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PET Imaging in Gastric Carcinoma

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1. Introduction

Gastric carcinoma is the fourth most common carcinoma in the world, with an estimated one million new cases every year, and it is the second most common cause of death from carcinoma (Ferlay et al., 2010). Surgery is the mainstay of treatment of gastric carcinoma. Despite recent advances in surgical treatment, the overall prognosis of patients with gastric carcinoma has not improved significantly because the neoplasm is often diagnosed at an advanced stage of the disease. Local and systemic recurrences are common, even after complete resection of the primary tumour and regional lymph nodes. Multimodality therapy, consisting of surgery with adjuvant or neoadjuvant radiotherapy, chemotherapy or both, has been used recently as a means to improve the survival rate of patients with gastric carcinoma. Current data suggest that this carcinoma is best managed with a tailored therapeutic regimen based on thorough preoperative staging of the tumour and an understanding of established prognostic factors (Stein et al., 2000).

The International Union Against Cancer (Unio Internationalis Contra Cancrum: UICC) TNM Classification of Malignant Tumours, 7th edition (Sobin et al., 2009), provides the latest, internationally agreed-upon standards to describe and categorise cancer stages and progression. Staging of gastric carcinoma was performed according to the UICC TNM staging for the T stage, N stage and M stage. The T stage refers to the depth of the invasion of the primary tumour, the N stage refers to the number of metastatic lymph nodes and the M stage indicates the presence or absence of systemic metastases (Table 1). For the N stage, the UICC TNM staging detailed in the 7th edition (Sobin et al., 2009) is a classification system based on the number of metastatic lymph nodes, a variable that has proved to be an independent prognostic factor in gastric carcinoma. In contrast, the Japanese Classification of Gastric Carcinoma (JCGC), 13th edition, provides lymph node station numbers for anatomically separate sites of regional lymph nodes (Japanese Gastric Cancer Association [JGCA], 1998). This classification is based on the study of lymphatic flow and surgical results. There was a difference in the two classification systems, particularly regarding lymph node metastasis, but near standardization was reached in 2010. For the year 2011, not enough data have been collected based on the new standards. We describe lymph node metastasis based on the JCGC, 13th edition, which classifies lymph node metastasis according to the anatomic sites of metastatic lymph nodes (Table 2). Current preoperative staging techniques, such as endoscopy, barium studies, computed tomography (CT) and endoscopic ultrasonography (EUS), are of limited accuracy, and invasive procedures often are used for better assessment of the stage of the disease. Positron emission tomography (PET) has been evaluated recently in the staging of gastric carcinoma.
Management of Gastric Cancer

T – Primary tumor
TX: Primary tumour cannot be assessed
T0: No evidence of primary tumour
Tis: Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria, high grade dysplasia
T1: Tumour invades lamina propria, muscularis mucosae, or submucosa
  T1a: Tumour invades lamina propria or muscularis mucosae
  T1b: Tumour invades submucosa
T2: Tumour invades muscularis propria
T3: Tumour invades subserosa
T4: Tumour perforates serosa or invades adjacent structures
  T4a: Tumour perforates serosa
  T4b: Tumour invades adjacent structures

N – Regional Lymph Nodes
NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Metastasis in 1 to 2 regional lymph nodes
N2: Metastasis in 3 to 6 regional lymph nodes
N3: Metastasis in 7 or more regional lymph nodes
  N3a: Metastasis in 7–15 regional lymph nodes
  N3b: Metastasis in 16 or more regional lymph nodes

M – Distant Metastasis
M0: No distant metastasis
M1: Distant metastasis

Stage Grouping
Stage 0: Tis, N0, M0
Stage IA: T1, N0, M0
Stage IB: T2, N0, M0
  T1, N1, M0
Stage IIA: T3, N0, M0
  T2, N1, M0
  T1, N2, M0
Stage IIB: T4a, N0, M0
  T3, N1, M0
  T2, N2, M0
  T1, N3, M0
Stage IIIB: T4b, N0, M0
  T3, N2, M0
  T4b, N3, M0
  T1, N3, M0
Stage IVA: Any T, Any N, M1

Table 1. UICC TNM, 7th edition, staging for gastric carcinoma

Extent of lymph node metastasis (N)
N0: No evidence of lymph node metastasis
N1: Metastasis to Group 1 lymph nodes, but no metastasis to Group 2 or 3 lymph nodes
N2: Metastasis to Group 2 lymph nodes, but no metastasis to Group 3 lymph nodes
N3: Metastasis to Group 3 lymph nodes
NX: Unknown

Table 2. JCGC, 13th edition, N staging for gastric carcinoma
The regional lymph nodes are classified into three groups depending upon the location of the primary tumour. This grouping system is based on the results of studies of lymphatic flow at various tumour sites, together with the observed survival rate associated with metastasis at each nodal station.

2. PET imaging

PET instrumentation has been available for over 35 years. Recently it has become clear that PET, using the glucose metabolism tracer $^{18}$F-fluoro-2-deoxy-D-glucose (FDG), will have a major role in the management of patients, particularly in oncology. Imaging with FDG-PET is based on the altered glucose uptake of neoplastic cells (Fig. 1). FDG is a radiolabelled glucose analogue that accumulates in cells after cellular uptake, mainly by glucose transporters (GLUTs) located on the cell membrane and intracellular phosphorylation by hexokinases. GLUT-1 is the main cell surface protein facilitating the active uptake of FDG. Neoplastic cells overexpress GLUT-1 on their membranes, resulting in higher uptake. The expression of GLUT-1 itself correlates with tumour aggressiveness and carcinoma-related mortality (Kawamura et al., 2001).

Fig. 1. Representative FDG-PET image of a patient with primary gastric carcinoma. (A) Whole-body anterior projection image of FDG-PET examination highlighting tumour FDG uptake in the gastric wall. (B) Transversal slice of whole-body FDG-PET examination with tumour FDG uptake in the gastric wall.
Apart from visual analysis, an often-used semi-quantitative method to assess the uptake of FDG in a tumour is the standardised uptake value (SUV):

$$\text{SUV} = \frac{\text{Regional radioactivity concentration}}{\text{Total injected dose / body weight}} \quad \text{(Lindholmet al., 1993).}$$

This value is the measurement of FDG uptake in a tumour volume normalised on the basis of the distribution volume. SUVs are dependent on several parameters, such as time after FDG injection, tumour size, blood glucose level and spatial resolution of the reconstructed image (Boellaard et al., 2004; Thie, 2004). Relative values, such as SUV changes, measured with accorded and comparable protocols are reliable. Moreover, inter-observer correlations are consistently high (Ott et al., 2003).

2.1 Patient preparation

Patient preparation for a whole-body FDG-PET examination is essential, both to optimise image quality and to minimise physiologic variants and artifacts (Shreve et al., 1999). Patients should fast for a minimum of four hours to ensure that serum glucose and endogenous serum insulin levels are low at the time of FDG administration. Glucose competes with FDG for cellular uptake, and there is some evidence that elevated serum glucose levels will lower the observed FDG uptake in malignant neoplasms (Lindholm et al., 1993). Equally significantly, elevated serum insulin promotes FDG uptake in muscle (Fig. 2. A), so a recent carbohydrate meal or even a snack or the administration of exogenous insulin to lower blood glucose levels can yield extensive muscle uptake. Such muscle uptake will not interfere with the evaluation of centrally located abnormalities such as lung nodules or mediastinal lymph nodes. In general, a serum glucose level of less than 150 mg/dL at the time of FDG accumulation is preferred; a level lower than 200 mg/dL is acceptable. With serum glucose levels above 200 mg/dL, noticeable degradation in image quality due to reduced tissue uptake of FDG and sustained blood pool tracer activity can occur. It is relatively easy to measure serum glucose prior to FDG administration, and this measurement is routine at many centres. Use of exogenous insulin to reduce serum glucose immediately prior to FDG administration is not generally recommended since it will result in accelerated FDG uptake in muscle (Fig. 2. B).

2.2 Image acquisition

2.2.1 Attenuation correction

Whole-body FDG-PET imaging is performed with attenuation correction. As patient movement between the transmission and emission image acquisitions may result in registration artifacts in the attenuation-corrected images, the emission and transmission image acquisitions should be temporally as close as possible when sealed-source transmission scans are used.

2.2.2 Image acquisition time

Image acquisition time and FDG dose are related, but not in the entirely inverse fashion of single-photon radiotracer imaging. Regarding sealed-source transmission scans with image segmentation, acquisition time per bed position is two minutes or less. CT-based attenuation
Fig. 2. A and B. Effect of endogenous and exogenous insulin. (A) Whole-body anterior projection image of a patient who ate candies prior to FDG administration and had a serum glucose level of 220 mg/dL, and (B) a patient given 6 units of regular insulin intravenously prior to FDG administration to reach a normalised serum glucose level of 95 mg/dL. In both cases, there is extensive skeletal muscle uptake, uniform and symmetrical, due to the action of insulin.

Correction allows a whole-body transmission scan without noise or segmentation errors to be performed in less than 30 seconds with multi-detector helical CT. Shallow relaxed breathing is essential to minimise image registration errors when X-ray CT is used for the transmission image sonogram because when CT acquisition is performed during free breathing, the temporal relation (seconds) is quite different from the PET emission acquisition (a few to several minutes).

2.2.3 Radiopharmaceutical dose
Due to the nature of contaminating scatter and random coincidence events, the relationship between the FDG dose and usable image counting statistics is neither direct nor linear. This relationship depends on the geometry of the tomograph, the type of detector crystal, the size of the patient and the reconstruction algorithm used. In general, ring tomographs in 2D mode with thick axial septa will increase usable true coincidences with increasing administered dose to the upper range of the dosimetry-limited FDG dose (about 700 MBq) (Jones et al., 1982). Increasing the administered dose can reduce the emission image acquisition time, for example, from eight minutes to four minutes per bed position.
Tomographs with greater axial cross-plane acceptance and finer septa, and especially tomographs operating in full 3D mode, will reach limiting random coincidence count rate contributions with administered doses as low as 200 MBq or less.

2.2.4 Time of imaging after tracer injection
Imaging acquisition following FDG administration for body imaging is commenced 40 to 60 minutes following FDG administration. This delay is based in part on the time required for a majority of the activity to clear from the blood pool and for most of the tumour accumulation of the tracer to occur. In fact, there is continued accumulation of FDG in malignant neoplasms and other FDG-avid tissues such as bone marrow beyond one hour, with continued clearance of blood pool activity (Hamberg et al., 1994). Hence, a longer delay in the commencement of image acquisition has been advocated to enhance the tumour-to-background ratio and to allow more complete clearance of upper urinary tract activity. For tomographs that are count-rate limited, a longer delay of 90 to 120 minutes, with a correspondingly higher FDG dose, may provide optimal whole-body imaging.

2.2.5 Imaging display and interpretation
Whole-body FDG-PET images are routinely displayed as a series of orthogonal tomographic images in the transversal, coronal and sagittal planes, together with a whole-body rotating projection image. The rotating projection image provides an invaluable rapid assessment of the overall status of FDG-avid malignancy in the body and can be very helpful in discerning the 3D relationships of abnormalities to normal structures. Interpretation of whole-body images is thus best accomplished using both the rotating whole-body projection image and the serial tomographic images.

Some disagreement remains over the use of semi-quantitative measures of FDG uptake for routine application in oncology, with some centres using SUV routinely and others relying entirely on visual interpretation. SUV cannot be relied upon as an absolute criterion of malignancy because the degree of FGD uptake implies a probability of malignancy rather than an established diagnosis. Even more importantly, the SUVs reported in publications have been obtained using varying methods and do not represent a standardised parameter (Keyes et al., 1995). On the other hand, when a patient undergoes serial PET imaging using the same tomograph in order to assess a change in FDG uptake for therapy monitoring, SUV or a similar semi-quantitative measurement may well be a necessary adjunct to visual interpretation.

2.3 Clinical utility of FDG-PET in gastric carcinoma
2.3.1 Primary tumour staging (T stage)
Most studies included in this review examined the feasibility of primary tumour detection by FDG-PET in gastric carcinoma. The studies show that FDG-PET is not an accurate imaging technique for the primary diagnosis of a gastric primary tumour as it combines high specificity with low sensitivity. About 20% of patients with gastric carcinoma are non-assessable by FDG-PET. The sensitivity rate for detecting the primary tumour varies between 58 and 94% amongst studies (median 81.5%), and the specificity ranges from 78 to 100% (median 98%) (Chen et al., 2005; Mochiki et al., 2004; Mukai et al., 2006; Stahl et al., 2003; Yeung et al., 1998; Yoshioka et al., 2003; Yun et al., 2005). The detection of gastric carcinoma by FDG-PET is complicated by background signalling, partly due to the high
physiological uptake of FDG in the normal gastric wall. Moreover, variable and sometimes intense, highly located uptake background activity is observed in the normal gastric wall, resembling false-positive pathological uptake (Mochiki et al., 2004; Stahl et al., 2003). Actively creating gastric distension by water ingestion could augment FDG-PET specificity (Kamimura et al., 2007, 2009; Ott et al., 2003; Yun et al., 2005). After water ingestion, the physiological FDG uptake in the gastric wall became a cystic structure with a mild and even distribution of FDG along the thin wall, and the focal tumour uptake was more clearly visualised under gastric distension by water ingestion (Fig. 3) (Kamimura et al., 2009).

Fig. 3. FDG-PET images of a patient before and after water ingestion. A 63-year-old male with gastric carcinoma of the lower part of the stomach (moderately differentiated tubular adenocarcinoma). Transversal (left), coronal (middle) and sagittal (right) FDG-PET images of the patient. (A) Before ingestion of water, diffuse physiological FDG uptake in the stomach is higher than that in the liver, and it is difficult to distinguish the tumour uptake from physiological FDG uptake in the stomach. (B) After ingestion of water, diffuse physiological FDG uptake in the gastric wall is reduced, and the focal tumour uptake is more clearly visualised (arrows).
Sensitivity of primary tumour identification by FDG-PET is influenced by several other determinants. The location of the tumour (i.e. upper/middle/lower one-third) has been shown to influence the sensitivity of FDG-PET (Mochiki et al., 2004; Mukai et al., 2006; Ott et al., 2003; Stahl et al., 2003). Even in the normal gastric wall, different SUV uptakes have been found between the upper and lower parts of the stomach. Two studies found a higher detection rate by FDG-PET of a gastric carcinoma located in the proximal part of the stomach compared to a distal carcinoma (Koga et al., 2003; Mukai et al., 2006). A second determinant is tumour size or T stage. The sensitivity of FDG-PET ranges from 26 to 63% in early gastric carcinoma (median 43.5%; SUV range 2.1–2.8) to 93–98% in locally advanced gastric carcinoma (median 94%; SUV range 4.3–7.9) (Chen et al., 2005; Mochiki et al., 2004; Mukai et al., 2006; Stahl et al., 2003; Yeung et al., 1998; Yoshioka et al., 2003; Yun et al., 2005). FDG-PET as part of screening programs for the detection of gastric carcinoma in asymptomatic patients yields even worse results (Shoda et al., 2007). A sensitivity of 10% was found, with primarily false-positive findings (Shoda et al., 2007). There are various explanations for this difference. Several studies report a correlation between tumour invasion as an independent factor and overexpression of GLUT-1 receptors. Possibly, the increased need for glucose due to augmented cell metabolism and cell division in advanced carcinoma is the cause of GLUT-1 overexpression and higher FDG uptake (Yamada et al., 2006). The relative volume effect may be a reason for the higher detection rate of advanced gastric carcinoma as the discrimination between physiological and pathological gastric wall uptake increases. This effect makes FDG-PET an inaccurate method for screening and primary tumour detection (Shoda et al., 2007). Furthermore, a clear difference in the sensitivity of FDG-PET is found between different histological carcinoma subtypes. According to the Japanese Classification (JGCA, 1998), gastric carcinoma can be divided into papillary, tubular (well-differentiated type, moderately differentiated type), poorly differentiated (solid type, non-solid type), mucinous adenocarcinoma and signet ring cell carcinoma. The non-intestinal (i.e. diffuse) subtype and carcinomas containing signet ring cells display a consistently low detectability by FDG-PET (Mukai et al., 2006; Ott et al., 2003; Stahl et al., 2003). For tubular adenocarcinoma and moderately differentiated adenocarcinoma, SUV counts of 7.7 to 13.2 were found, which were significantly higher compared to those for mucinous adenocarcinoma and signet ring cell carcinoma (4.1 to 7.7) (Chen et al., 2005; Mochiki et al., 2004; S. K. Kim et al., 2006; Yoshioka et al., 2003; Yun et al., 2005). This result is due to a higher expression of GLUT-1 on the cell membrane of the neoplastic cells, as proven for cohesive gastric carcinoma (i.e. tubular adenocarcinoma, poorly differentiated adenocarcinoma) (Kawamura et al., 2001; W. S. Kim et al., 2000). Other factors influencing the low FDG uptake in mucinous adenocarcinoma and signet ring cell carcinoma are the diffuse growth pattern of non-intestinal gastric carcinoma, the high content of metabolically inert mucus and the low tumour cell density (Kawamura et al., 2001; Ott et al., 2003; Stahl et al., 2003). For these entities, FDG-PET seems to have little value in the primary detection of gastric carcinoma.

2.3.2 Regional lymph node metastases (N stage)
In the N stage, the UICC TNM staging uses a classification system based on the number of metastatic lymph nodes only (Sobin et al., 2009). We describe lymph node metastasis based on the JCGC, 13th edition, which classifies lymph node metastasis according to the anatomic sites of metastatic lymph nodes (JGCA, 1998).
Five studies investigated the value of FDG-PET in detecting lymph node metastasis (Fig. 4) (Chen et al., 2005; S. K. Kim et al., 2006; Mochiki et al., 2004; Mukai et al., 2006; Yun et al., 2005). Sensitivity for metastasis to N1 lymph nodes was very low, ranging from 18 to 46% (median 27.5%) compared to CT (sensitivity of 58–89%; median 68%). This lack of sensitivity could be explained by the relatively low spatial resolution of FDG-PET (5 to 7 mm). The perigastric lymph nodes, therefore, cannot be distinguished from the primary tumour or the normal stomach wall. FDG-PET and CT have low sensitivities of 33–46% and 44–63% in detecting metastases at the N2 and N3 lymph node stations, respectively. Specificity, in contrast, was higher in N1 and N2 lymph node stations with FDG-PET, ranging between 91 and 100% (median 96%), compared to CT (Chen et al., 2005; Mochiki et al., 2004; Mukai et al., 2006; Yun et al., 2005). FDG-PET has a better positive predictive value for lymph node metastasis in comparison to CT, which may alter the planning of therapy, as treatment strategies, especially for N3 lymph node metastasis, change from curative surgery to palliative measures (Chen et al., 2005; Mochiki et al., 2004). A combination of anatomy-based imaging by CT and metabolically based imaging by FDG-PET using PET/CT might, therefore, augment the detection or denial of lymph node involvement.

Fig. 4. Representative FDG-PET images of a patient with primary gastric carcinoma with regional lymph node involvement. A 79-year-old male with gastric carcinoma of the upper part of the stomach (moderately differentiated tubular adenocarcinoma). Anterior whole-body projection (A), transversal (B) and coronal (C) FDG-PET images of the patient show intense tumour FDG uptake (T arrows) in the gastric wall and regional lymph node metastasis (LN arrows).
2.3.3 Distant metastatic disease (M stage)

Not much is known about the role of FDG-PET in detecting distant metastasis. However, whole-body FDG-PET can point out distant metastases in some cases (Fig. 5).

Fig. 5. Representative FDG-PET images of a patient with primary gastric carcinoma with liver metastases. A 75-year-old male with gastric carcinoma of the middle part of the stomach (moderately differentiated tubular adenocarcinoma). Anterior whole-body projection (A), transversal (B) and coronal (C) FDG-PET images of the patient show avid tumour FDG uptake (T arrow) in the gastric wall and multiple liver metastases (M arrows).

One series found respective sensitivities and specificities of 85% and 74% for the detection of liver metastasis, 67% and 88% for lung metastasis, 50% and 63% for peritonitis carcinomatosis, 24% and 76% for ascites, 4% and 100% for pleuritis carcinomatosis and 30% and 82% for bone metastasis (Yoshioka et al., 2003). As is the case for peritoneal carcinomatosis, the low number of metastatic tumour cells in ascites, pleura and bone may explain the low FDG-PET sensitivity. Two patterns of FDG uptake are known to be indicators of peritoneal metastasis: diffuse uptake spreading uniformly throughout the abdomen and pelvis, thus obscuring visceral outlines, and discrete foci of uptake located randomly and anteriorly within the abdomen or independently within the pelvis and unrelated to solid viscera or nodal stations (Lim et al., 2006; Turlakow et al., 2003). Lim et al. demonstrated that although the sensitivity of PET to detect peritoneal metastasis was significantly lower than that of CT (35 vs. 77%), the specificity of PET was significantly
higher than that of CT (99 vs. 92%) (Lim et al., 2006). Current CT scanning has poor sensitivity as well, showing specificity even worse than that of FDG-PET. Diagnostic laparoscopy still plays an undefined role in staging gastric carcinoma. It is highly sensitive for peritoneal metastasis detection; however, it has little value in predicting regional lymph node metastasis (Burke et al., 1997; Lowy et al., 1996). The risks and morbidity of a staging laparoscopy outweigh the benefits, as eventually only a small number of patients will benefit from it (Lehnert et al., 2002). With the higher sensitivity of CT and the higher specificity of PET, fusion of these imaging modalities may be more useful than either one alone. In case of suspicion of peritoneal carcinomatosis based on PET and/or CT, diagnostic laparoscopy could be performed to prevent unnecessary laparotomies.

2.3.4 Assessment of response to therapy
The use of neoadjuvant chemotherapy in the treatment of gastric carcinoma has evolved greatly in recent years (Cunningham et al., 2006; Hartgrink et al., 2004; Schuhmacher et al., 2001). Better surgicopathological results could be obtained with this treatment modality, especially by reducing microscopically irradical resections, residual tumour positive lymph nodes and tumour invasion in adjacent organs upon surgery. It is vital to discriminate between responders and non-responders to chemotherapy, as chemotherapy in the latter group could result in unnecessary risk for therapy-related morbidity with co-existing tumour growth. In 80% of all patients, gastric tumours are assessable by FDG-PET, and around 30–40% of gastric carcinoma patients are responders with current chemotherapy regimens as defined by tumour regression (Di Fabio et al., 2007; Ott et al., 2003). Histopathological complete tumour regression is infrequently found (Cunningham et al., 2006; Hartgrink et al., 2004; Ott et al., 2003; Schuhmacher et al., 2001). Thoracoabdominal CT scanning is commonly used to monitor tumour response. CT-observed tumour response depends on tumour size reduction, which is a relative late sign of response (RECIST criteria) (Therasse et al., 2000). An earlier sign of response is chemotherapy-induced reduction in tumour metabolic rate, which can be detected by FDG-PET. Two relatively small studies (44 and 22 patients) showed that the fractional change in glucose consumption could be assessed by FDG-PET immediately following the first cycle of chemotherapy (Di Fabio et al., 2007; Ott et al., 2003). Moreover, FDG-PET has been shown to be a predictor of not only neoadjuvant chemotherapy-induced clinical and histopathological response but also overall survival (Di Fabio et al., 2007; Ott et al., 2003). Patients with a metabolic response had a two-year survival rate of 90%, in contrast to 40% in non-responders (Ott et al., 2003). In addition, 100% of the non-responders were detected by FDG-PET and were subsequently withdrawn from neoadjuvant therapy in order to proceed to immediate surgery. FDG-PET evaluated treatment correctly in ~80% of responders and non-responders combined (Di Fabio et al., 2007; Ott et al., 2003). Future goals are the delineation and validation of SUV-decrement thresholds with adequate sensitivity and specificity to discriminate between beneficiaries and non-beneficiaries of neoadjuvant chemotherapy. Currently, a 35% decrease in SUV as the cut-off level shows 75% sensitivity (Di Fabio et al., 2007; Ott et al., 2003). The role of FDG-PET in monitoring tumour response in gastric carcinoma must be examined further, with the potential for clinically interesting results.

2.3.5 Detection of recurrent disease
Tumour recurrence is directly associated with gastric carcinoma-related mortality, particularly early recurrence (< 1 year disease-free survival) (Shiraishi et al., 2000).
Peritoneal recurrence is especially common (Shiraishi et al., 2000). No curative treatment modalities are left for these patients, and the aim of care is palliation. An exception to this rule is late recurrence (> 5 years disease-free survival), which coincides with sporadic carcinoma mortality (Shiraishi et al., 2000). The extent of lymph node metastasis at primary diagnosis is the most important independent factor determining the timing of tumour recurrence (Shiraishi et al., 2000). Clinical surveillance is the most frequently used follow-up modality, as current endoscopic and radiologic (ultrasonography, barium study and CT) techniques are not sensitive enough for early recurrence detection and no reliable biochemical markers are known to correlate with recurrence (Jadvar et al., 2003; De Potter et al., 2002). Radiological examination, based on anatomical findings, is limited by postoperative non-cancerous changes. The detection of active neoplastic metabolism theoretically increases the advantage of FDG-PET over CT. However, FDG-PET lacks diagnostic accuracy in the early detection of recurrence, with sensitivity and negative predictive values of 70 and 60%, respectively (Jadvar et al., 2003). The high physiological remnant gastric uptake and the low spatial resolution of current hardware prevent the detection of early recurrence by FDG-PET (Jadvar et al., 2003; Yun et al., 2005). Creating gastric distension by water ingestion increases the ability of FDG-PET to discriminate between physiological and pathological gastric uptake and could reduce false-positivity (Kamimura et al., 2009; Yun et al., 2005). On the other hand, the use of PET/CT fusion images could decrease the number of false-positive FDG-PET scans by locating FDG-avid foci on anatomical landmarks.

2.4 Tumour imaging with other tracers

Other potentially useful PET tracers for the evaluation of gastric carcinoma are 3-deoxy-3-¹⁸F-fluorothymidine (FLT) and ¹¹C-choline (choline). FLT is a pyrimidine analogue that has proven to be a stable PET tracer that accumulates in proliferating tissue and malignant tumours (Shields et al., 1998). FLT is a substrate for thymidine kinase 1, which is an enzyme involved in the production of thymidine monophosphate. Hermann et al. performed a pilot study assessing the feasibility of FLT-PET compared to FDG-PET in gastric carcinoma (Herrmann et al., 2007). They found a sensitivity of 100% of FLT-PET for primary tumour detection (60% of tumours were signet ring cell carcinoma), compared to a sensitivity of FDG-PET of 69%. Background activity was low. These findings suggest that FLT-PET is a potentially useful imaging modality for the detection and staging of gastric carcinoma, especially for histologic subtypes with low FDG uptake. Kameyama et al. also reported that the sensitivity of FLT-PET was as high as that of FDG-PET for the detection of gastric carcinoma (Kameyama et al., 2009). The cellular uptake of choline presumably reflects its incorporation into phosphatidylcholine, a cell membrane constituent (Hara et al., 1998). The increased uptake of choline in tumour cells is thought to be related to the high rate of tumour cell duplication and cell membrane biosynthesis. In patients with oesophageal carcinoma, Kobori et al. reported that choline-PET was more sensitive than FDG-PET for detecting very small mediastinal lymph node metastases (Kobori et al., 1999). However, FDG-PET was more sensitive than choline-PET in detecting metastases in the upper abdomen due to intense normal uptake of choline in the liver. On the other hand, Pieterman et al. reported that both FDG and choline-PET visualised primary tumours of thoracic carcinoma but that the detection of lymph node metastases was inferior and the detection of brain metastases was superior to those of FDG-PET (Pieterman et al., 2002). Choline-PET does not appear to have been applied to the evaluation of gastric carcinoma.
Further investigations are needed to determine the value of FLT and choline-PET in gastric carcinoma.

3. Conclusion

FDG-PET has a limited role in primary tumour detection due to its low sensitivity, especially in early and non-intestinal gastric carcinoma. However, gastric distention by oral water may decrease physiological gastric uptake of FDG to result in better diagnostic accuracy for advanced gastric carcinoma. FDG-PET has a slightly better positive predictive value for the detection of lymph node metastasis in comparison to CT; furthermore, it has reasonable sensitivity for liver and lung metastases. FDG-PET, therefore, improves preoperative staging in advanced gastric carcinoma. FDG-PET could have a significant role in monitoring tumour response during neoadjuvant chemotherapy because it adequately detects therapy responders at an early stage. Furthermore, FDG-PET is accurate in predicting histopathological response and even long-term prognosis, making it a valuable adjunct to neoadjuvant gastric carcinoma treatment. The results of positron emission tomography in the evaluation and monitoring of gastric carcinoma may improve in the near future. The use of PET/CT fusion imaging has improved diagnostic performance in several carcinoma types (Czernin et al., 2007), and its use in gastric carcinoma is currently under investigation (Hur et al., 2010). The use of other PET tracers, such as FLT and choline, holds promise for the future. Therefore, continued research into PET imaging in gastric carcinoma should be advocated.

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5. References


PET Imaging in Gastric Carcinoma


Gastric cancer is the fifth most common cancer and the second most common cause of cancer death worldwide. More than 50% of the patients have advanced disease at diagnosis and in this case the disease has a poor outcome. The staging of gastric cancers is based on endoscopic ultrasound, computed tomography, magnetic resonance imaging, positron emission tomography, in addition to the laparoscopic staging. Many improvements in the surgical techniques have been seen in the last decade. Laparoscopic surgery is an emerging approach which offers important advantages: less blood loss, reduced postoperative pain, accelerated recovery, early return to normal bowel function and reduced hospital stay. D1 lymphadenectomy, with a goal of examining 15 or greater lymph nodes is a standard. D2 dissection is considered as a standard in several institutions especially in eastern Asia. Perioperative chemotherapy and adjuvant concurrent radiochemotherapy are recognized as standards treatments. Palliative chemotherapy is the mainstay treatment of advanced stages of the disease (metastatic and non-operable tumors). Despite these treatment advances, the prognosis of gastric cancer remains poor with a 5-year survival ranging from 10 to 15% in all stages combined.

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