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COMMENT

^{18}F-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography in the Management of Metastatic Colorectal Cancer

Are we there yet?

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التصوير المقطعي باستخدام ^{18}فلوروديوكسي جلوكوز البوزيترون الانبعاثي/التصوير المقطعي في تشخيص وعلاج سرطان القولون والمستقيم المنتشر

هل وصلنا؟

خالد النعمانى و سهام السنانية

Colorectal cancer (CRC) is the second most commonly diagnosed cancer in females and the third in males. More than 1.2 million cases around the globe are diagnosed every year and it is the estimated cause of death for more than half a million people each year. Metastatic CRC is the first presentation in approximately one-fourth of patients.[1] Another 30% of patients initially diagnosed with localised bowel cancer will subsequently develop liver metastases.[1] The five-year survival rate for patients with stage IV CRC with liver metastases is approximately 6%.[2] However, if the liver is the only site involved and the metastases are amenable to surgical resection, then the five-year survival rate increases to 25–40%.[2]

The clinical evaluation of patients with CRC requires multiple imaging modalities such as computed tomography (CT), contrast-enhanced CT, magnetic resonance imaging (MRI), ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) and PET/CT. All of these imaging modalities play a major role in the diagnosis and staging of CRC. In the February 2015 issue of SQUMJ, Jafferbhoy *et al.* retrospectively evaluated the value of ^{18}F-FDG-PET/CT imaging in the management of patients with metastatic CRC.[3]

^{18}F-FDG-PET imaging has an important role in the diagnostic and staging algorithm. Current evidence-based indications for ^{18}F-FDG-PET in the UK recommend the use of this imaging modality in the staging of patients with synchronous CRC and metastases at presentation, before considering surgical resection.[4] This recommendation is similar to the North American National Comprehensive Cancer Network guidelines for the initial staging of CRC, which suggests the use of CT or MRI of the chest, abdomen and pelvis;^{18}F-FDG-PET/CT imaging should be reserved for situations in which curative resection is being considered.[5] The incorporation of ^{18}F-FDG-PET scanning can facilitate the detection of extrahepatic disease and, therefore, can reduce the need for non-therapeutic laparotomies; however, we have to keep in mind that PET can be unreliable in certain settings where there is increased metabolic activity due to inflammation. In addition, mucinous adenocarcinomas may show a false-negative PET result.[6,7]

Wiering *et al.* performed a systematic review of data looking at the superiority of PET imaging over CT alone in the detection of extrahepatic disease.[6] For hepatic disease or metastases, pooled sensitivity and specificity for PET was 80% and 92%, respectively, in comparison to 91% and 98% for extrahepatic disease or metastases.[6] Corresponding values for CT imaging were 83% and 84% for hepatic metastases and 61% and 91% for extrahepatic metastatic disease. The use of PET imaging led to a 25% change in clinical management.[6]

A randomised trial demonstrated that combining PET with triphasic CT imaging reduced the number of unnecessary laparotomies from 34 (45%) in the control group to 21 (28%) in the experimental group. This combination of PET and triphasic CT imaging

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prevented unnecessary surgery in one of six patients, with a relative risk reduction of 38%.[7]

Similar findings were reported by Jafferbhoy *et al*.[3] ^{18}F-FDG-PET/CT imaging had a major impact on 72.7% of patients in the preoperative group; the intent of treatment was changed from curative to palliative due to the presence of inoperable disease in 36.3%, resectable metastases were identified after indeterminate CT scanning in 27.3% and 9.1% avoided unnecessary surgery after negative ^{18}F-FDG-PET/CT results.[3]

The previously reported benefit of PET in reducing unnecessary laparotomies was disputed by Moulton *et al*. in a recently published randomised trial in which 404 patients with potentially resectable isolated colorectal liver metastases (CRLM) were randomly assigned to either undergo preoperative integrated PET/CT or forego PET/CT entirely.[8] Only 8% of those who had undergone preoperative PET/CT had a change in surgical management. The frequency of liver resections were similar in both groups (91% versus 92% in the experimental and control groups, respectively). Additionally, there was no change in survival, with both groups demonstrating a two-year survival rate of 80%.[8] Due to the differences in outcomes of these studies, more data are required to evaluate the impact of ^{18}F-FDG- PET and PET/CT imaging on the clinical management of patients with CRLM.

Several studies have investigated the role of ^{18}F-FDG-PET and PET/CT in patients with CRLM undergoing selective internal radiation therapy (SIRT) with yttrium-90 (^{90}Y) microspheres.[9–12] Radio-embolisation using ^{90}Y resin or glass microspheres, also known as a palliative treatment, reduces the mass of a liver tumour, eventually permitting surgical resection.[13] A recently published evidence-based review of the literature by Annunziata *et al*. included 19 studies looking at the role of ^{18}F-FDG-PET and PET/CT in patients with CRLM undergoing SIRT with ^{90}Y microspheres in 833 patients. The role of ^{18}F-FDG-PET or PET/CT was evaluated in planning and assessing the response to treatment and evaluating PET as a prognostic tool.[14]

At present, the role of ^{18}F-FDG-PET or PET/CT in planning SIRT for CRLM is still questionable. Different studies have revealed different outcomes and therefore no strong conclusion can yet be drawn.[11,15,16] Further studies are needed to assess the role of ^{18}F-FDG-PET or PET/CT in planning treatment before advising SIRT for patients with CRLM. A few recently published studies have investigated the role of ^{18}F-FDG-PET or PET/CT imaging in the evaluation of patient response to SIRT.[9,17,18] All these studies confirmed the usefulness of ^{18}F-FDG-PET and PET/CT imaging.

Furthermore, the role of ^{18}F-FDG-PET or PET/CT as a prognostic tool has been evaluated by a few recently published studies.[10,18–20] Gulec *et al*. looked at the relationship between functional tumour volume (FTV), total lesion glycolysis (TLG) and clinical outcomes. They demonstrated a correlation between semi-quantitative factors such as FTV and TLG with patient outcome and survival.[19] Similarly, Fendler *et al*. reported the use of TLG in predicting survival in patients with CRLM; FTV and TLG were found to correlate with outcome and survival in these patients using the Response Evaluation Criteria In Solid Tumors.[20]

Zerizer *et al*. investigated the role of early ^{18}F-FDG-PET/CT in predicting progression-free survival.[18] Early ^{18}F-FDG-PET/CT was found to be superior to contrast-enhanced CT imaging in predicting progression-free survival in patients with CRLM treated with ^{90}Y radioembolisation.[18]

^{18}F-FDG-PET/CT is an emerging prognostic tool in patients with CRLM undergoing SIRT. However, this finding should be confirmed with larger prospective studies. Unfortunately, PET technology is currently not available in Oman at the present time and patients requiring PET scans are sent to nearby countries. With the establishment of an oncology service at the Sultan Qaboos University Hospital and an oncology centre at the Royal Hospital in Muscat, Oman, PET imaging is becoming a necessity. According to personal sources, a PET scanning facility will be installed this year. This will definitely improve the oncology services available in Oman and reduce the expenses required to send patients abroad.

In summary, the role of integrated PET/CT imaging in selecting optimal CRLM surgical candidates and in the follow-up of surgical patients is uncertain. Until additional data are available, ^{18}F-FDG-PET scans are recommended for CRC staging and in selecting treatment options for patients, including the resection of metastases and SIRT. At present, limited evidence supports the use of ^{18}F-FDG-PET/CT as a tool for planning SIRT, assessing treatment response and predicting progression-free survival.

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