PO Box 2345, Beijing 100023, China
www.wjgnet.com
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REVIEW

Positron emission tomography/computer tomography: Challenge to conventional imaging modalities in evaluating primary and metastatic liver malignancies

Long Sun, Hua Wu, Yong-Song Guan

Long Sun, Hua Wu, Minnan PET Center, The First Hospital of Xiamen, Fujian Medical University, Xiamen 316003, Fujian Province, China
Yong-Song Guan, West China Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China
Yong-Song Guan, State Key Laboratory of Biotherapy, West China Medical School, Sichuan University, Gaopeng Street, Keyuan Road 4, Chengdu 610041, Sichuan Province, China
Correspondence to: Yong-Song Guan, West China Hospital of Sichuan University, Chengdu 610041, China. yongsongguan@yahoo.com
Telephone: +86-28-85421008 Fax: +86-28-85538359
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Abstract

Computer tomography (CT) and magnetic resonance imaging (MRI), as conventional imaging modalities, are the preferred methodology for tumor, nodal and systemic metastasis (TNM) staging. However, all the noninvasive techniques in current use are not sufficiently able to identify primary tumors and even unable to define the extent of metastatic spread. In addition, relying exclusively on macromorphological characteristics to make a conclusion runs the risk of misdiagnosis due mainly to the intrinsic limitations of the imaging modalities themselves. Solely based on the macromorphological characteristics of cancer, one cannot give an appropriate assessment of the biological characteristics of tumors. Currently, positron emission tomography/computer tomography (PET/CT) are more and more widely available and their application with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) in oncology has become one of the standard imaging modalities in diagnosing and staging of tumors, and monitoring the therapeutic efficacy in hepatic malignancies. Recently, investigators have measured glucose utilization in liver tumors using ^{18}F-FDG, PET and PET/CT in order to establish diagnosis of tumors, assess their biologic characteristics and predict therapeutic effects on hepatic malignancies. PET/CT with ^{18}F-FDG as a radiotracer may further enhance the hepatic malignancy diagnostic algorithm by accurate diagnosis, staging, restaging and evaluating its biological characteristics, which can benefit the patients suffering from hepatic metastases, hepatocellular carcinoma and cholangiocarcinoma.

INTRODUCTION

Positron emission tomography (PET) is a noninvasive imaging technique that provides a functional or metabolic assessment of normal tissues or diseased conditions[1-3]. PET is now widely applied in clinical oncology. The development of the resolution and sensitivity of PET have been improved by the availability of newer scanners with a larger field of view and introduction of integral PET and computer tomography (CT) systems in 2000[4,5]. An additional factor is the decision by the Centers for Medicare and Medicaid Services to approve reimbursement for several oncologic clinical indications for PET, including the staging and restaging of non-small-cell lung, esophageal, colorectal, breast, and head and neck cancers, cervical cancer, as well as lymphoma and melanoma, and the monitoring of the response to treatment of breast cancer[6].

Asian and Western populations have their own characteristic disease spectrum and cancer incidence[7]. Hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) are the major primary hepatic malignancies in the world. In the United States, about 150 000 patients are diagnosed with colon cancer each year, and more than 50 000 of them will develop liver metastases[8]. HCC is one of the most common cancers in Asians and its mortality is just secondary to lung cancer in urban regions and gastric carcinoma in rural regions in China[9]. The incidence of CC is increasing worldwide and CC is a devastating malignancy with a high mortality that presents late and is difficult to diagnose[10]. At present, PET and PET/CT with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) have joined the

team for the workup and management of selected patients suffering from hepatic colorectal metastases, HCC or CC[11]. This review focuses on the application of PET and PET/CT with ^{18}F-FDG as a radiotracer in the evaluation of hepatic malignancies, including their diagnosis, staging and restaging, evaluation of their biologic characteristics, making a treatment plan and monitoring their responses, detection of early recurrence and assessment of their prognosis.

PET AND PET/CT *VS* CONVENTIONAL IMAGING MODALITIES

Compared to conventional imaging technologies, including CT and conventional magnetic resonance imaging (MRI), PET provides information about functional or metabolic characteristics for detection of malignancies, characterization of tumor stage, assessment of therapeutical response, and tumor recurrence, whereas CT predominantly shows the anatomical or morphologic features of tumors (i.e. size, density, and shape, *etc*)[12,13]. Conventional imaging modalities reveal morphology of lesions with largely nonspecific features. Therefore, differentiation between malignant and benign lesions could be improved by PET with its metabolic assessment[14]. Furthermore, PET has a high sensitivity in identifying areas involving cancer at an early stage. In general, accelerated radiotracer activity occurs before changes occur in anatomical structure. In many circumstances, this specific feature permits more accurate assessment of treatment and enables early detection of cancerous lesions[15].

Several radiotracers have been used in detecting hepatic malignancies by PET or PET/CT, and provide insight into their physiologic features, including glucose consumption (assessed with ^{18}F-FDG) and lipid synthesis (^{11}C-acetate)[16], cell-membrane metabolism and tumor proliferation (^{18}F-fluorocholine)[17]. Of these radiotracers, ^{18}F-FDG is by far the most commonly used in oncologic PET and the only oncologic PET tracer approved by the Food and Drug Administration (FDA) for routine clinical use[18]. ^{18}F-FDG is transported into tumor cells by glucose transporter proteins on the cell surface and then phosphorylated by hexokinase to FDG-6-phosphate. FDG-6-phosphate cannot be further metabolized in most tumor cells, thereby it selectively accumulates in cancer tissues. The amount of tumoral ^{18}F-FDG uptake is often expressed as the standardized uptake value (SUV) with a semiquantitative measure. The SUV is calculated by dividing the tissue activity by the injected dosage of radioactivity per unit body weight. The SUV ratio is expressed as the tumor to non-tumor ratio. Iwata *et al*[19] found that the median SUV is significantly lower in HCC than in metastatic liver cancer or CC, and the median SUV ratio is significantly lower in HCC than in metastatic liver cancer or CC and significantly higher in multiple HCC than in single HCC, while the median SUV and median SUV ratio are significantly higher in the presence of portal vein thrombosis than in the absence of such thrombosis.

However, PET lacks anatomical landmarks for topographic orientation, and it is difficult to identify the abnormal glucose metabolic activity in regions close to organs with variable physiological ^{18}F-FDG uptake. Thus combination with some other forms of imaging, such as CT, is desirable for differentiating normal from abnormal radiotracer uptake[20]. PET/CT is an integral combination of the cross-sectional anatomic information provided by CT and the metabolic information provided by PET. Anatomical and metabolic information is acquired during a single examination and images of the two series can be fused. ^{18}F-FDG PET/CT has several advantages over PET alone, the most important one is the ability to accurately localize increased ^{18}F-FDG activity to specific normal or abnormal anatomic locations, which can be difficult or even impossible with PET alone[21]. The main commercially available PET/CT systems in the world are PET with multi-detector computed tomography (MDCT), so that its most units can perform full dose diagnostic CT scan for selected patients who need additional CT scan after conventional ^{18}F-FDG PET/CT imaging. Comparison of several PET-derived imaging modalities with their features in detecting liver malignancies is shown in Table 1.

Table 1 Characteristics of PET and its novel sister modalities in detecting liver malignancies

Modalities	Characteristics
PET	By detecting ^{18}F-FDG uptake, producing functional images but with very poor anatomical details
PET/CT	Integrated PET and CT system, locate ^{18}F-FDG in specific anatomical sites
PET/MDCT	Best to monitor response to treatment, especially early ones with fine details

EVALUATION OF HEPATIC MALIGNANCIES

Diagnosis of hepatic metastases

PET has emerged as an important diagnostic tool in the evaluation of metastatic liver diseases[22-26]. A greater metabolic activity in malignant tissue is accompanied with a greater glucose uptake than that in surrounding normal tissue. This greater focal glucose uptake can be identified with ^{18}F-FDG PET, which allows for the identification of malignant tumor foci. Wiering *et al*[27] reported the results of a meta-analysis of the current literature about the usefulness of ^{18}F-FDG PET for the selection of patients to undergo resection of colorectal liver metastases. The sensitivity and specificity of ^{18}F-FDG PET in hepatic metastatic diseases were 79.9% and 92.3%, respectively, and 91.2% and 98.4% in extrahepatic diseases, respectively. The pooled sensitivity and specificity of CT were 82.7% and 84.1% in hepatic lesions, respectively, and 60.9% and 91.1% in extrahepatic lesions, respectively. ^{18}F-FDG PET results led to changes in clinical management from the first decision, with a percentage of 31.6% (range, 20.0%-58.0%). The combination of sensitivity with specificity in ^{18}F-FDG PET indicated that ^{18}F-FDG PET has an added value in the diagnostic workup of patients with colorectal liver metastases. ^{18}F-FDG PET can be considered as a useful tool in preoperative staging by

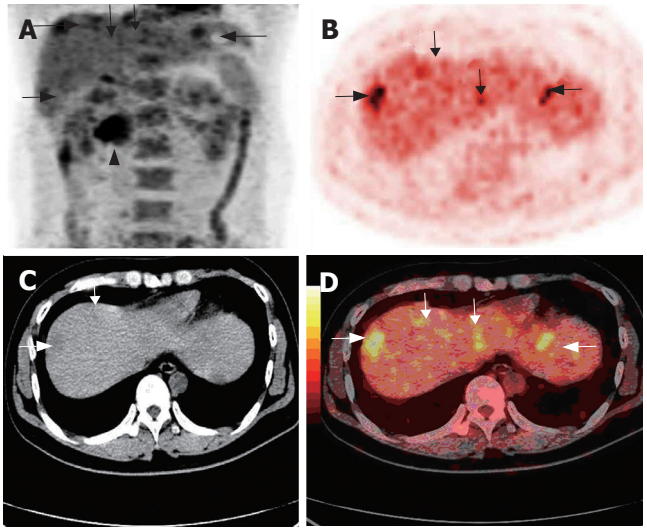

Figure 1 A 33-year-old man undergoing ascending colon cancer resection two years ago. Coronal PET image (**A**) also showing recurrent lesion (arrow head) at the root of mesentery, ^{18}F-FDG PET (**B**) and PET/CT fused imaging (**D**) demonstrating multiple hepatic metastases (arrow), and non-enhanced CT (**C**) detecting fewer lesions than PET/CT fused imaging (**D**).

producing superior results compared with conventional diagnostic modalities, especially in excluding or detecting extrahepatic metastatic disease.

Conventional PET scanning is associated with several shortcomings. The major drawback relates to its poor resolution and lack of concise anatomic illustration of PET images, making exact localization of ^{18}F-FDG uptake difficult. For example, a right adrenal gland metastasis might be misinterpreted as a liver metastasis[28,29]. Additionally, confirmation of a positive ^{18}F-FDG PET uptake by histology is sometimes impossible because of the lack of morphologic information. The new PET/CT technique allows exact identification of the lesions, which enables accurate biopsies and targeted surgery to be performed. Compared with contrast-enhanced CT, PET/CT provides comparable findings for the detection of primary liver metastases. However, PET/CT is more helpful than contrast-enhanced CT for detection of recurrent intrahepatic tumors after hepatectomy, extrahepatic metastases, and local recurrence at the site of the initial colorectal surgery[30]. Information provided by PET/CT results in a change from the initial decision on therapeutic strategies in about a fifth of the patients. Routinely performing PET/CT on all patients being evaluated for liver resection for metastatic colorectal cancer is recommended (Figure 1)[31]. To the patients with metastatic colorectal cancer, a routine PET/CT scan is recommended for making therapeutic decisions, such as liver resection.

Diagnosis of HCC

PET is an imaging technique reflecting cellular metabolism. However, the feasibility of PET in diagnosis of HCC is limited because of its vague images and high cost. Several investigators have reported controversial conclusions telling an inadequate sensitivity of PET (50%-55%)[32]. Shin *et al*[33] reported a group of 32 HCC patients verified by surgical pathology or clinical course using imaging studies (CT, MRI or angiography) within 3 mo after PET. The sensitivity and specificity of ^{18}F-FDG PET were 65.5% and 33.3% respectively. The positive predictive value was 90.5%. The diagnostic accuracy was 62.5%. Chen *et al*[34] reported that the sensitivity, specificity and accuracy were 73.3%, 100% and 74.2%, respectively for detecting recurrence with ^{18}F-FDG PET in patients with unexplained rise of serum alpha-fetoprotein (AFP) levels after the treatment of HCC. Hanajiri[35] and Beadsmoore *et al*[36] found that ^{18}F-FDG PET is more sensitive than conventional CT and MRI in detecting suspected vein tumor thrombus in patients with HCC. The reported positive rate of perihepatic lymph node involvement in patients undergoing hepatic resection is approximately 5% for hepatocellular carcinoma. ^{18}F-FDG PET is useful in detecting distant metastases from a variety of malignancies and shows superior accuracy to conventional CT and MRI in identification of perihepatic lymph nodes and distant metastases[37,38]. ^{18}F-FDG PET could provide additional information and contribute to the management of HCC patients who are suspected of having extrahepatic metastases.

Of the noninvasive imaging techniques for studying HCC, triple-phase MDCT and contrast enhanced MRI have been widely applied[39,40]. PET/CT combines the advantages of CT with the functional studying ability of PET, through the fusion of PET and CT images acquired at the same time that may help accurately localize the focal metabolic activity. Currently available data indicate that PET/CT is more sensitive and specific than either of its constituent imaging methods alone and probably more so than images obtained separately from PET and CT and viewed side by side (Figure 2). However, ^{18}F-FDG PET/CT cannot replace separate diagnostic CT for HCC. Additional full dose enhanced triple-phase MDCT scan at the same time followed by ^{18}F-FDG PET/CT whole body scan may be needed to take in some suspected HCC patients, especially those at high risk[41].

Diagnosis of CC

Surgical resection is considered the only curative strategy for intrahepatic CC at present. Accurate staging is essential for appropriate management of patients with CC. MRI or CT combining endoscopic ultrasound and PET provide useful diagnostic information in certain patients[10]. In diagnosing malignant diseases in patients with biliary stricture, ^{18}F-FDG PET may give better sensitivity and specificity than CT, and is more sensitive than cytological examination of bile in sensitivity[42]. ^{18}F-FDG PET could be useful in cases of suspected hilar CC by radiological findings with non-confirmatory biopsy[43]. Anderson *et al*[44] reported that the sensitivity of ^{18}F-FDG is 85% in detecting nodular morphology, 65% in detecting metastases of CC, 78% in detecting gallbladder carcinoma, and 50% in detecting extrahepatic metastases. PET is accurate in predicting the presence of nodular CC (mass > 1 cm) but may be not helpful for the diagnosis of infiltrating type of CC. PET is also helpful for detecting residual gallbladder carcinoma following cholecystectomy and has led to a change in management of 30% of patients with CC.

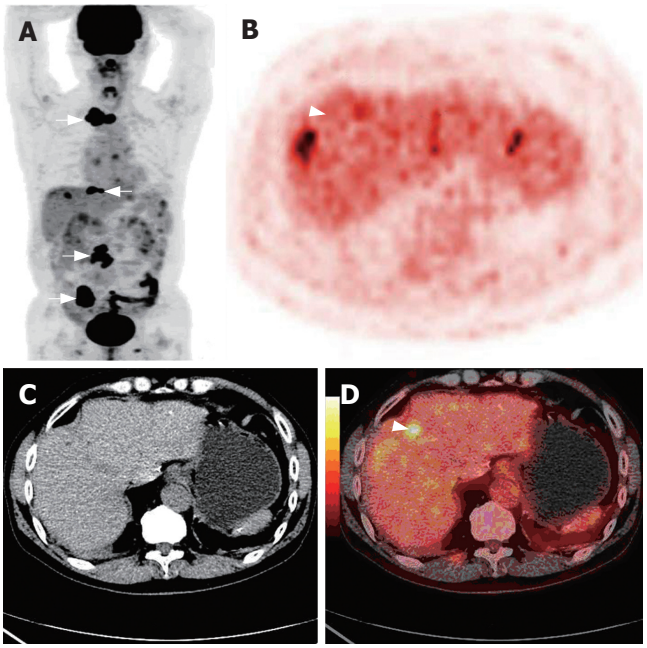

Figure 2 A 68-year-old male undergoing HCC resection 28-mo ago. Multiples bone metastases (arrow) on the image of whole body PET (**A**), non-enhanced CT (**C**) detecting no recurrence lesion in the liver, ^{18}F-FDG PET (**B**) and PET/CT fused imaging (**D**) showing a high metabolism recurrent lesion (arrow head).

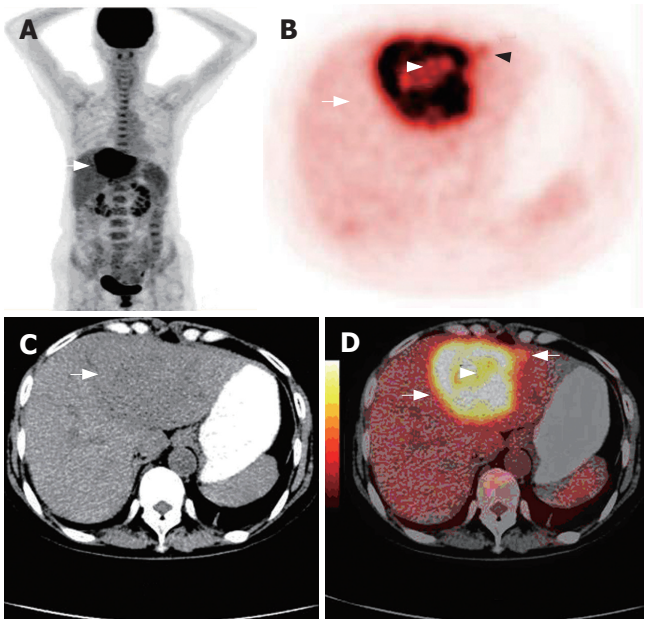

Figure 3 A 68-year-old female complaining of uncomfortable left upper abdomen for one month with increasing of CA19-9 (> 700 μ/L) (**A**), non-enhanced CT (**C**) detecting a low density lesion in the left lobe of the liver (white arrow), ^{18}F-FDG PET (**B**) and fused imaging of PET/CT (**D**) showing necrosis (arrow head) in the center of the mass with a satellite lesion (black arrow). CC was confirmed by liver biopsy.

The number of metastatic lymph nodes is a significant prognostic factor for CC. The reported positive rate of perihepatic lymph node involvement ranges 30%-50% in patients with hilar CC[45], and 47%-58% in those with intrahepatic CC[46]. The involvement of paraaortic and regional nodes in advanced hilar cholangiocarcinoma is 14.4%. There is no consensus regarding the optimal technique for evaluating the status of perihepatic lymph nodes at the time of liver resection for intrahepatic CC. Some have advocated routine nodal sampling before resection, while others have advocated routine subhilar lymphadenectomy. Without liver resection, the optimal decision to sample lymph nodes can be only guided by information gathered from preoperative imaging studies and the intraoperative assessment of perihepatic nodes[47].

Petrowsky *et al*[48] reported that ^{18}F-FDG-PET/CT and contrast-enhanced CT may provide a comparable accuracy for the primary intra- and extra-hepatic CC. Regional lymph node metastases were detected with PET/CT and contrast-enhanced CT in only 12% *vs* 24%. All distant metastases were detected with ^{18}F-FDG PET/CT, while only 25% were detected with contrast-enhanced CT. PET/CT findings resulted in a change of management in 17% of patients deemed resectable after standard work-up. PET/CT is particularly valuable in detecting unsuspected distant metastases which have not been diagnosed with standard imaging. Thus, PET/CT staging has an important impact on selection of adequate therapy. However, false positive rates have been found in patients with inflammatory disease, such as primary sclerosing cholangitis and cholecystitis. Therefore, a multidisciplinary diagnostic approach using ^{18}F-FDG PET or PET/CT in conjunction with conventional modalities seems essential to a precise differential diagnosis.

EVALUATION OF HEPATIC MALIGNANT BIOLOGICAL CHARACTERISTICS

There is a dilemma that the five-year survival rate (ranging from 30% to 50%) of patients after curative resection of HCC almost does not increase in the past decade. The treatment procedures of cancer must face the core biological characteristics of cancer-aggressiveness and metastasis[49]. The diagnosis, treatment, prognosis standardizations of hepatic malignancies rely exclusively on the macromorphological characteristics, which is not enough to evaluate the biological characteristics of such malignancies. Molecular imaging in oncology is the noninvasive imaging of the key molecules and molecule-based events that are characteristic of the genotype and phenotype of human cancer. Since tumors with increased ^{18}F-FDG uptake are more metabolically active and more biologically aggressive[50,51], PET and PET/CT with ^{18}F-FDG would play a key role in evaluating the biological characteristics of hepatic malignancies (Figure 3).

It has been reported that the higher the glucose metabolism seen on ^{18}F-FDG PET imaging, the worse the prognosis of tumors, especially untreated tumors[52,53]. It is clear that a great deal of biological information is contained within the ^{18}F-FDG PET SUV that reflects the level of glycolysis, and strongly correlates to an adverse patient prognosis[49]. Although HCC accumulates ^{18}F-FDG to various degrees, a high positive rate of ^{18}F-FDG accumulation has been reported in patients with high-grade HCC[54] and in those with markedly elevated AFP levels. Preoperative ^{18}F-FDG uptake reflects tumor differentiation and P-glycoprotein expression and may be a good predictor of outcome in HCC[55]. The SUV ratio is related significantly to disease-related deaths as well as

other predictive factors, including the number, size and stage of tumors, involvement of vessels and the capsule, and provides information of prognostic relevance in patients with HCC before surgery[56]. A significant survival benefit is correlated with low ^{18}F-FDG uptake in patients with metastases of colorectal cancer[57].

Approximately 50% of patients with resected hepatic malignancy may have a tumor recurrence. Thus, it is of importance to predict the relapse and to tackle it with additional treatment. A better understanding of biological characteristics of hepatic malignancy could lead to adequate use of adjuvant surgical treatments and hopefully better treatment outcome[58]. For example, if patients at high risk of tumor recurrence could be identified before the resection, they would benefit from additional treatments, such as neoadjuvant and adjuvant therapy, biotherapy, or the three. It is not necessary for patients at a low risk of tumor recurrence to receive the above therapies.

SELECTION OF LIVER TRANSPLANTATION CANDIDATES

Liver transplantation is the only option capable of simultaneously curing both HCC and the underlying liver disease. Prevention of postoperative tumor recurrence to improve the patients' long-term survival remains the primary concern as well as the major difficulty in liver transplantation for HCC[59]. The key problem is thus the selection of patients who can benefit from liver transplantation, so that it is necessary to identify patients at low risk of recurrence. The stringent morphologic criteria (solitary nodule < 5 cm, 3 nodules < 3 cm each) have been implemented to list HCC patients for liver transplantation, leading to a big improvement in survival rate of transplanted HCC patients in the last 10 years. Nevertheless, several recent studies have shown the limitations of such criteria in prediction of prognosis[60,61]. All conventional imaging modalities in current use with the common HCC staging procedures (TNM, Milan criteria) have their own limits to identify primary tumors and may be even more limited in their ability to define the extent of metastatic spread[62]. Furthermore, relying exclusively on the macromorphological characteristics of tumors may result in misdiagnosis mainly due to the limits of imaging techniques. The macromorphological characteristics of cancer also give an imprecise estimate of the tumor's aggressiveness[63].

With the advantages of whole-body scanning and high sensitivity in tumor detection, ^{18}F-FDG PET/CT can be instrumental in preoperative evaluation of liver transplantation for HCC (such as modification of clinical staging) and early detection of postoperative recurrent tumors. Histological grade of differentiation and macroscopic vascular invasion are strong predictors of both survival and tumor recurrence in patients with cirrhosis who receive transplants because of HCC[64]. Cillo *et al*[65] reported that candidates for liver transplantation can be selected using HCC grades (G1 and G2) based on preoperative fine needle aspiration biopsy, which is associated with an extremely low rate of tumor recurrence, comparable with that of incidentally detected HCC. Histological examination using percutaneous needle biopsy may be the most definite assessment of HCC grades. However, it is invasive and the specimen retrieved does not always represent the entire lesion owing to sampling errors[66]. Histological grade and vascular invasion cannot be determined preoperatively. PET and PET/CT with ^{18}F-FDG imaging could also be a good preoperative tool for estimating the post-liver transplantation risk of tumor recurrence, importantly, tumor recurrence can be highly anticipated for PET-imaging-positive HCC patients who satisfy the Milan criteria. Yang *et al*[32] supported that PET-imaging-positive HCC patients should be selected cautiously for liver transplantation.

SELECTION OF PATIENTS WITH HEPATIC COLORECTAL METASTASES FOR HEPATECTOMY

Hepatic resection, a potentially curative approach for patients with liver metastases from colorectal carcinoma, carries a 5-year survival rate of 30%-50%. The resection rate of hepatic metastases from colorectal carcinoma varies from 20% to 50%[67]. Some clinical and pathological factors have been identified as important prognostic determinants of survival after surgical resection of colorectal liver metastases, including sex and age of the patients, stage of tumor, the number and size as well as distribution of hepatic metastatic lesions, presence of extrahepatic distant metastases, type of hepatectomy, and adjuvant chemotherapy, *etc*[68]. Antoniou *et al*[69] reported that a repeated hepatectomy is safe and may provide survival benefit equal to that of the first liver resection based on their results from a meta-analysis of repeated hepatectomy for patients with colorectal cancer metastases.

^{18}F-FDG PET is a useful tool in preoperative staging. It may be better than conventional diagnostic modalities, especially for staging and re-staging after hepatectomy[70]. Kinkel *et al*[71] reported that the mean weighted sensitivity of ultrasonography, CT, MRI, and ^{18}F-FDG PET is 55%, 72%, 76% and 90% respectively, in the detection of hepatic metastases from colorectal, gastric, and esophageal cancers. Results of pair wise comparison between imaging modalities demonstrated a greater sensitivity of ^{18}F-FDG PET than ultrasonography, CT and MRI. At equivalent specificity, ^{18}F-FDG PET is the most sensitive noninvasive imaging modality for the diagnosis of hepatic metastases from colorectal, gastric, and esophageal cancers.

^{18}F-FDG PET/CT provides important additional information in patients with presumed resectable colorectal metastases to the liver, leading to a change of therapy in one fifth of patients[30]. The most significant additional information relates to the accurate detection of extrahepatic spread of tumor. ^{18}F-FDG PET/CT is particularly valuable in detecting local recurrence at the margin of a previous liver resection and at the site of the primary colorectal surgery[72]. It also increases the accuracy and certainty of locating lesions in colorectal cancer. More definitely normal and abnormal lesions could be identified

with PET/CT than with PET alone with an improved staging and restaging accuracy of 78%-89%[73]. This test should be used for patients at high risk for extrahepatic disease and evaluated prospectively for all patients under consideration for liver resection.

VIABLE TUMORS *VS* NECROSIS OR FIBROSIS AFTER TREATMENT

Less than 20% of patients with hepatic metastases, HCC and CC have been treated surgically. Palliative treatment of inoperable hepatic metastases, HCC and CC has been reported[74]. Despite initial resection or remission of hepatic malignancy, the survival benefits are not satisfactory because of frequent recurrences following the treatment[75]. Early detection of a residual or locally recurrent tumor after palliative treatment is critical to early successful retreatment. Conventional CT and MRI are disadvantageous in early evaluation of the local treatment efficacy and recurrent diseases[76].

An important contribution of restaging with PET among patients without any other clinical or biochemical evidence of disease is the possibility of distinguishing between viable tumors and necrosis or fibrosis in residual masses that may be present after treatment[75]. PET and PET/CT with ^{18}F-FDG are not affected by scar tissue and artificial materials. ^{18}F-FDG PET and PET/CT accurately monitor the local efficacy of radiofrequency ablation (RFA) for treatment of liver metastases and can recognize early incomplete tumor ablation, which may not be detectable on contrast-enhanced CT alone. Conversely, CT and MRI may be false-positive at the rim of the lesions because of hyperperfusion after RFA[77,31]. Zhao *et al*[78] reported that ^{18}F-FDG PET/CT is better than CT in judging tumor residue of HCC after treatment with transcatheter arterial chemo-embolization (TACE) combined with RFA or surgery and in guiding further treatment of HCC. Furthermore, integrated PET/CT can provide a value especially for the postoperatively distorted liver with scar tissue and artificial materials, where the sensitivity and specificity CT and MRI are relatively low.

PREDICTORS OF POSTOPERATIVE RECURRENCE IN ASYMPTOMATIC PATIENTS

An unexplained rise of tumor markers (e.g., among patients with colorectal cancer and elevated levels of serum carcinoembryonic antigen (CEA) or HCC patients with elevated serum AFP levels after the treatment) after the treatment of hepatic malignancy is an early indicator of tumor recurrence or extrahepatic metastases[79]. However, conventional imaging techniques have a limited sensitivity for detecting recurrent disease in such patients. ^{18}F-FDG PET has been proved to be an effective whole-body imaging technique that detects metabolic changes preceding structural findings. Several studies have persuasively demonstrated that tumor restaging with PET can detect and localize disease recurrence among patients with no or mild symptoms and elevated tumor marker level. PET also can provide information about whether the detected disease is resectable[80,81].

Table 2 Comparison between PET/CT and conventional imaging modalities of their values in examination of liver malignancies

Modalities	Specificity	Sensitivity	Accuracy
18F-FDG-PET/CT	+++	+++	+++
Ultrasound	+	++	-
CT	++	+++	+
MRI	++	++	++

- poor; + fair; ++ good; +++ excellent.

Flamen *et al*[82] have reported the results of ^{18}F-FDG PET for unexplained rising CEA in postoperative colorectal cancer patients, showing that a patient-based analysis revealed that the sensitivity of ^{18}F-FDG PET in detecting tumor recurrence is 79%, and the positive predictive value is 89%, while a lesion-based analysis displayed that the sensitivity of ^{18}F-FDG PET in detecting tumor recurrence is 75%, and the positive predictive value is 79%. ^{18}F-FDG PET whole-body scan also provides a valuable imaging tool for detecting extrahepatic metastasis and contributes to the management of HCC patients suspected of having extrahepatic metastases[83]. ^{18}F-FDG PET/CT provides fused images demonstrating the complementary role of functional and anatomic assessment in the diagnosis of cancer recurrence through the precise localization of suspected ^{18}F-FDG uptake foci and their characterization as malignant or benign[84]. ^{18}F-FDG PET/CT is better than common CT in judging tumor residue of HCC after treatment, and in guiding further treatment of HCC.

EVALUATION OF PROGNOSIS OF HEPATIC MALIGNANCIES

At present, despite careful preoperative staging with conventional imaging modalities and colonoscopy, most patients with colorectal liver metastases have recurrence after liver resection. The overall 5-year survival rate is 30%, ranging 12%-41%. These results have not steadily improved over time[85,86]. Accordingly, to reduce the frequency of futile hepatic resections, more effective staging tools are needed. ^{18}F-FDG PET appears to define a new cohort of patients in whom tumor grade is a very important prognostic variable[22]. The current study focused on the prognostic value of pretreatment metabolic activity in metastases measured with ^{18}F-FDG PET, which was investigated as an indicator of survival in colorectal cancer.

The overall 5-year survival in patients screened with ^{18}F-FDG PET before hepatic resection for metastatic colorectal cancer is 58.6%, which is a substantial improvement in overall survival when compared with the results from a large number of historical series in which ^{18}F-FDG PET was not used[87]. A significant survival benefit has been shown in patients with low ^{18}F-FDG uptake in

metastases of colorectal cancer[58]. ^{18}F-FDG PET is useful not only for the evaluation of malignancy of hepatocellular carcinoma but also for the prediction of outcome in patients with hepatocellular carcinoma[88]. The SUV of ^{18}F-FDG PET in high-grade HCCs is significantly higher than that in low-grade HCCs. The SUV ratio is related significantly to disease-related deaths as well as other predictive factors, including the number, size and stage of tumors, and involvement of vessels as well as capsule[19]. Evaluation of examination results from these imaging modalities is illustrated in Table 2.

CONCLUSION

^{18}F-FDG PET has advantages over conventional imaging techniques in designing and evaluating managements of hepatic malignancies with biological characteristics for an optimal patient outcome. With combined functional and anatomical image, PET/CT is more and more widely applied in clinical practice. It is more sensitive and specific than PET, with a lower false-positive and false-negative rate. Multiple avenues of investigation that can be used to improve the ability of PET and PET/CT with ^{18}F-FDG to enhance the diagnostic algorithm of hepatic malignancies, which can benefit the patients suffering from hepatic metastases, HCC and CC by more accurate diagnosis, staging, restaging and further evaluation of their biologic characteristics.

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