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Role of Positron Emission Tomography/Computed Tomography (PET/CT) in Assessment and Follow-up of Gastrointestinal Tract Malignancies

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Abstract

Positron Emission Tomography/Computed Tomography (PET/CT) is a highly advanced imaging method that has several uses in oncology, such as determining the stage of cancer, evaluating the effectiveness of treatment, reevaluating the stage of cancer, and monitoring for the return of cancer over time. PET advancement has brought out a new capacity in medical diagnosis: being able to non-invasively examine the physiological condition of interior tissues. The integration of PET with simultaneous CT combines two procedures that enable the diagnosis of metabolic or receptor-specific abnormalities together with precise anatomical localization. In comparison to PET alone, the PET/CT combination is more effective in accurately identifying the location of abnormalities and distinguishing between normal and abnormal uptake of FDG along with additional tracers. PET/CT has become an essential component of management guidelines in many diseases such as lung, breast, and lymphoproliferative malignancies. The ability to image metabolic processes like glucose metabolism adds to the information provided by structural imaging, especially in the context of treatment monitoring, where metabolic changes can often precede structural changes.

Keywords: Gastrointestinal Tract Malignancies, PET/CT.

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1. Introduction

PET has revolutionized medical diagnostics by allowing non-invasive imaging of the physiological condition of inside tissues. The provided article discusses the advancement of PET technology, with a specific focus on the glucose analog known as 2-deoxy-2-18F-D-glucose (FDG) [1]. PET/CT has come to be as an essential component of management guidelines in many diseases such as lung, breast, and lymphoproliferative malignancies [2]. The ability to image metabolic processes like glucose metabolism adds to the information produced by structural imaging, especially in the context of treatment monitoring, where metabolic changes can often precede structural changes. While FDG remains the most often utilized tracer in PET imaging, there have been significant advancements in the creation of more sensitive and specific tracers, some of which are currently being utilized and others that are still in the process of being developed. Moreover, the sensitivity and specificity of PET have progressively improved because of the introduction of advanced ligands and enhancements in procedure. Ultimately, PET has evolved into a valuable instrument for evaluating the effectiveness of therapy and determining the most appropriate therapeutic approach, so greatly enhancing its practicality [1]. The integration of PET with simultaneous CT combines two procedures that enable the diagnosis of metabolic or receptor-specific abnormalities together with precise anatomical localization. The combination of PET/CT is more effective contrasted to PET alone in accurately identifying the location of lesions and distinguishing between normal and abnormal uptake of FDG and additional tracers [3].

2. Overview of Gastrointestinal FDG Uptake

Due to the high FDG-avidity of several gastrointestinal (GI) cancers, FDG-PET/CT is an efficient instrument for the purposes of diagnosing, staging, assessing therapy response, and conducting monitoring. However, the abdomen poses unique challenges since several of its organs have varying and considerable physiological uptake. The existence of FDG uptake in the bowel is often a result of normal physiological activity and may be enhanced by medicines like metformin [4]. The urinary system

consistently eliminates FDG, resulting in high renal absorption and an ongoing existence of FDG in the bladder and collecting system. The existence of increased uptake of the FDG in the bowel may be attributed to infectious or inflammatory conditions which include infectious, abscesses, diverticulitis, appendicitis and inflammatory colitis, and colitis associated to immunotherapy [5]. While FDG-PET/CT may be a very accurate and precise test for assisting in the identifying and management of gastrointestinal cancers, infections, and inflammatory diseases, further specialized diagnostic imaging and clinical correlation are frequently required [1].

3. Specific Tumors

3.1. Esophageal Cancer

At the time of baseline staging, both CT and PET/CT do not seem to have any significant role in T-staging as they can't accurately evaluate the extent of the invasion of the tumor and therefore endoscopic ultrasound (EUS) continues to be the most important investigation. It also allows for sampling, which is necessary for confirmation of the disease [6]. 18F-FDG-PET/CT has additional limitations in that it is unable to reliably differentiate confounding changes like inflammation from actual malignant pathology. However, in confirmed cases of esophageal malignancy, the semi-quantitative parameters derived from PET/CT (like SUVmax, metabolic tumor volume [MTV], and total lesion glycolysis [TLG]) can predict a locally advanced tumor in the period prior to operation with good accuracy. High SUVmax has also been demonstrated to anticipate early recurrence and low survival [7]. The patterns of early nodal dissemination are determined by the location of the main tumour. Cervical esophageal malignancies often metastasize first to upper thoracic or paraoesophageal cervical lymph nodes, in addition to supraclavicular and low anterior cervical lymph nodes. Mid-esophageal cancers metastasize first to paraoesophageal nodes or subcarinal nodes located in close proximity to the main location. Gastric cardia, paraoesophageal nodes close to the main tumor, and gastrohepatic nodes are all affected by GE junction cancers (Figure 1, 2) [8].

3.2. Gastric Cancer

Like esophageal cancers, gastric cancers have a low 5-year survival of ~30% and most cases (36%) are detected with distant metastases at baseline. For all practical purposes, gastroesophageal junction tumors behave similarly to esophageal tumors and the above-mentioned concepts are applicable to those lesions. Conversely, non-junctional tumors may exhibit varying levels of 18F-FDG avidity. Tumors that are bigger in size, have non-signet cell histology, and express Glucose transporter-1 tend to have greater levels of avidity [10]. If there is a presence of diffuse or focused metabolic activity on an FDG PET-CT scan for reasons unrelated to the stomach, it is advisable to undergo clinical examination. If there are clinical complaints linked to the stomach, endoscopy is advised. The sensitivity of FDG PET-CT for identifying the main tumor at an early stage is often low, with reported rates ranging from 26 to 63%. This sensitivity is much lower for tumors that produce mucin. While many gastric tumors may exhibit significant metabolic activity, others have relatively modest metabolic activity that falls within the normal range for the stomach (Figure 3) [11].

3.3. Small Intestinal Malignancies

Survival improves significantly with curative resection and therefore accurate staging is paramount. As with other GI malignancies, PET/CT by itself is insufficient for assessing tumor depth and hence T-staging. Dedicated studies on the use of 18F-FDG PET/CT in small intestinal malignancies is rare and most literature has focused on lymphomas and neuroendocrine tumors. Still, PET/CT seems to provide a benefit in the evaluation of metastatic sites, particularly distant metastases because of whole-body imaging and sensitivity of 18F-FDG to metabolic changes. Furthermore, the utilization of PET/CT enterography can enhance the evaluation of primary disease, by improving rater confidence and reducing false positives [12].

3.4. Colorectal Malignancies

Colorectal malignancies are usually detected at an earlier stage and consequently have a good 5-year survival. As with other GI tumours, the role of PET/CT in the evaluation of T-stage is limited by its lower resolution, inadequacies in the assessment of true depth of involvement, physiological 18F-FDG activity, and confounding inflammatory lesions. The combination of PET with CT colonography can improve specificity and allow for noninvasive assessment of obstructive lesions, where colonoscopy examination is not feasible. However, PET/CT colonography possess a ristricted role in evaluation of small polyps (<10 mm). Recently, PET/ MRI demonstrated to improve both local and distant staging, when compared to PET/CT [13]. (Figure 4).

3.5. Lymphoma

The avidity of 18F-FDG in the lymphomas is dependent on the subtype. Many GI lymphomas including MALTomas, diffuse large B-cell type, Follicular type, and T-cell type show significant 18F-FDG uptake [14, 15]. Lymphomas can account for nearly a fifth of GI malignancies and this involvement can be primary or secondary. In primary lesions, 18F-FDG PET/CT allows for the assessment of extent of involvement and in secondary lesions, it can detect other sites of involvement. Furthermore, measures such as TLG have demonstrated potential as prognostic indicators. PET/CT is more effective than CECT for staging and restaging due to its capability to identify metabolic alterations even when there are no structural alterations and in the case of tiny lesions. Therefore, PET/CT is crucial in determining whether to extend or modify treatment [16].

3.6. Gastrointestinal Stromal Tumors

GI stromal tumours (GIST) are a kind of tumour that originates from the mesenchymal tissue and might happen in any part of the GI tract. One of the major factors, which weigh heavily on management is the differentiation of benign from malignant lesions. The use of tumor diameter and Ki67 have not proven feasible in risk stratification. GIST lesions usually

show high 18F-FDG avidity, which in turn correlates with stage, risk group, and mitotic index. In addition, 18F-FDG PET/CT influences management among individuals when used for restaging by accurately detecting or ruling out local/distant recurrence with a sensitivity and specificity of 89% and 97%, correspondingly. PET/CT is now one of the most accurate methods for assessment the responses for treating in GIST. The SUVmax, measured either before or after treatment, is helpful for assessing the response to treatment and predicting the prognosis among individuals who are either responsive or unresponsive to Imatinib therapy [17]. The assessment of therapy response in GISTs involves several problems and conflicting methodologies, with the most important ones being the standard RECIST and Choi criteria (Table 1). The Choi criterion suggests that a reduction in the tumor's attenuation is a significant predictor of tumour response and is typically considered a more reliable measure of responses [9].

3.7. Neuroendocrine Tumors

Neuroendocrine tumors (NET) are rare tumors, many of which are nonfunctioning, i.e., They do not induce symptoms with the peptides they secrete. Thus, many patients present with symptoms related to local effects like obstruction or distant metastases. Both 18F-FDG and another radiotracer namely 68Ga-DOTA-peptides (which bind to somatostatin receptors) have been used for imaging this tracer. The differentiation and Ki67 determine the selection of radiotracer, since well-differentiated lesions have a strong affinity for 68Ga-DOTA-peptides, whereas poorly differentiated ones exhibit a strong affinity for 18F-FDG. The 68Ga-DOTA-peptide-PET/CT scan is very sensitive and specific in detecting NETs, with a sensitivity and specificity of over 90%. It has been demonstrated to alter the treatment plan in up to 50% of participants. A recent study demonstrated that incorporating CT enterography with PET imaging might significantly enhance the sensitivity (up to about 90%) for detecting unknown primary NETs [18].

3.8. Hepatocellular Carcinoma

HCC may manifest as a large solitary tumor, often exhibiting necrosis, adipose components, and varying degrees of calcification. It may also manifest as a condition characterized by the presence of many nodules or localized areas, with or without central necrosis. It may manifest as a condition that spreads throughout the tissue, making it difficult to differentiate from cirrhosis that is already existing. Imaging strategies commonly use contrast-enhanced CT (CE CT) to detect certain characteristics. These characteristics include an enhancement mass with invasion of the portal vein, late arterial enhancement with quick removal of contrast, or an arterioportal shunt with wedge-shaped perfusion defects that are linked to focal steatosis or focal fatty sparing. Fibrolamellar HCC may have a central scar, comparable to that seen in focal nodular hyperplasia. Magnetic resonance imaging (MRI) is often used to analyze and identify particular characteristics. It reveals vascular enhancement with the combination of T1 and Gd, which is quickly eliminated, often leaving behind a continuous rim of enhancing. Diffusion weighted imaging (DWI) MR scan displaying a prominent intra-tumoral signal is indicative of HCC. The sensitivity of the usual enhancement pattern observed with CE CT or MR is about 60%, despite its excellent specificity. Regrettably, the use of FDG PET in HCC remains restricted. Moderately or well-differentiated HCC often exhibits similar metabolic activity to that of the liver (Figure 5) [19].

3.9. Cholangiocarcinoma

Adenocarcinoma is responsible for 90% of occurrences of CC, whereas squamous cell carcinoma responsible for the remaining 10%. CC has a complex categorization system. Tumours may be classed anatomically as intrahepatic, extrahepatic (specifically hilar or Klatskin tumors), or distal extrahepatic (involving the common bile duct). Additional categorization methods for CC have been devised, focusing on the macroscopic development pattern, microscopic characteristics, and cell of origin [20]. The outlook for patients with CCC is often unfavorable. Surgical excision is the only remedy for CC. Regrettably; it is common for CCC to manifest at a later stage with extensive, untreatable illness. The main focus of treatment is palliative, particularly including biliary drainage. In some situations, radiation therapy, photodynamic therapy, chemotherapy, and molecular targeted therapies may also be used. The efficacy of FDG PET-CT in CC varies. Intrahepatic cholangiocarcinoma is usually very metabolically active and may manifest as big, round masses (Figure 6) [20].

3.10. Gallbladder Carcinoma

Gallbladder tumor and its metastases usually exhibit increased metabolic activity on FDG PET-CT scans. There is a lack of sufficient evidence about the effect of FDG PET-CT in gallbladder cancers. The NCCN guidelines do not include FDG PET as a recommended imaging modality for managing gallbladder cancers. Instead, they recommend using contrast-enhanced CT or MRI of the abdomen and pelvis, as well as a CT scan of the chest. Nevertheless, a recent meta-analysis of the existing data on the effectiveness of FDG PET-CT in detecting gallbladder cancers revealed a combined sensitivity of 96% and specificity of 91% for identifying local illness. Additionally, the research found a combined sensitivity and specificity of 96% and 91% for detecting metastatic disease. The combined sensitivity for nodal illness was 75%, whereas the specificity was 91% [21]. The information about nodal illness is important since lymph nodes affected by gallbladder cancers are often tiny and pose a difficulty for CT scans. While existing research suggests that FDG PET-CT might be beneficial in evaluating gallbladder cancers, more studies on a bigger scale are necessary. It is crucial to be aware that there are instances when false positive results occur due to FDG uptake in the gallbladder. These instances include both chronic and acute cholecystitis, xantho-granulomatous cholecystitis, and papillary hyperplasia [22].

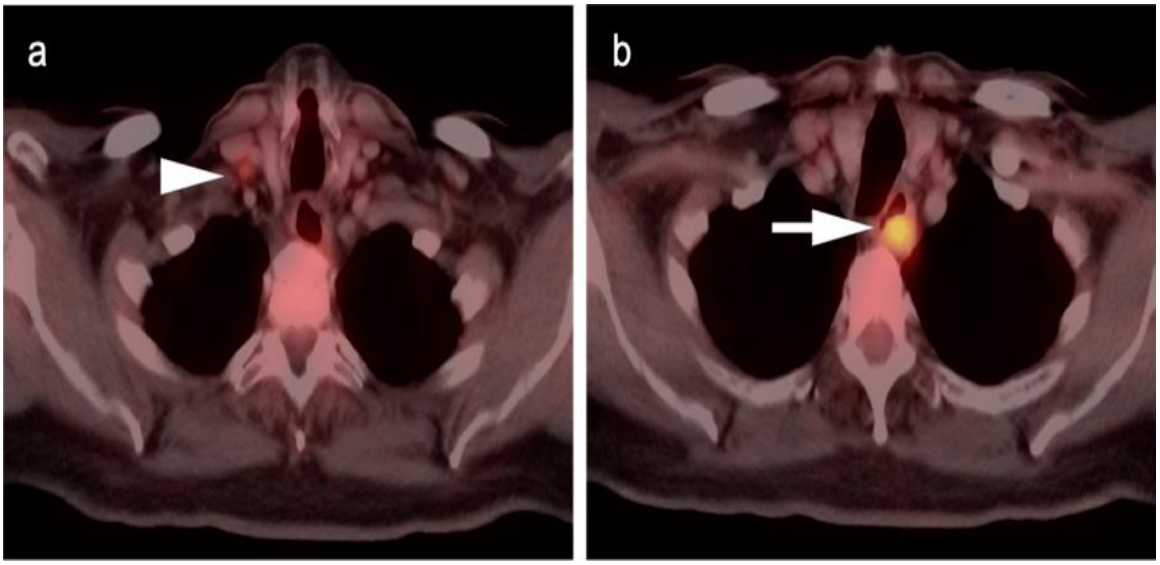

Figure 1. Tumors of the upper thoracic esophagus. (a) The axial fused FDG PET-CT picture indicates a single hypermetabolic low right level 3 cervical node (white arrowhead); (b) The axial fused FDG PET-CT image reveals that the main tumor is a hypermetabolic eccentric mass in the upper thoracic esophagus (white arrow). Upper esophageal tumours often spread to the lymph nodes in the lower neck or supraclavicular area. [9]

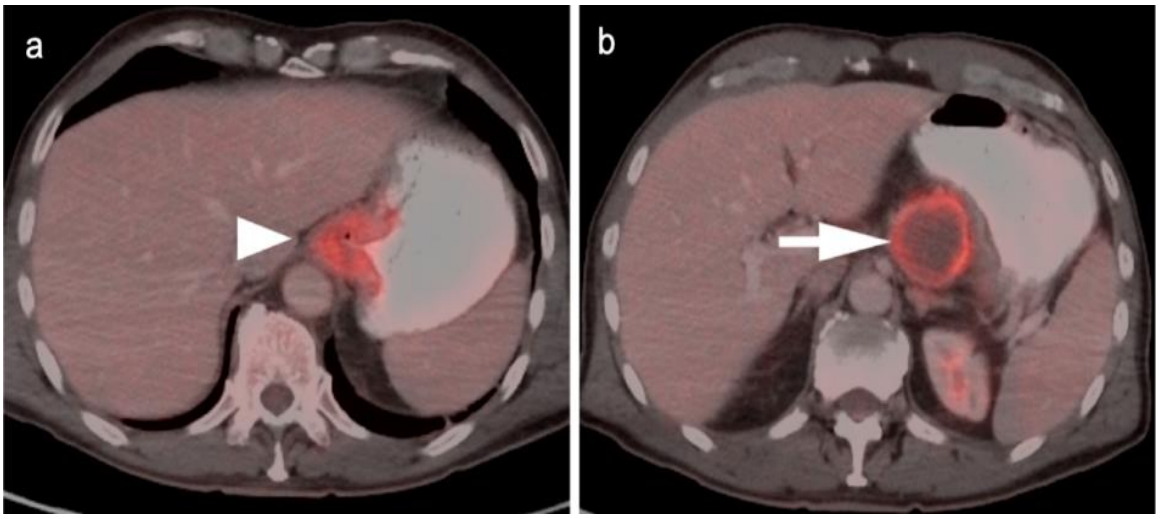

Figure 2. The patient had GE junction esophageal cancer, as evidenced by FDG PET-CT images of the upper abdomen (a) showing a GE junction tumor extending slightly into the gastric cardia (white arrowhead) via axial fused FDG PET-CT; (b) showing a typical pattern of nodal spread to lymph nodes in the gastro-hepatic ligament (white arrow) via axial fused FDG PET-CT [9]

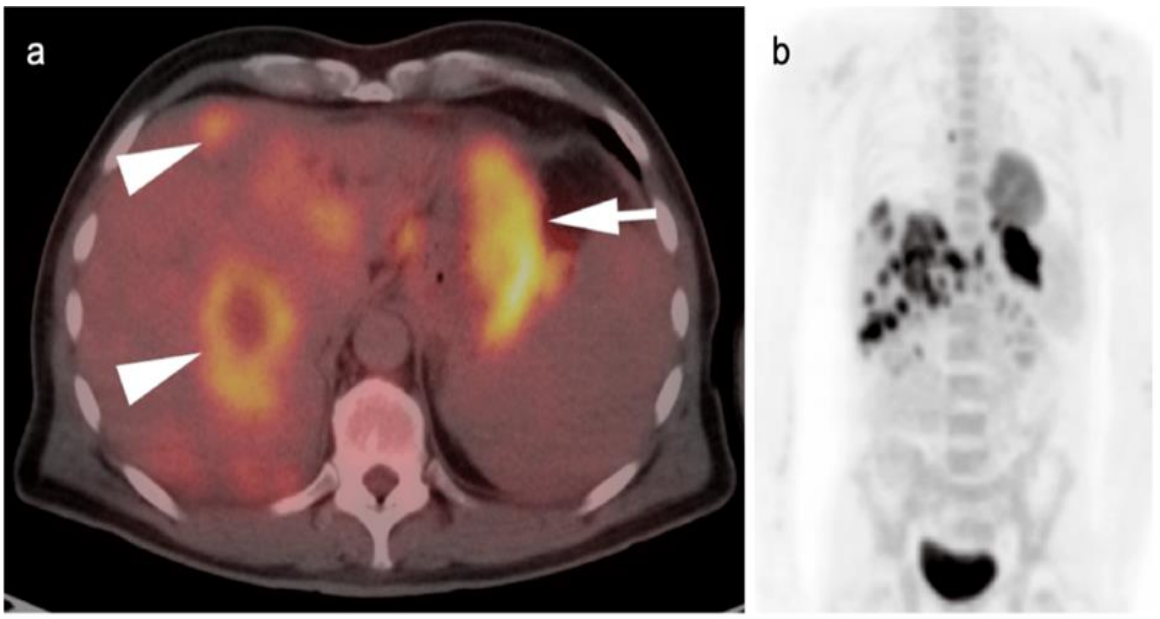

Figure 3. Metastatic gastric cancer (a) Axial FDG PET-CT and (b) MIP image. Markedly hypermetabolic in gastric carcinoma (white arrow) with widespread hepatic metastases (white arrowheads) [9]

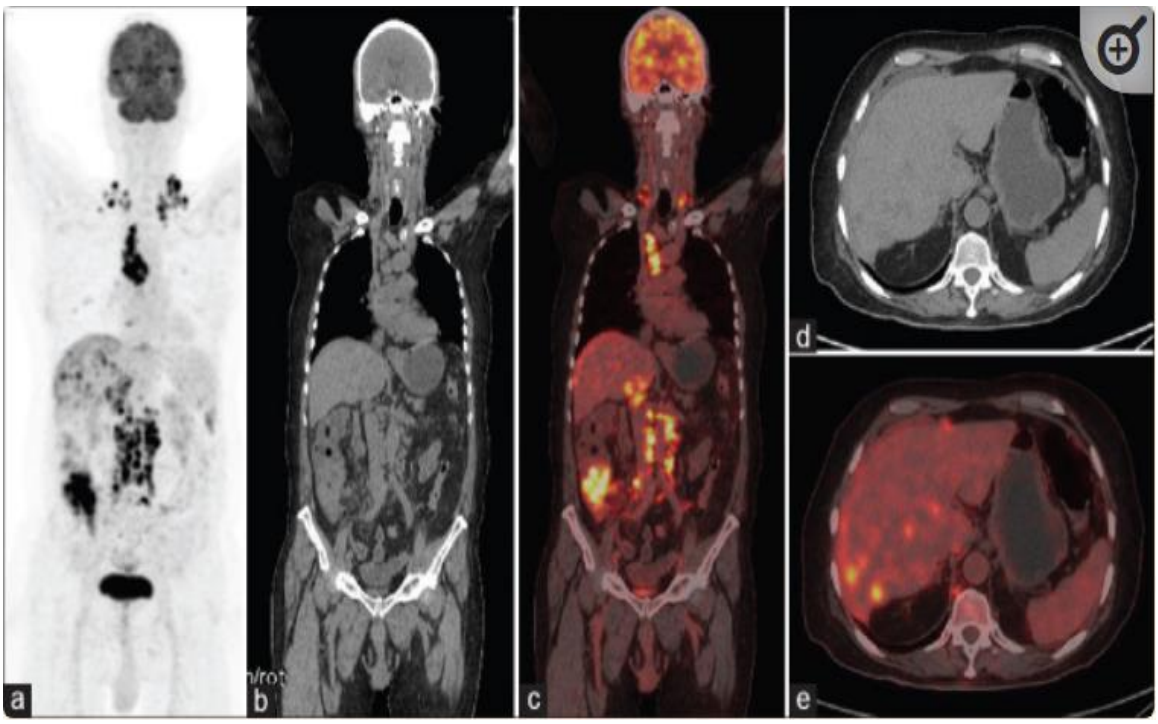

Figure 4. Case of 73-year-old male who was diagnosed with adenocarcinoma of the caecum with hepatic and retroperitoneal lymph nodal metastases. He was referred for 18F-FDG PET/CT for metastatic workup (MIP [a], Coronal CT [b], Coronal PET/CT [c], Axial CT [d], Axial PET/CT [e]}. PET/CT showed a FDG avid mass involving the caecum and ascending colon with metabolically active retroperitoneal lymphadenopathy (b and c) and liver metastases (d and e) (all of which had already been identified). In addition, PET/CT have the ability to detect involvement of cervical and mediastinal lymph-nodes (a-c). These additional sites of involvement did not impact the management in this patient [9].

Table 1. Comparison of response criteria for GISTS [9]

RECIST Criteria	Response	Choi Criteria
All lesions disappeared. no newly formed lesions.	Complete (CR)	Disappearance of all lesions. No new lesions.
Decrease by 30%. no more increase.	Partial (PR)	≥10% decrease in size OR ≥15% decrease in density (HU on CT). No new lesions. No obvious progression of non-measurable disease.
Does not satisfy the requirements for PR or PD.	Stable disease (SD)	Does not meet criteria for complete response, partial response of progression. No clinical deterioration attributed to tumor progression
20% increase in size AND criteria for PR, CR or SD not met prior to increased disease	Progression (SD)	≥10% increase in tumor size AND does not meet criteria of PR by tumor density on CT. New lesions. New intratumoral nodules or increase in size of previous intratumoral nodules.

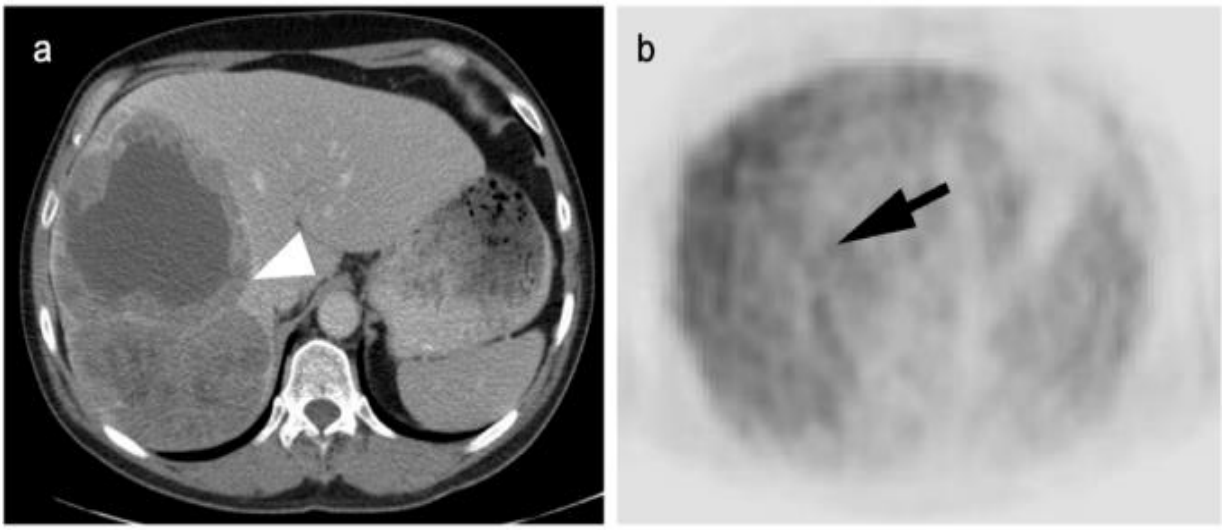

Figure 5. Well-differentiate HCC shown on the contrast enhanced CT (a) and axial FDG PET (b). The large lesion on CT (white arrowhead) is isometabolic to the remainder of the liver on FDG PET-CT (black arrow), which is a typical feature of well-differentiated HCC [9]

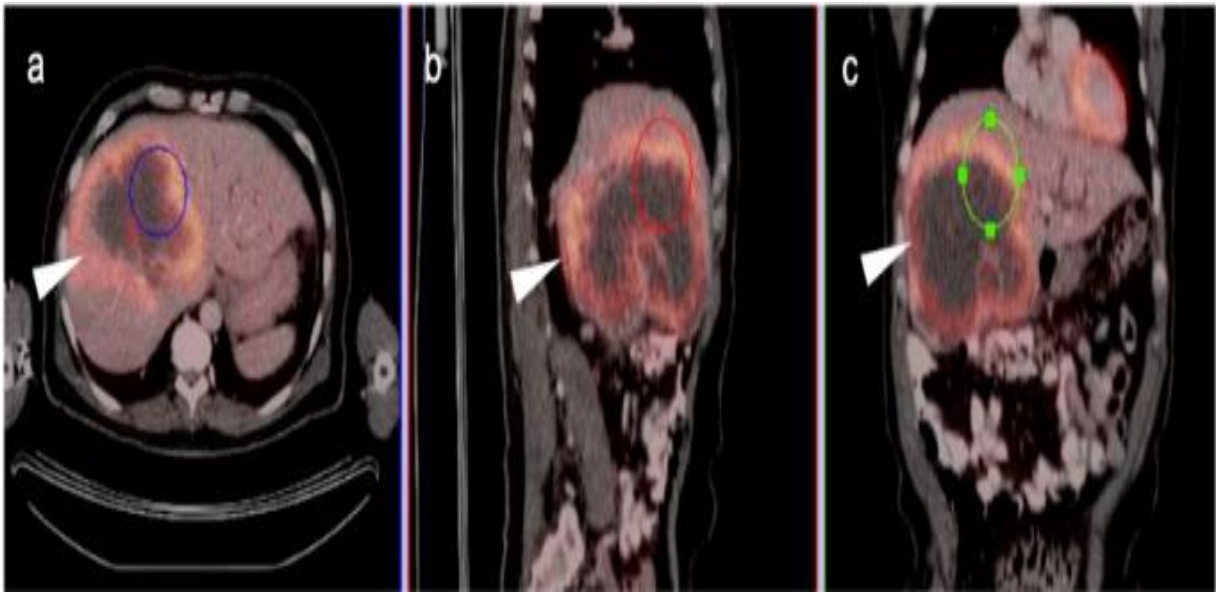

Figure 6. Intrahepatic cholangiocarcinoma. Axial (a), Sagittal (b) and Coronal (c) projections of a fused FDG PET-CT scan show a typical hypermetabolic ring-shaped area of increased metabolic activity with central necrosis (white arrowhead). SUV max in shown region of interest (ROI) is 10.3 [9]

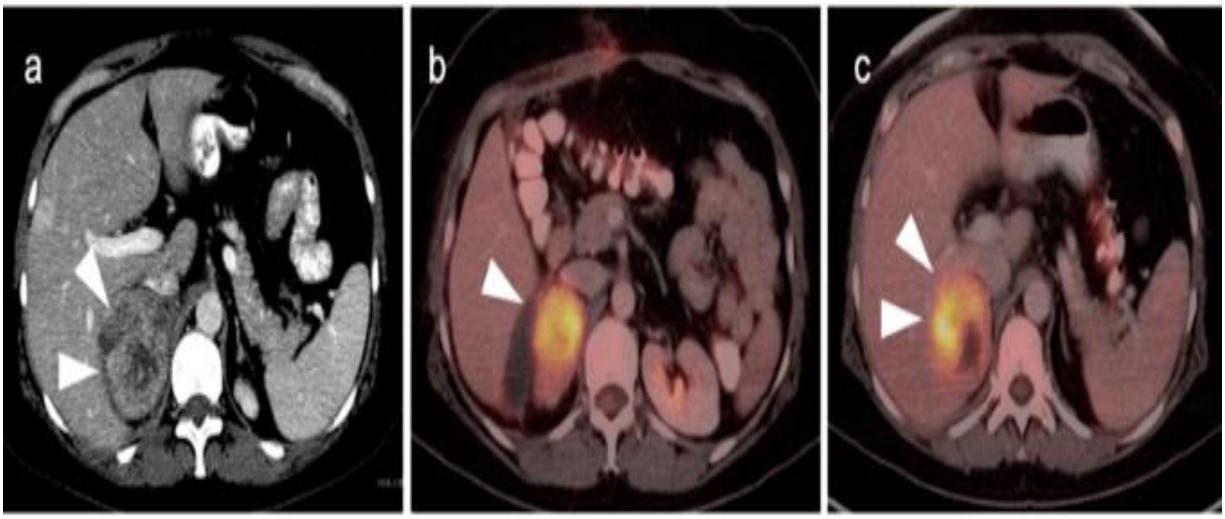

Figure 7. Adrenal cortical carcinoma. (a) a CT scan before surgery revealed a right adrenal mass that had uneven enhancement and areas of necrotic tissue. The mass was confirmed to be an adrenal cortical carcinoma after pathological examination (b, c) axial fused images from an FDG PET-CT scan taken 7 months after the removal of the adrenal cortical carcinoma demonstrate a recurring hypermatabolic mass in the right adrenal fossa ((b, c), white arrowheads). There is a possibility that the mass has invaded the nearby liver, as there is no clear boundary between the mass and the liver (white arrowheads, (c)) [9]

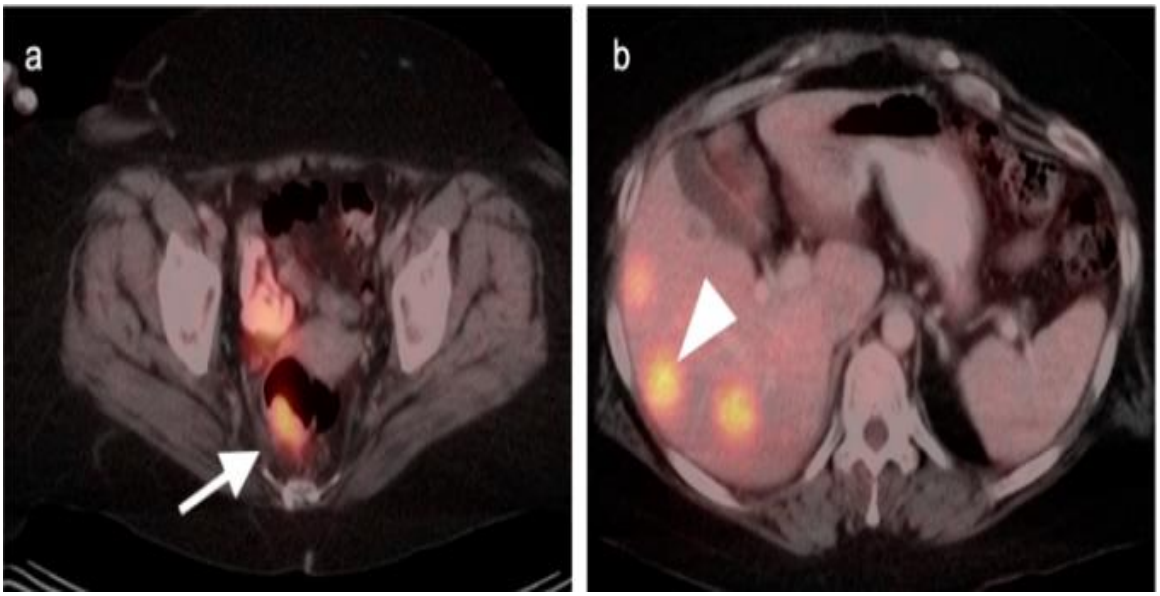

Figure 8. Rectal carcinoma with hepatic metastases, (a) The axial fused PET-CT picture of the pelvis reveal a rectal mass with increased metabolic activity (shown by the white arrow): (b) The axial fused PET-CT scan of the upper abdomen demonstrates many metastatic liver tumors with heightened metabolic activity (indicated by the white arrowhead). Usually, both primary colorectal carcinomas and their metastasis have high metabolic activity, while mucinous tumors may have lower levels pf activity [9]

Individuals who have stents inserted in their common bile duct often have an increase in activity in the gallbladder wall, which is most likely caused by inflammation and partial blockage. However, in cases when anatomic imaging is inconclusive, FDG PET-CT may be beneficial in the treatment of some individuals with gallbladder cancers [23].

3.11. Adrenal Cancer

Adrenocortical carcinomas and their metastases usually have a high affinity for FDG. Nevertheless, oncocytic adrenocortical cancer has been demonstrated to have a modest level of FDG absorption. Hence, the absence of significant metabolic activity on FDG PET-CT does not rule out the occurrence of adrenocortical cancer. Furthermore, there are no established metabolic patterns identified by FDG PET-CT that can accurately differentiate adrenocortical tumours from other potential diagnoses. Adrenocortical carcinomas are uncommon. If an adrenal nodule or mass is seen on FDG PET-CT and there are no signs of aberrant hormone secretion, the chances are much higher that the lesion is either a benign adrenal lesion or metastases from other origin, rather than an adrenocortical cancer. The presence of a significant size and certain imaging features seen by CT and MRI, like heterogeneous enhancement, necrotic tissues, and invasion into nearby organs, strongly indicate that an adrenal mass is most likely a malignant tumor (Figure 7). FDG PET-CT may be useful in determining the presence of a primary tumour when a potential adrenal metastases is detected [24].

3.12. Bowel Adenocarcinoma: Colon, Rectum, Small Bowel

The benefit of FDG PET-CT in detecting adenocarcinoma of the bowel is widely recognized. Generally, both the main tumor and any metastasis to other areas of the body show increased metabolic activity (Figure 8). However, there are certain difficulties and challenges when using PET-CT for colorectal or small-bowel adenocarcinomas. False negative results can occur, so it is crucial to carefully examine the CT scan. Mucinous signet-ring cell variations of adenocarcinoma and their metastasis may have reduced metabolic activity. Similarly, mucinous metastatic tumors in the peritoneum, known as pseudomyxoma peritonei, typically exhibit minimal activity and specific characteristics of attenuation [25].

4. Conclusions

The PET/CT imaging technique proved to be an efficient diagnostic tool to evaluate the progress of patients with managed gastric malignancies by accurately identifying any remaining stomach lesions. PET/CT imaging is a very sensitive modality that allows for targeted imaging of metabolic processes and clubs these with structural changes. In most GI lesions, it demonstrated to enhance identifying of distant metastasis, aid in prognostication, treatment planning, and post treatment surveillance. The function of FDG PET-CT is well recognized in the staging, assessing of therapeutic

effectiveness, and monitoring of various gastrointestinal cancers.

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