Roles of PET/CT in Evaluating Gallbladder and Hepatobiliary Tumors

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Introduction

Gallbladder carcinoma is a common carcinoma in the biliary cells and in the gastroenteric system as well [1]. An early diagnosis seems to be difficult due to its anatomical location, lack of typical symptoms, and aggressive biologic characteristics. In addition, gallbladder carcinoma is a highly aggressive malignancy. The 5-year survival rate of gallbladder cancer is reported at less than 15% [2]. In a recent study, 80% of the patients had metastatic disease and only 20% had potentially resectable disease at the time of diagnosis [3]. Thus, accurate evaluation and staging are important to provide a suitable indication of surgery [4].

Several diagnostic tools have been used in this setting, including ultrasonography (US), computed tomography (CT), magnetic resonance (MR), endoscopic retrograde cholangiopancreatography (ERCP), and percutaneous transhepatic cholangiography (PTC). This chapter introduces a new and elegant molecular imaging technique using positron emission tomography (PET).

Value of FDG-PET for Oncological Cases

Fluorine-18-fluorodeoxyglucose (FDG) and PET/CT have been proposed as a noninvasive imaging method to assess the disease extent in patients with various cancer.

Since most of the malignant lesion use glucose as an energy source, FDG as a marker of exogenous glucose utilization has been used for detecting and characterizing malignant lesions using whole-body PET imaging. FDG PET has been proposed for diagnosis, staging, the effectiveness of treatment and the prediction of long-term survival in different malignancies [5–8]. Hybrid PET/CT device permits enhanced detection and characterization of neoplastic lesions, by a combination of the functional data obtained by PET with morphological data obtained by CT.

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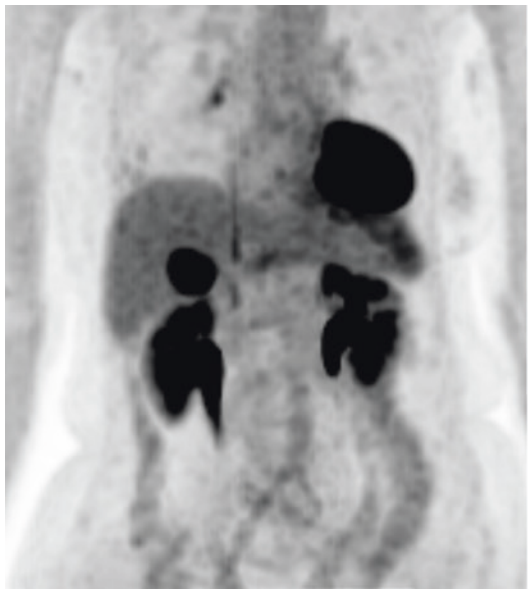
Clinical Applications of FDG-PET for Gallbladder Cancer

The typical example of FDG PET-CT in a patient with gallbladder cancer is shown in Fig. 1. A high FDG uptake is well observed in an area of gallbladder cancer.

There are a number of reports showing different values of sensitivity and specificity for diagnostic accuracy of FDG PET or PET/CT [1, 4, 9–25]. In addition, a systematically reviewed and meta-analyzed report has also indicated the value and limitation for the diagnostic value of FDG PET for diagnosing gallbladder carcinoma [26]. Their pooled results of the meta-analysis indicate that FDG PET studies showed good sensitivity (87%) and specificity (78%) in the evaluation of primary tumors with a high value of the AUC (0.88) in patients with gallbladder carcinoma. Possible sources of false positive results are inflammatory diseases of the gallbladder (Fig. 2). On the other hand, possible false negative results are small size and/or low-grade tumors (Fig. 3). Regarding the diagnostic work-up of patients with gallbladder carcinoma, FDG PET and PET/CT may have little diagnostic advantage over traditional imaging modalities in detecting primary gallbladder carcinoma [4].

FDG PET and PET/CT may have important roles complementary to US, MR, CT, PTC, and ERCP in staging gallbladder carcinoma patients. Since FDG PET is a whole-body scanning technique, it allows the detection of unsuspected metastatic lymph nodes or distant spread that may lead to major changes in the surgical management of patients with biliary tract cancer [24] (Fig. 4). Since incidental diagnosis of gallbladder carcinoma is increasing, the role of PET/CT for an effective treatment has been discussed [27]. The pT1b patients on PET/CT may be observed as the chance of relapse is low. On the other hand, chemotherapy may be needed for all pT2 patients due to the high incidence



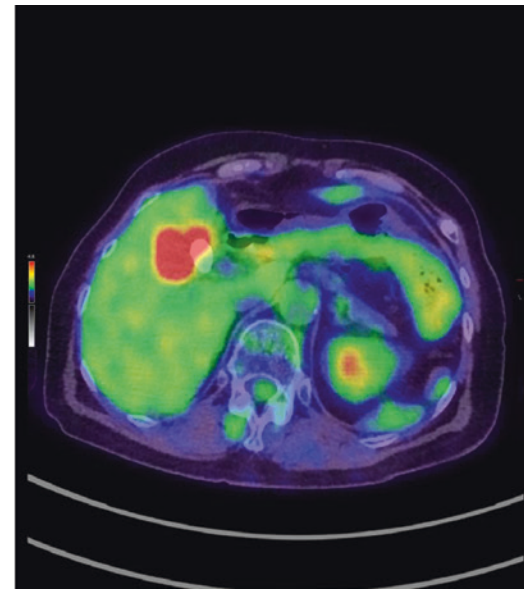
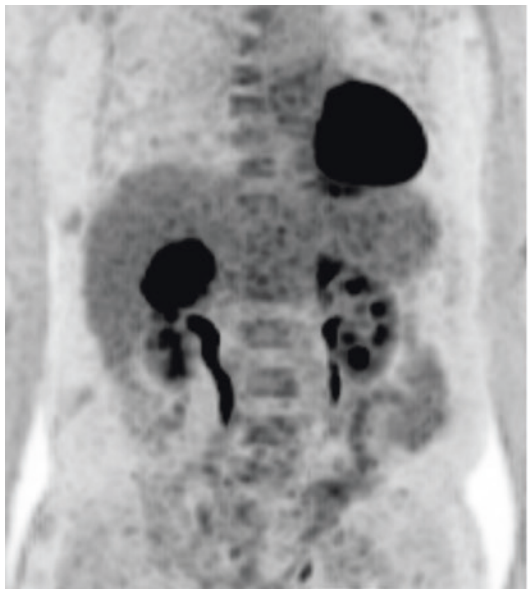


Fig. 1 FDG PET maximum intensity projection (MIP) image (left) and PET/CT fusion image (right) of a 76-year-old female patient with advanced gallbladder cancer MIP image shows focal area of high FDG uptake in the right upper abdomen. Fusion image reveals a calcified gallstone in the gallbladder and high uptake (SUV max 12.7) in wall thickening of the gallbladder body. High uptake area spread to segment 5 of the liver, suggested intrahepatic invasion. Two months later, she underwent surgery and adenocarcinoma of gallbladder was proved by pathological examination



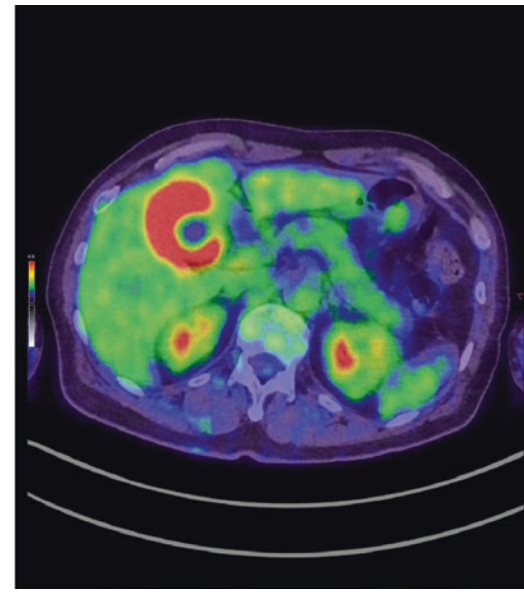
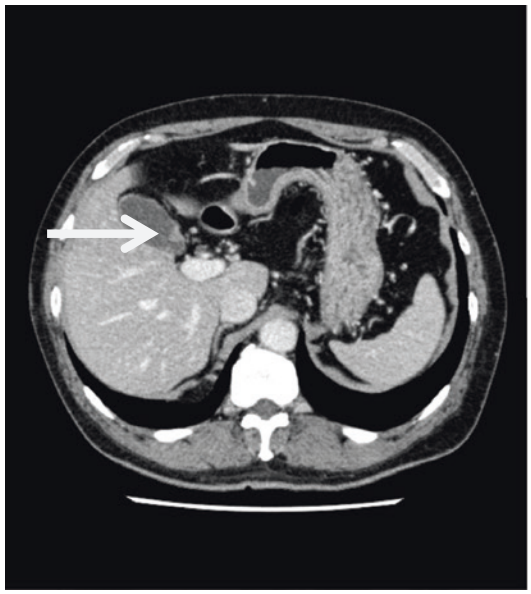


Fig. 2 FDG PET MIP image (left) and PET/CT fusion image (right) of a 65-year-old male patient with xanthogranulomatous cholecystitis (XGC). MIP image shows focal area of high FDG uptake in the right upper abdomen Fusion image reveals high uptake (SUV max 16.5) as along wall thickening from fundus to body of the gallbladder. Two months later, he underwent surgery and xanthogranulomatous cholecystitis was proved by pathological examination



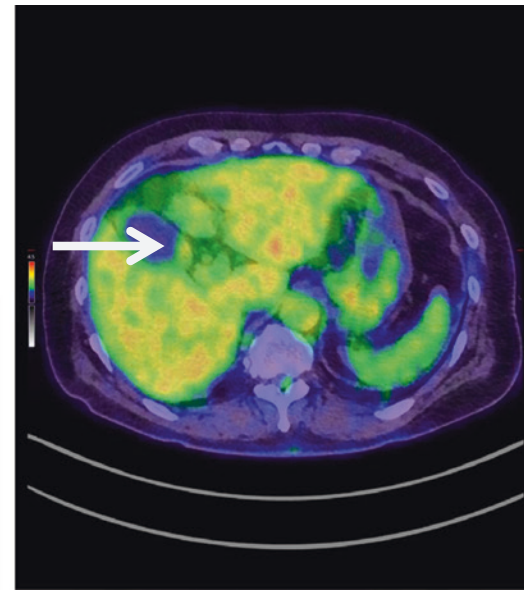


Fig. 3 Contrast-enhanced CT image (left) and FDG PET/CT fusion image (right) of a 68-year-old male patient with early gallbladder cancer Contrast-enhanced CT image shows focal wall thickening of the gallbladder neck. Fusion image reveals slightly high uptake (SUV max 3.0) in the gallbladder neck (white arrow). Two months later, he underwent surgery and adenocarcinoma (tub1 > tub2) of gallbladder was proved by pathological examination

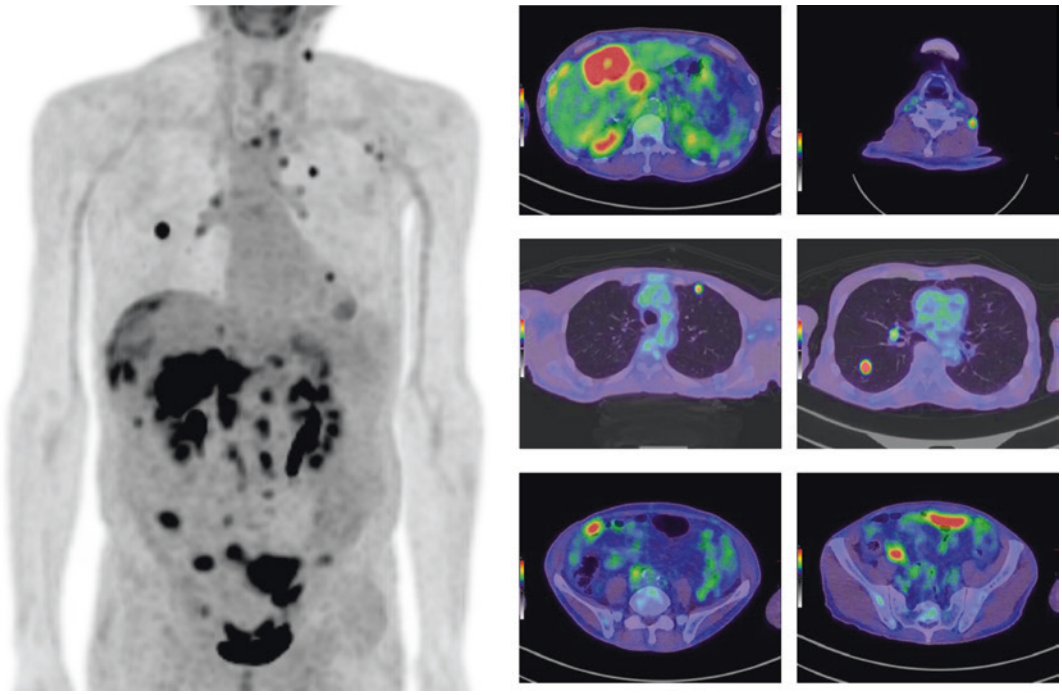


Fig. 4 FDG PET MIP image (left) and PET/CT fusion images (right) of a 75-year-old male patient with gallbladder cancer and systemic metastasis MIP image shows multiple focal high FDG uptakes in the abdomen, left supraclavicular fossa, chest, and pelvis. Fusion images reveal high uptake in the gallbladder tumor, left supraclavicular lymph node metastasis, pulmonary metastases, and peritoneal dissemination

of recurrence and nodal metastasis [27]. Since PET/CT was in good agreement with the final outcome compared to CT, PET/CT tended to show a better prediction on resectability than CT, especially due to unexpected distant metastasis [28]. There are a number of recent papers indicating diagnostic as well as prognostic values of PET/CT for patients with gallbladder carcinoma [29, 30].

Since most patients with gallbladder carcinoma are diagnosed incidentally after cholecystectomy, FDG PET is not commonly used for evaluating gallbladder carcinoma. On the other hand, FDG PET is typically used for initiating staging after cholecystectomy or restaging when recurrence is suspected [31, 32]. An increase in FDG uptake is well demonstrated in gallbladder carcinoma and has been helpful in identifying recurrence in the areas of incision when CT cannot differentiate scar tissue from tumor recurrence [26, 33]. While FDG PET may accumulate in both gallbladder carcinoma and inflammation, the addition of delayed imaging may improve differentiating between two lesions [13].

Clinical Applications of FDG-PET for Hepatobiliary Cancer

FDG PET/CT has also been used for assessing hepatobiliary carcinoma with reported sensitivity varied from 61 to 90% [10, 34, 35]. The diagnostic value may be highly dependent on the tumor form. FDG PET was more helpful in patients with nodular cholangiocarcinoma than those with the infiltrating variety (Fig. 5). Infiltrating cholangiocarcinoma may not have a sufficient cellular mass density due to the limited value of spatial resolution of PET (usually 4–7 mm in FWHM in recent high-performance PET camera). In addition, false positive findings may often be seen in patients with a biliary stent, probably

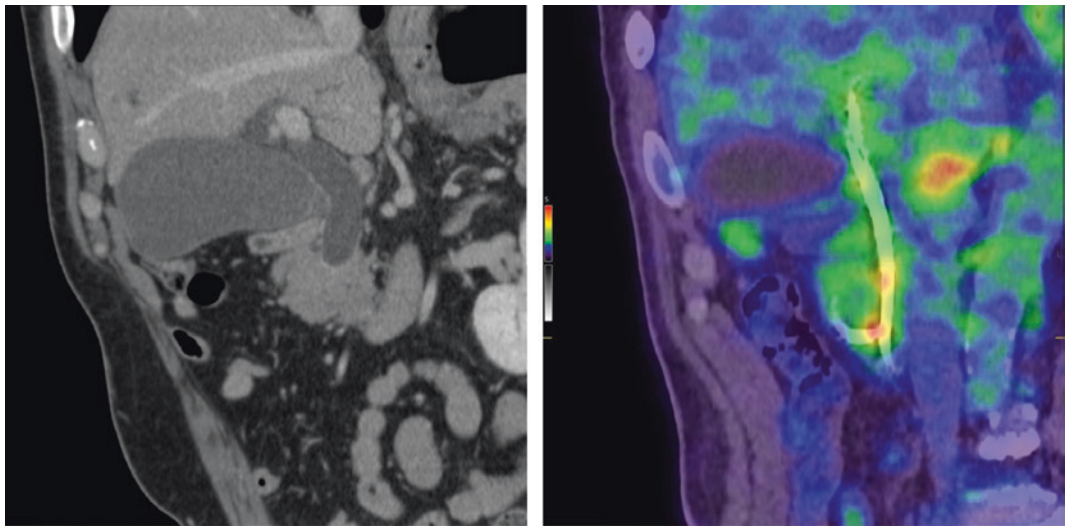


Fig. 5 Contrast-enhanced CT image (left) and FDG PET/CT fusion image (right) of a 67-year-old male patient with extrahepatic bile duct cancer Contrast-enhanced CT oblique-coronal plane image shows occlusion of distal common bile duct and dilatation of proximal common bile duct. Fusion image reveals high uptake in the distal common bile duct. High uptake in the lymph node in the hepatoduodenal ligament suggested lymph node metastasis. Two months later, he underwent pancreaticoduodenectomy. Adenocarcinoma (tub1 > por2, with sarcomatoid change) of distal bile duct and lymph node metastasis was proved by pathological examination

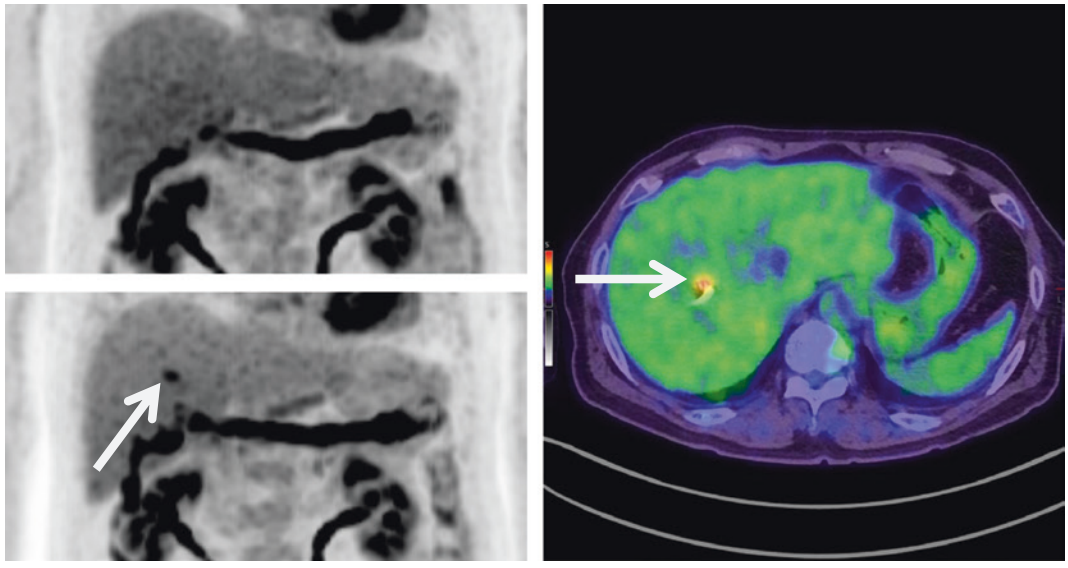


Fig. 6 FDG PET MIP images (left) and PET/CT fusion image (right) of a 67-year-old male patient with intrahepatic cholangiocellular carcinoma On 60-min MIP image (left top), no abnormal FDG uptake can be identified in the liver. On the other hand, 110-min MIP image (left bottom) and fusion image (right) reveal focal high uptake in the right hepatic duct (white arrow). Two months later, he underwent extended right hepatectomy and adenocarcinoma (tub1 > tub2 > por2) of right hepatic duct and bile duct was proved by pathological examination

due to inflammatory changes and also in patients with acute cholangitis where high FDG uptake may be seen. FDG PET has an important role in patient management since the metastatic diseases were unsuspected on the conventional imaging modalities. FDG PET findings may often show falsely negative for metastatic disease, but such lesions were detected during surgery. One of the limited sensitivities for detecting lesions may be due to the relatively high background activity of the FDG uptake in the liver. But a better contrast of the lesion may be seen by the delayed FDG imaging (90–120 min after injection) as compared to the conventional 60-min imaging after injection (Fig. 6) [13, 36, 37]. All extra-abdominal metastatic lesions were correctly detected by FDG PET [35].

Patients with primary sclerosing cholangitis may often develop cholangiocarcinoma. Therefore, a noninvasive method to detect cholangiocarcinoma small enough to allow for intended curative surgery is needed. CT and US have a poor sensitivity for the detection of such early cholangiocarcinoma. Dynamic FDG PET may hold a promise to detect cholangiocarcinoma and differentiates it from nonmalignant tissue [38].

Conclusions

We conclude that FDG PET may have an important role for evaluating biliary malignant tumors by detecting unsuspected distant metastasis, and thus, providing suitable patient management. However, FDG PET has high false negative rate for infiltrating cholangiocarcinoma, and also high false positive rate for acute inflammation. A wise use of FDG PET is required in a variety of clinical settings considering such values and limitations of FDG PET.

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