Perspective

The role of ^{18}FDG-PET in gastric cancer

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Imaging with ^{18}F-fluoro-2-deoxyglucose PET (^{18}FDG-PET) is based on the increased glucose uptake of neoplastic cells, which over-express the main cell-membrane glucose transporter GLUT-1 resulting in higher uptake of ^{18}FDG as well. More than visual analysis an often-used semi-quantitative method to assess tumor ^{18}FDG uptake is the standard value (SUV), which is the measurement of ^{18}FDG up-take in a tumor volume normalized on the basis of a distribution volume.

^{18}FDG-PET has been widely used to evaluate various types of malignant tumors, including lung, oesophageal, and colorectal cancer and lymphomas (1). However, the role of ^{18}FDG PET in gastric cancer is debatable. Although ^{18}FDG-PET is clinically useful in detecting recurrent gastric cancer after surgical resection (2,3), the role of ^{18}F-FDG PET in preoperative workup is limited due to its low sensitivity for primary tumour and lymph node (LN) metastasis (4,5). Furthermore, because only a few studies with a small number of patients have been performed, the role of ^{18}F-FDG PET in predicting prognosis of patients with gastric cancer is still contentious.

The primary site detection rate of ^{18}FDG-PET is about 50% in early gastric cancer and 92% in advanced gastric cancer. Sensitivity for detecting the primary tumour varies between 47 and 96% due to the different characteristics of enrolled patients (5-12) of the studies considered. The variable and sometimes intense physiological ^{18}FDG uptake in the normal gastric wall and differences of ^{18}FDG uptake in cancer lesions according to hystopathological subtypes of gastric cancer are the most significant contributing factors for the low detection rate of gastric primary tumours.

Normal gastric wall devoid of malignant lesions can displays an SUV exceeding 2.5 and benign gastric mucosal inflammation can show focal intense ^{18}FDG accumulation, which restricts detection of gastric cancer lesions (13-15). ^{18}FDG uptake in mucinous carcinoma can be positively correlated with tumour cellularity, but negatively correlated with the amount of mucin within the tumor mass, which accounts for low detectability of ^{18}FDG-PET for undifferentiated and mucinous tumors (16). Furthermore, an infiltrative growth pattern, high content of mucus and low concentration of cancer cells lead to low ^{18}FDG uptake in poorly differentiated cancer and signet-ring cell cancer, in spite of their aggressiveness. Detection rate is higher when tumors are larger than 3.5 cm and have deeper depth of invasion, and at a later stage. In many multivariate analyses, tumor size, spread of tumor cells beyond the muscle layer (≥ T2), and lymph node metastasis were statistically significant factors in primary site detection rate.

The sensitivity, specificity, and positive predictive value of ^{18}FDG-PET to lymph node metastasis are 60%, 85%, and 80%, respectively; sensitivity being lower compared to CT while specificity and positive predictive value are higher. PET is less sensitive than CT in the detection of lymph node metastasis located near to gastric wall in the regional stations, mainly due to its poor spatial resolution, which makes it unhelpful in discriminatine between lymph nodes and the primary tumor (17). Detection of lymph node metastases in the 12, 13, 14, 15, 16 stations can change the extent of lymph node dissection or may preclude unnecessary surgery. Metastases at these anatomical sites would theoretically be easier to identify at PET because they are located away from the primary lesions. In other words, the relatively low spatial resolution of PET does not adversely affect the detection of these metastases because they are remote from the primary tumor or from areas of intense FDG uptake. Sensitivity, specificity, and positive predictive value to distant metastasis are, respectively,

65%, 99%, and 88%, similar to CT. The major advantage of ^{18}FDG-PET over anatomic imaging modalities is its capacity to detect distant solid organ metastases. Metastases to the liver, lungs, adrenal glands, and ovaries can be readily identified at FDG PET (18). ^{18}FDG PET has a little value in diagnosing peritoneal carcinomatosis, again hampered by its low sensitivity (mean 32%) but relatively high specificity (mean 88.5%). Some authors have reported that peritoneal lesions show an extensive fibrosis around relatively few malignant cells, wich could explain the low sensitivity of this imaging modalità, the small size of peritoneal nodules (<5 mm) could represent another reason for the low detection rate (19). The study of Lee *et al.* (20) demonstrated that ^{18}FDG uptake in gastric cancer is an independent and significant prognostic factor for predicting cancer recurrence after curative surgical resection. Patients with negative ^{18}FDG uptake in gastric cancer showed a significantly recurrences rate after surgical resection than patients with positive 18FFDG uptake. Furthermor, recurrence-free survival was significantly different between patients with positive and negative 18F-FDG uptake. Therefore, although the detectability of ^{18}FDG-PET/CT for gastric cancer is low, preoperative 18F-FDG-PET/CT could provide effective information on the prognosis after surgical resection in patients with gastric cancer expecially in tubular and undifferenziated types. In addition, ^{18}FDG-PET has actually a significant role in monitorino the response to neoadjuvant chemotherapy, showing chemo-responders at early stage. It is anticipated that the use of new metabolic tracers, such as coline or methionine will improve the sensitivity of PET-CT in staging gastric cancer.

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