. The physician's suspicion or prediction of malignancy in the esophagus demonstrated a sensitivity of 87.5% and specificity of 78.1% ($p = 0.001$). However, no correlation was observed between the uptake pattern and the type of findings in the esophagus.

The Mann-Whitney U test unveiled substantial disparities between the SUVmax values of uptake sites exhibiting either normal endoscopic findings or solely inflammatory changes (median = 5.6, $n = 69$) and those with malignant conditions (median = 7.6, $n = 11$), with $U = 198.5$, $z = -2.53$, $p = 0.011$, $r = 0.28$. Nonetheless, despite the statistical significance of the difference and acceptable sensitivity, ROC curve analysis indicates low specificity in determining a cut-off value for SUVmax.

Stomach

As illustrated in Table 3, most incidental FDG uptakes in the stomach were inflammatory – chronic gastritis comprised 43.3% (42/97) and no abnormalities were found in 42.3% (41/97). There were 6 cases of adenocarcinomas (1 diffuse type and 5 intestinal type), 5 lymphomas, 1 high-grade dysplasia, and 2 melanoma metastases. Regarding uptake patterns, 38 cases (39.2%) exhibited diffuse uptake, 42 cases (43.3%) displayed focal uptake, and 17 cases (17.5%) were not specified in the report. Among the malignancies, 4 out of 6 adenocarcinomas exhibited focal uptake, while in 2 pattern uptake was not specified; 2 out of 5 lymphomas showed focal uptake, with 3 unspecified; both metastases displayed focal uptake, and the high-grade dysplasia exhibited focal uptake as well. Hence, 64.3% of malignancies demonstrated focal uptake, while 35.7% were unspecified in the report.

There was a significant association between the location of incidental FDG PET/CT uptake and malignant findings. Fourteen incidental uptakes corresponded to a malignant finding in the stomach, and they were significantly more frequent in the body of the stomach (likelihood ratio = 10.095, $p = 0.018$).

Qualitative analysis by the nuclear medicine specialist was available in 44 patients, indicating a benign nature in 32 cases (72.7%) and suspicion for malignancy in 12 cases (27.3%). A significant association was observed between the qualitative assessment provided in the 18F-FDG-PET/CT report and the nuclear medicine physician's interpretation (LR = 9.850, $p = 0.002$). The physician demonstrated the ability to discern the presence of malignancy with a sensitivity of 83.3% and specificity of 81.6%.

Regarding pattern uptake in the stomach, 44 uptakes (45.4%) exhibited a focal pattern, while 38 uptakes (39.2%) displayed a diffuse pattern. The uptake pattern

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Table 3. Upper GIT endoscopic findings

Location	*N*	%
Esophagus		
No changes	33	41.2
Inflammatory/benign findings	36	45
Reflux esophagitis LA grade A	14	
Reflux esophagitis LA grade B	13	
Reflux esophagitis LA grade C	2	
Esophageal candidiasis	2	
Leiomyoma	3	
Peptic stenosis	1	
Diverticulum	1	
Malignant findings	11	13.8
Adenocarcinoma	2	
Squamous cell carcinoma	9	
Stomach		
No changes	41	42.3
Inflammatory findings		
Chronic gastritis	42	43.3
Premalignant/malignant findings	14	14.4
Adenocarcinoma	6	
Adenoma with high-grade dysplasia	1	
Metastatic melanoma	2	
Follicular lymphoma	2	
Hodgkin lymphoma	1	
MALT lymphoma	1	
Diffuse large B-cell lymphoma	1	
Duodenum		
No changes	9	60.0
Inflammatory/benign findings	6	40.0
Brunner's gland hyperplasia	1	
Bulbitis	2	
Benign ulcers	3	
Total	193	100

MALT, mucosa-associated lymphoid tissue.

Table 4. Lower GIT uptake distribution

Location	*N*	%
Terminal ileum	3	1.5
Ascending colon	79	40.7
Transverse colon	15	7.8
Descending colon	57	29.4
Rectum	37	19.1
Anastomosis	3	1.5
Total	194	100

was not specified in the remaining 15 cases (15.5%). The pattern of uptake was significantly different according to the nature of the lesion, with focal uptake more commonly associated with malignant findings, while diffuse uptake was more frequently linked to inflammatory conditions or no findings during endoscopy (LR = 5.772, $p = 0.016$).

The SUVmax in the stomach varied significantly according to the nature of the lesion, being higher in malignant lesions (median SUV = 6.7 in benign lesions vs. median SUV 9.65 in malignant lesions, $p = 0.001$, $r = 0.34$). Additionally, ROC analysis revealed a statistically significant association between increases in SUVmax and malignant findings, with an AUC of 0.78 ($p = 0.001$). An optimal SUVmax cut-off of 8.2 was considered adequate to distinguish between benign and malignant findings, with 79% sensitivity and 76% specificity.

Duodenum

All 15 findings in the duodenum were benign in nature, 9 revealing normal mucosa, 2 bulbitis, 3 ulcers, and 1 Brunner's gland hyperplasia. The uptake was focal in 8 and diffuse in 2, not being specified in the remnant. The SUVmax of all incidental findings in duodenum was between 4.7 and 12.3.

Lower GIT

The distribution of the uptake in the lower GIT is summarized in Table 4. The nature of the lesion, revealed by the endoscopic study complemented with the histological examination, is detailed in Table 5.

As specified in Table 5, 92 of incidental uptakes (47.4%) were inflammatory or exhibited no changes at endoscopic examination, while 102 (52.6%) were premalignant or malignant – 46 adenomas with low-grade dysplasia, 5 sessile serrated lesions with no dysplasia, 23 adenomas with high-grade dysplasia (11.9%) (Fig. 2) and 23 incidental adenocarcinomas (11.9%) (Fig. 3). According to the above criterion, 57 (29.4%) incidental uptakes were advanced adenomas. Additionally, other notable findings comprised 3 lymphomas (2 diffuse large B-cell and 1 follicular), with 2 of them located at the terminal ileum, and the other one at the cecum. There were found 2 metastatic lesions (1 melanoma and 1 Meckel cell carcinoma).

Based on the pattern of uptake, 26 (13.4%) displayed diffuse uptake, 133 (68.6%) exhibited focal uptake, and 35 (18.0%) lacked specification in the report. Among the premalignant/malignant conditions, 72 (72.7%) demonstrated focal uptake, 10 (10.1%) showed diffuse uptake, and 17 (17.2%) were unspecified according to the report.

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Table 5. Lower GIT endoscopic findings

Location	*N*	%
Normal intestinal mucosa	74	38.1
Inflammatory/benign findings	18	9.3
Diverticula	9	
Anastomosis edema	1	
Benign ulcers	2	
Others inflammatory conditions	6	
Premalignant/malignant findings	102	52.6
Tubular/villous adenoma w/low-grade dysplasia	46	
Sessile serrated lesion	5	
Tubular/villous adenoma w/high-grade dysplasia	23	
Adenocarcinoma	23	
Meckel cell carcinoma metastasis	1	
Metastatic melanoma	1	
Diffuse large B-Cell lymphoma	2	
Follicular lymphoma	1	

60 patients with no alterations had focal uptake. There was no significant difference observed between the uptake pattern and the nature of the lesion.

However, we found a significant association between the location of the uptake and the nature of the lesion, with the left colon revealing significantly more premalignant/malignant findings, while the rectum exhibited significantly more benign findings (LR = 19.039, $p = 0.001$). The nuclear medicine physician conducted a qualitative analysis in 73 patients, indicating a benign nature in 22 cases (30.1%) and suspicion for malignancy in 51 cases (69.9%). A significant association was observed between the qualitative analysis and the nature of the lesion ($x^2 = 11.926$, $p = 0.001$), with the nuclear medicine physician demonstrating 87.2% sensitivity in identifying premalignant/malignant findings, albeit with 50% specificity.

There were significant differences between median SUVmax in benign versus premalignant/malignant lesions (7.9 vs. 9.4, $p = 0.004$, $r = 0.21$). However, no optimal cut-off was found due to low specificity.

Patient Management

There was a dichotomy in patient management based on the location of the findings. Among the 11 patients diagnosed incidentally with malignancy in the esophagus, only two underwent intended curative treatment, both for squamous cell carcinoma. The remaining patients were referred to palliative care due to either metastatic lesions or low performance status. Similar results were observed in the stomach, where the majority of patients diagnosed incidentally with adenocarcinoma (5 out of 6) were referred to palliative care, with only one undergoing curative treatment through surgery. The patient with adenoma with high-grade dysplasia underwent endoscopic submucosal dissection. As for lymphomas, all patients underwent curative-intent treatment, while both patients with metastatic lesions were referred to palliative care. In contrast to the upper GIT, among the 23 patients diagnosed incidentally with cancer in the colon/rectum, 15 (65.2%) underwent intended curative treatment (surgery with or without radiotherapy and/or chemotherapy). Eight patients (34.8%) received palliative treatment due to the primary cancer stage or comorbidities.

Discussion

The objective of this study was to characterize the unexpected 18F-FDG-PET/CT findings in the upper and lower GIT, correlate them with endoscopic findings, analyze their significance, and determine whether the incidental diagnosis of GIT malignancy alters patient management. Many studies focusing on FDG-avid lesions in the GIT, both upper and lower, have involved a limited number of patients [5, 9, 15]. To the best of our knowledge, this study represents the largest investigation to date concerning the upper GIT.

The utilization of 18F-FDG-PET/CT has been on the rise due to its efficacy in staging or monitoring malignancies. Approximately 1 to 3 percent of patients undergoing 18F-FDG-PET/CT exhibit gastrointestinal uptake [16, 17]. At our institution, given the scarcity of data regarding the management of these patients, all individuals with incidental

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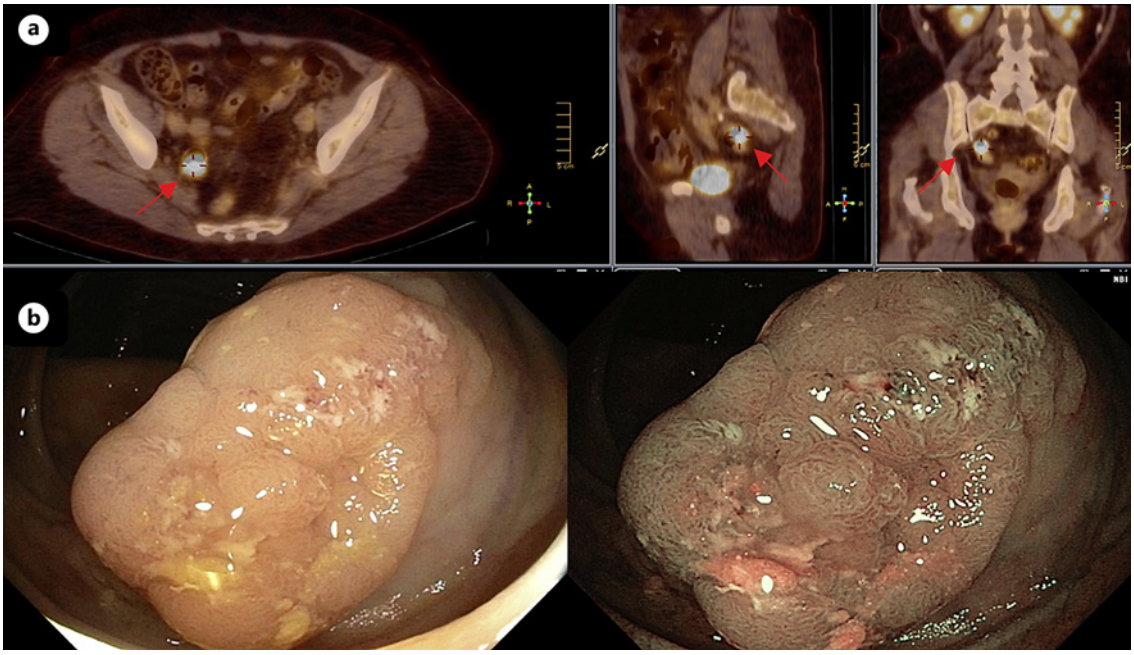

Fig. 2. Sixty eight-year-old man was submitted to 18Fluorine-FDG PET/computer tomography in the context of a hematological disorder. There was incidental FDG uptake in the ascending colon. The patient underwent colonoscopy, which showed a tubulo-villous adenoma which harbors high-grade dysplasia. **a** Fused PET/CT image showing FDG uptake (standardized uptake value, SUVmax 9.8) in the ascending colon (arrow) in axial, coronal and sagittal planes. **b** Colonoscopy image showed a lateral spreading tumor granular homogenous type in white light and narrow band image.

GIT uptake are referred for endoscopic examination. However, this practice burdens the endoscopy unit and presents challenges for clinicians triaging the examinations.

Existing literature predominantly focuses on the lower GIT [14, 18], exemplified by a study conducted by Kousgaard et al. [13], which identified a 12% risk of malignant lesions and a 72% risk of premalignant lesions. Consistent with these findings, our study revealed that 29.4% of incidental uptakes in the lower GIT corresponded to advanced polyps, and 11.9% to malignant lesions. In the upper GIT, malignancy was identified in 13.8% of esophageal and 14.4% of gastric incidental uptakes, with only one premalignant condition (adenoma with high-grade dysplasia) in the stomach. The implications of these findings on patient management are significant. Existing literature predominantly addresses changes in diagnosis and treatment in the lower GIT, with reported alterations ranging from 40% to 90% [13, 19, 20]. Similarly, our study demonstrated that 65.2% of patients with colorectal cancer underwent curative treatment. In contrast, in the upper GIT, only 22.2% (2/9) of patients with esophageal cancer and 28.6% (2/7) of those with gastric cancer or high-grade dysplasia received curative treatment. This underscores the importance of carefully selecting patients for additional diagnostic work-up, particularly those eligible for further treatment.

In similarity with other studies [5, 21–24], we also tried to find an optimal cut-off value for SUVmax, although it significantly rises with premalignancy/malignancy, the SUVmax does not appear to be a good tool for the distinction between benign and premalignant/malignant findings in most locations, except for the stomach, were a cut-off of 8.2 can be considered, with moderate to good sensitivity (79%) and specificity (76%). Most of the available studies were not able to find an optimal cut-off of SUVmax [5]. However, more recently, Hosni et al. [22] found the value of 9.2 to be the value with the highest sensitivity (0.76) and specificity (0.88) but in opposition to our data, this value was referred to all GIT not adjusted to the location. Lee et al. [24] found a value of 7.6, with a sensitivity of 0.686 and a specificity of 0.688, to distinguish between cancer and pre-cancerous lesions but only at the colon.

In our study, the location of incidental uptake in 18F-FDG-PET/CT examinations appears to be significant. Incidental uptake tended to be benign in nature at the GEJ and in the rectum, consistent with findings reported in the literature [24]. In the GEJ, this can be attributed to inflammation caused by acid reflux from the stomach. In the rectum, although the explanation is less precise, an enlarged hemorrhoids could be a plausible cause. Conversely,

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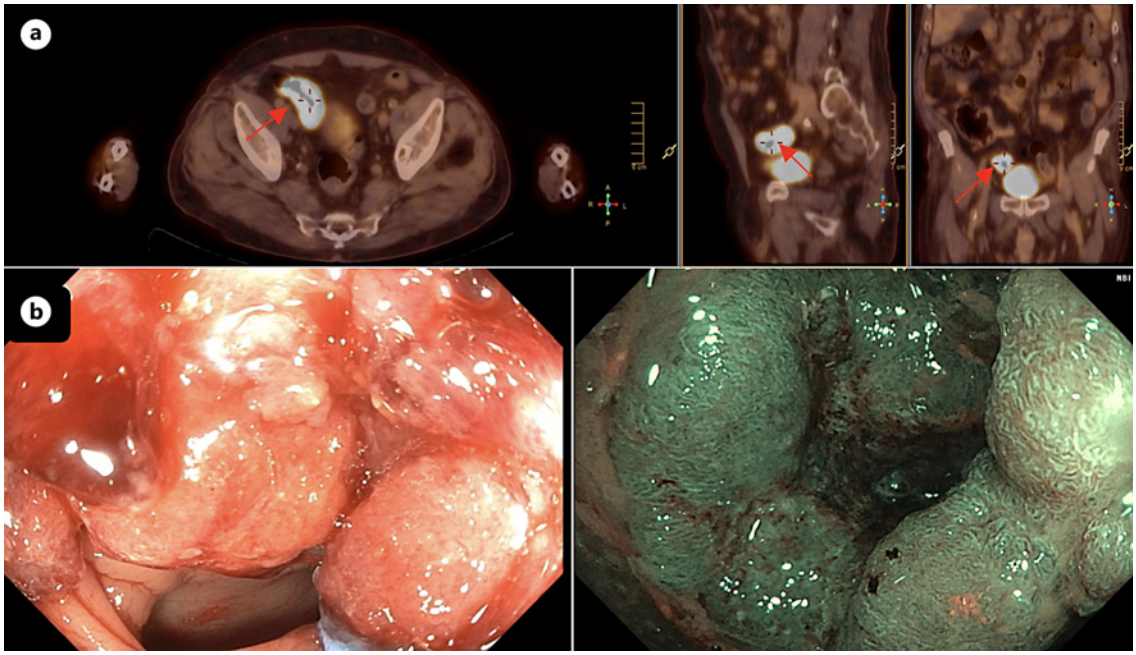

Fig. 3. Seventy two-year-old man was submitted to 18Fluorine-FDG PET/computer tomography in the context of a hematological disorder. There was incidental FDG uptake in the right colon. The patient underwent colonoscopy, which showed an adenocarcinoma. **a** Fused PET/CT image showing FDG uptake (standardized uptake value, SUVmax 17.9) in the ascending colon (arrow) in axial, coronal and sagittal planes. **b** Colonoscopy image showed a lateral spreading tumor granular homogenous type in White Light and Narrow Band Image.

incidental uptake in the mid-esophagus, body of the stomach, and descending colon were significantly more often associated with at least premalignant conditions. Regarding other characteristics of the uptake, existing literature suggests that focal uptake is predictive of at least a premalignant condition [22, 24, 25]. However, we found that focal uptake was predictive of at least a premalignant condition only in the stomach, possibly due to the fact that 18.8% of all reports did not specify the type of uptake. Our analysis of 260 uptakes in the GIT with endoscopic examinations without any changes or inflammatory findings revealed that 147 (56.5%) displayed focal uptake, 64 (24.6%) showed diffuse uptake, and 49 (18.9%) had unspecified uptake according to the report. Among 127 premalignant/malignant conditions, 87 (68.5%) exhibited focal uptake, 14 (11.0%) diffuse uptake, and 26 (20.5%) had unspecified uptake in the report. Based on these data, albeit limited by the nature of the study, we propose that upper GI uptakes with SUVmax of at least 8.2 and focal in nature should be promptly evaluated.

To the best of our knowledge, this study is the first to incorporate the qualitative analysis of the nuclear medicine physician as a metric for evaluating incidental uptake, and it has proven to be highly effective in predicting outcomes across the GIT, particularly in ruling out premalignancy/malignancy. However, further studies are required to validate this parameter as a method to assist in selecting incidental uptakes that require further evaluation.

This is a retrospective single-center study, which with the inherent limitations, could restrict the generalizability of the findings. To mitigate potential confounding factors that may contribute to heterogeneity among studies, a prospective, multicenter investigation employing standardized imaging parameters is necessary. Achieving an optimal management approach necessitates a comprehensive evaluation of the patient's medical history and clinical presentation. However, due to the extensive analysis and considerable number of patients/uptakes and statistically significant PET parameters this study may give some valuable information about the characteristics of the uptakes at GIT and which should prompt endoscopic examination.

Conclusion

Our results fill an important knowledge gap in this field, providing valuable evidence to support the prioritization of certain endoscopic examinations and

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potentially reduce the burden of unnecessary procedures, allowing to select those who need further endoscopic examination.

Statement of Ethics

This study protocol was reviewed and approved by Comissão de Ética para a Saúde of Instituto Português de Oncologia de Lisboa Francisco Gentil, Approval No. GQR.MOD.09.1. Patient consent was waived in accordance with institutional protocol, as consent is not required for cohort studies that utilize only global anonymous data without presenting any individually identifiable information.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Luís Correia Gomes and Davide Fraga were involved in manuscript drafting, data collecting and statistical analyses. Pedro Lage, Isabel Claro, and Lucília Salgado were involved in manuscript critical revision. All authors approved the final version.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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