FDG PET/CT in Pancreatic and Hepatobiliary Carcinomas

Value to Patient Management and Patient Outcomes

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KEYWORDS

• ^{18}F-FDG PET/CT • Pancreatic cancer • Hepatocellular carcinoma

KEY POINTS

- Fludeoxyglucose F 18 (^{18}F-FDG) PET/CT has not been shown to offer additional benefit in the initial diagnosis of pancreatic cancer, but studies show benefit of ^{18}F-FDG PET/CT in staging, particularly in the detection of distant metastasis, and in patient prognosis.
- There is good evidence for ^{18}F-FDG PET and ^{18}F-FDG PET/CT in the staging and prognosis of both cholangiocarcinoma and gallbladder cancer.
- ^{18}F-FDG PET/CT has shown promise in the staging of liver malignancies by detecting extrahepatic metastasis.
- There is good evidence supporting the ability of PET/CT in predicting prognosis in patients with hepatocellular carcinoma (HCC).
- Evidence is evolving for the role of ^{18}F-FDG PET/CT in predicting prognosis and survival in patients with colorectal liver metastasis (CRLM).

INTRODUCTION

Pancreatic cancer is the tenth most common malignancy and fourth most common cause of cancer deaths in the United States, with a lifetime risk of 1.5%.[1] It was estimated that 46,420 people were expected to be diagnosed with pancreatic cancer in the United States in 2014. The average 5-year survival rate is drastically low at 6%, which is commonly attributed to the late presentation. At the time of diagnosis, only 20% of tumors are curative with resection.[2] Invasive ductal adenocarcinoma is the most common pancreatic malignancy, accounting for more than 80% of pancreatic cancers. Other less common malignancies include neuroendocrine tumors and exocrine acinar cell neoplasms.[3,4] Although smoking is the most highly studied risk factor, other factors include age, obesity, chronic pancreatitis, and

Disclosure: Dr Subramaniam – Phillips Health Care Molecular Imaging board meeting and Bayer Health Care – Clinical trials.

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PET Clin 10 (2015) 327–343
http://dx.doi.org/10.1016/j.cpet.2015.03.001
1556-8598/15/$ – see front matter

diabetes mellitus.[5] The National Comprehensive Cancer Center (NCCN) guidelines at this time recommend CT or MR imaging for evaluation, when there is clinical suspicion of pancreatic cancer and/or evidence of pancreatic ductal dilation.[6] The NCCN has stated that PET/CT is not a substitute for high-quality, contrast-enhanced CT (CECT).[6] Recently, the benefits of contrast-enhanced ^{18}F-FDG PET/CT, incorporating a 3-phase CECT and ^{18}F-FDG PET, have been shown in staging and treatment planning of pancreatic cancer.[3]

Two common cancers of the liver include HCC and liver metastasis, especially from colorectal cancers. HCC accounts for approximately three-fourths of all liver cancers. HCC is the sixth most common cancer and third most common cause of cancer deaths worldwide. It was estimated that 33,190 people were expected to be diagnosed with HCC in the United States in 2014.[1] The average 5-year survival rate (including intrahepatic bile duct cancer) is 16%, which is commonly attributed to the late presentation. In patients with either regional lymph node or distant metastasis, however, the survival rate decreases to approximately 10% and 3%, respectively.[1] Risk factors for HCC include alcohol-related cirrhosis, obesity, nonalcoholic steatohepatitis, and hepatitis B and C infections.[1] Current work-up for diagnosis and staging of HCC includes CT, MR imaging, ^{18}F-FDG PET, and bone scintigraphy, if clinically indicated.[7] Like pancreatic cancer, studies have suggested the benefit of ^{18}F-FDG PET/CT in the staging, treatment planning, and outcome of HCC.[8,9] CRLM, however, is common among patients with colorectal cancer. Metastasis to the liver is the most common location for stage IV colorectal cancer. The 5-year survival rate for patients who have resection of liver metastasis is approximately 25% to 40%.[10] ^{18}F-FDG PET/CT has been found to play a role in predicting prognosis and survival in patients with CRLM.

Biliary tract cancer commonly includes cholangiocarcinoma and gall bladder cancer. Cholangiocarcinoma is a malignancy arising from bile duct epithelial cells and can be divided into intrahepatic, extrahepatic, and the most common, perihilar cholangiocarcinoma, with an overall incidence of 1.67 per 100,000 in the United States.[11] Approximately 2000 to 3000 people in the United States are diagnosed with cholangiocarcinoma each year. Localized intrahepatic bile duct cancer has a 5-year survival rate of 15%, whereas the 5-year survival rate for extrahepatic bile duct cancer is 30%. With an average age of onset between 70 and 73, common risk factors for cholangiocarcinoma include primary sclerosing cholangitis, bile duct stones, and liver fluke infection, most commonly seen in Asia.[11] According to the NCCN guidelines, the conventional imaging work-up for diagnosis and staging of intrahepatic cholangiocarcinoma on suspicion and findings of an isolated intrahepatic mass includes CT or MR imaging, possible laparoscopy, esophagogastroduodenoscopy, and colonoscopy. Work-up for extrahepatic cholangiocarcinoma includes CT or MR imaging and noninvasive cholangiography. The only curative approach at this time is surgical resection.[6] Gallbladder carcinoma is also an uncommon malignancy that often presents late in the course of the disease. It was estimated that 6000 new cases of gallbladder cancer were expected to be diagnosed in the United States in 2014, with a 5-year survival rate ranging from 80% for stage 0 (TisN0M0) cancer to 2% in patients with stage IVB cancer. Common risk factors include gallstones, porcelain gallbladder, gall bladder polyps, and infection, among others. Likewise, both ^{18}F-FDG PET and ^{18}F-FDG PET/CT have been recently found to play a promising role in the staging, treatment planning, and outcome of gallbladder cancer.

^{18}F-FDG PET/CT is a valuable imaging test in the management of many human solid tumors.[3,12–19] In this review, the focus is on the value of ^{18}F-FDG PET/CT in the management and outcome of patients with pancreatic and hepatobiliary malignancies.

THE ROLE OF PET/COMPUTED TOMOGRAPHY IMAGING IN DIAGNOSIS, MANAGEMENT, AND OUTCOME

Fludeoxyglucose F 18 PET/Computed Tomography in the Diagnosis of Pancreatic Cancer

As discussed previously, the guidelines by the NCCN and the American College of Radiology suggest CT as the reference standard for the diagnosis and initial management of pancreatic cancer. There is no consensus that ^{18}F-FDG PET/CT is superior to CT in this regard, although debate exists. In 2014, a meta-analysis of 35 studies by Rijkers and colleagues[20] calculated pooled sensitivity (SN), specificity (SP), positive predictive value, and negative predictive value of 90%, 76%, 90%, and 76%, respectively, for ^{18}F-FDG PET, and 90%, 76%, 89%, and 78%, respectively, for ^{18}F-FDG PET/CT in the diagnosis. The investigators compared their values to pooled SN and SP of 91% and 85% for CT, and 84% and 82% for MR imaging, from a previous meta-analysis. The investigators, therefore, concluded that ^{18}F-FDG PET and ^{18}F-FDG PET/CT offered no additional benefit. Rijkers and colleagues discussed the promising role of ^{18}F-FDG PET/CT,

however, in the diagnosis of pancreatic cancer in the future as advances in the modality occur. Conversely, in a 2009 study of 38 patients by Kauhanen and colleagues[21] comparing ^{18}F-FDG PET/CT to multidetector helical CT (MDCT) and MR imaging, the investigators found a higher diagnostic accuracy with PET/CT, with an SN of 85% and SP of 94%, whereas SN and SP for MDCT were 85% and 67%, respectively, and for MR imaging 85% and 72%, respectively. Casneuf and colleagues[22] discussed that although ^{18}F-FDG PET/CT may have higher SN and accuracy compared with CT, multidetector row CT is easily accessible with lower associated costs and radiation.

Although ^{18}F-FDG PET/CT may not be the first choice for diagnosis of pancreatic cancer at this time, it remains useful in early work-up. Numerous studies have shown benefit of ^{18}F-FDG PET/CT in differentiating carcinoma from inflammation.[3] One of the key differentiating features between pancreatic carcinoma and pancreatitis is the distribution of uptake detected by ^{18}F-FDG PET/CT: focal versus diffuse. Lee and colleagues[23] studied 17 patients with atypical image findings of autoimmune pancreatitis who then underwent ^{18}F-FDG PET/CT for further characterization. The investigators compared these readings to the ^{18}F-FDG PET/CT of 151 patients with known pancreatic carcinoma. Both diffuse pancreatic uptake and ^{18}F-FDG accumulation in the salivary gland on PET/CT were most commonly found in patients with autoimmune pancreatitis compared with those with pancreatic cancer ($P<.001$ and $P = .003$, respectively). ^{18}F-FDG accumulation was more localized in patients with pancreatic cancer. The investigators concluded that ^{18}F-FDG PET/CT is helpful in differentiating the 2.

Fludeoxyglucose F 18 PET/Computed Tomography in Staging and Therapy Planning of Pancreatic Cancer

TNM staging of pancreatic cancer by the American Joint Committee on Cancer (AJCC) remains the most widely accepted staging system. Staging is important in this aggressive disease to plan appropriate therapy and is done most commonly with CT, endoscopic ultrasound, MR imaging, and PET/CT. At this time, CT is the reference standard for staging.[6] Its value stems from the accurate delineation of anatomic structures, for example, the vessels (superior mesenteric artery) that pancreatic malignancies can invade.

Over the course of a decade, ^{18}F-FDG PET and ^{18}F-FDG PET/CT have shown promise in the staging of pancreatic malignancies. In earlier studies, ^{18}F-FDG PET was able not only to detect metastasis but also differentiate benign versus malignant tumors.[24,25] Recently, ^{18}F-FDG PET/CT has been on the forefront of research for clinical use. The addition of functional imaging to anatomic imaging has proved beneficial—altering staging, decreasing the need for exploratory surgery for staging, and changing clinical management. Specifically, ^{18}F-FDG PET/CT has been found to have high accuracy, SN, and SP in detecting distant metastasis, resulting in a change in therapy planning. In a 2005 study of 59 patients with suspected pancreatic cancer deemed surgically resectable after conventional imaging, the investigators[26] found that ^{18}F-FDG PET/CT detected distant metastasis in an additional 5 patients (8.5%) not detected by conventional staging measures, with an SN of 81% and SP of 100% (**Fig. 1**). ^{18}F-FDG PET/CT was also able to locate 2 patients (3.4%) with coexisting rectosigmoid cancer. Thus, ^{18}F-FDG PET/CT altered the management of 16% of patients with pancreatic cancer. In the study by Kauhanen and colleagues[21] discussed previously, the investigators found ^{18}F-FDG PET/CT more sensitive compared with MDCT and MR imaging in the detection of distant metastasis to the liver (88%, 38%, and 38% respectively). With evidence of distant metastases, management would have been altered in 29% of patients (11 of 38) with the use of ^{18}F-FDG PET/CT compared with MDCT. Surgical intervention would have thus been avoided in 6 patients. The investigators found no additional benefit using PET/CT to detect lymph node metastasis, with similar sensitivities of 30% for PET/CT and MR imaging (**Fig. 2**).

Other studies have shown, however, that PET/CT does play a role in distant as well as locoregional metastasis. In the study by Casneuf and colleagues[22] discussed previously, the investigators found ^{18}F-FDG PET/CT more accurate than CT or PET alone in locoregional staging (85.3% vs 83.8% vs 79.4%, respectively). In a 2013 study of 71 patients by Topkan and colleagues,[27] the investigators used ^{18}F-FDG PET/CT to restage patients (after conventional staging) with unresectable locally advanced pancreatic carcinoma prior to chemoradiotherapy; 19 patients (26.8%) were found to have distant metastases that were not found initially on conventional imaging. The treatment intent for these patients was changed from curative to palliative. ^{18}F-FDG PET/CT also detected 3 additional metastatic lymph nodes in 3 patients. Overall, management was changed in 36.6% of patients (26 of 71) (**Fig. 3**). In a study by Asagi and colleagues,[28] in 2013, the investigators evaluated the N and M staging of 31 patients with stage IVa pancreatic ductal cancer, comparing ^{18}F-FDG PET/CECT with abdominal CECT. The

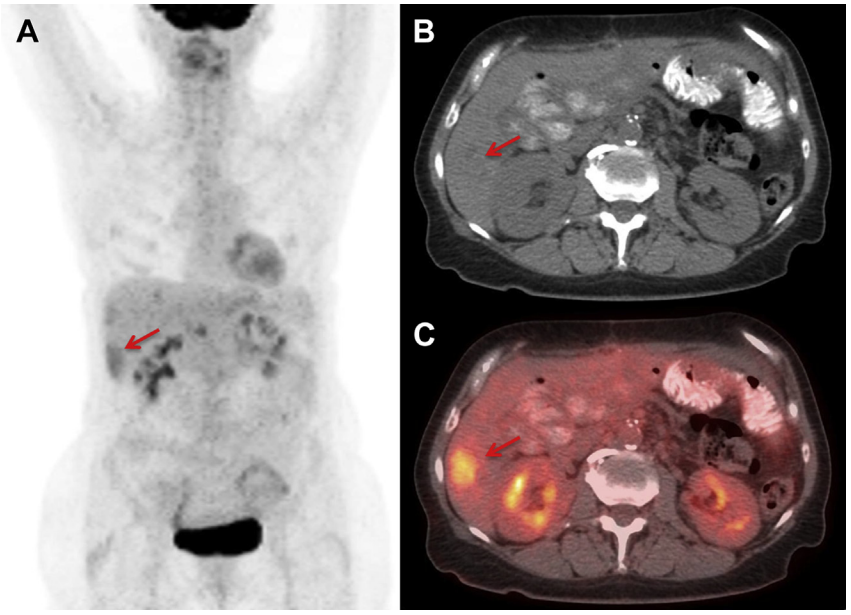

Fig. 1. Pancreas cancer–restaging of metastatic disease: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of a 73-year-old woman with pancreatic adenocarcinoma post–Whipple surgery who underwent a restaging ^{18}F-FDG PET/CT study. The study demonstrates hypermetabolic (SUVmax 3.08) metastatic liver lesions (*red arrows*), which were confirmed to be metastatic pancreatic cancer by hisyopathology.

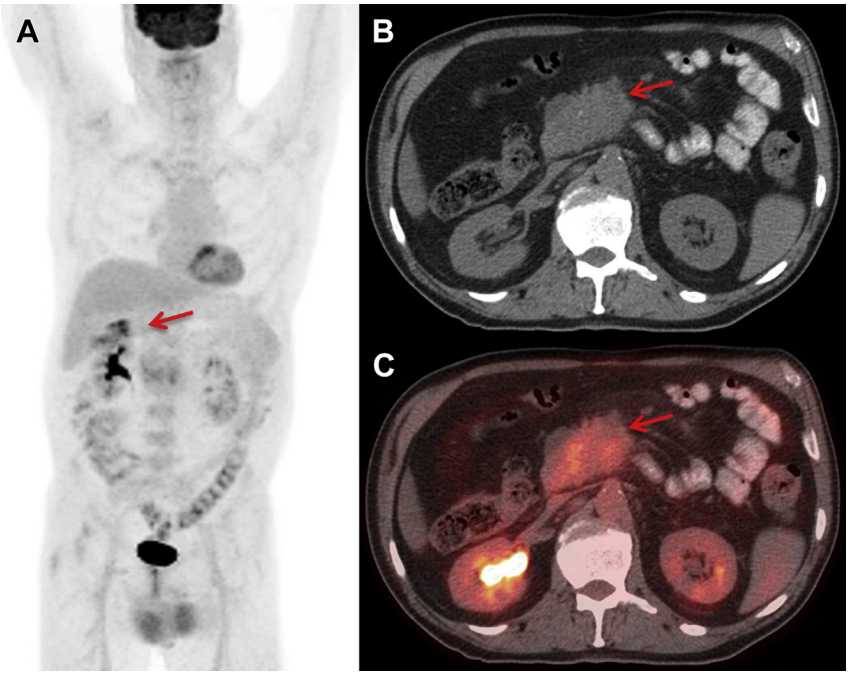

Fig. 2. Pancreas cancer staging: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) images of a 66-year-old man with newly diagnosed pancreatic adenocarcinoma who underwent a staging ^{18}F-FDG PET/CT study. The study demonstrates a moderately hypermetabolic (SUVmax 3.16), infilitrating mass (*red arrows*) in the head of the pancreas.

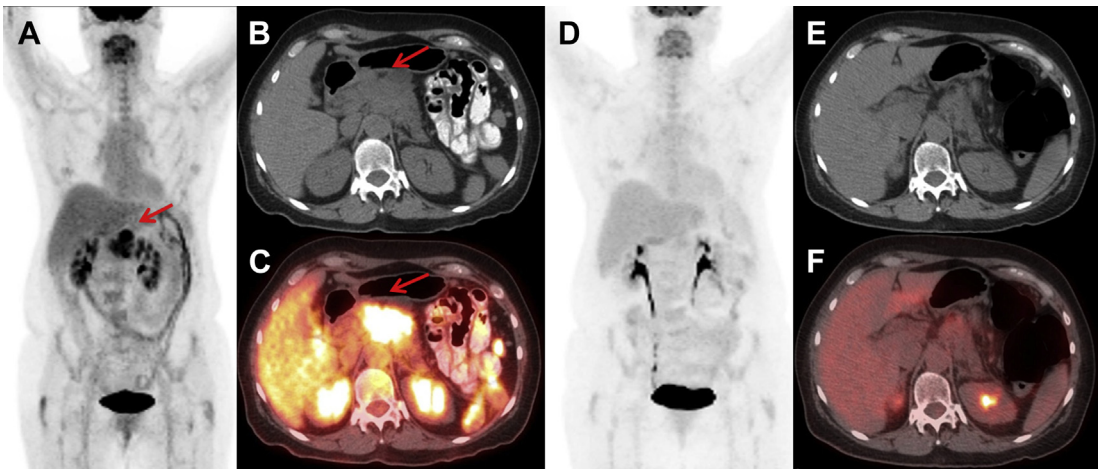

Fig. 3. Pancreas cancer—treatment response assessment: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of a 59-year-old woman with pancreatic adenocarcinoma who underwent a staging ^{18}F-FDG PET/CT study. The study demonstrates a hypermetabolic (SUVmax 9.31) pancreatic body mass (*red arrows*). The patient underwent chemoradiation. The anterior maximum intensity projection (*D*), axial CT (*E*), and axial fused PET/CT (*F*) of the restaging PET/CT study shows significant interval response to treatment.

accuracies of N and M classifications were greater for PET/CECT compared with CECT. Although the accuracy of N staging was suboptimal for PET/CECT (42%), CECT performed worse (35%). PET/CECT proved beneficial in M staging with an accuracy of 94% (29 of 31 patients). A summary of the studies evaluating staging in pancreatic cancer is in **Table 1**.

Pancreatic Cancer: Patient Outcome and Prognosis

^{18}F-FDG PET/CT may play a role in the prognosis of patients with pancreatic cancer. Specifically, multiple studies have found that the use of ^{18}F-FDG PET/CT can help predict patient outcome, in terms of both overall survival (OS) and progression-free survival (PFS).[29–31] In a study of 122 patients with resectable pancreatic ductal adenocarcinoma by Xu and colleagues,[29] the investigators studied various volumetric parameters of ^{18}F-FDG PET/CT to determine factors that can predict OS and recurrence-free survival (RFS). Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were found independent risk factors. The hazard ratio for OS and RSF increased with larger values of MTV and TLG. A doubling of the MTV on ^{18}F-FDG PET/CT led to an increase in the hazard ratio of OS by 1.27 times and a decrease in RFS by 1.25 times. A more recent study in 2014 by Lee and colleagues[30] also showed the prognostic value of MTV and TLG on patient outcome. In a retrospective study, Schellenberg and colleagues[31] aimed to determine the impact of ^{18}F-FDG PET/CT on the outcome of patients with unresectable pancreatic cancer undergoing stereotactic body radiotherapy (SBRT). The investigators concluded that both standardized uptake values (SUVs) and metabolic tumor burden (MTB) from PET scans are independent prognostic factors for both OS and PFS. The median OSs in months in patients with maximum SUV (SUVmax) below and above the median SUVmax value were 15.3 months and 9.8 months, respectively (P<.01). Likewise, a recent study by Moon and colleagues[32] showed the pretreatment SUVmax on ^{18}F-FDG PET/CT as a prognostic factor of PFS postpalliative chemotherapy (P = .046). Studies evaluating the role of PET and PET/CT in patient prognosis and outcome in pancreatic cancer are summarized in **Table 2** (**Fig. 4**).

FLUDEOXYGLUCOSE F 18 PET/COMPUTED TOMOGRAPHY IN STAGING AND THERAPY PLANNING OF BILIARY TRACT CANCERS

TNM staging for cholangiocarcinoma and gallbladder cancer by the AJCC is again the most widely used staging system. Staging can dramatically alter the therapy plan for a patient. ^{18}F-FDG PET and ^{18}F-FDG PET/CT have shown added benefit to the staging of cholangiocarcinoma. ^{18}F-FDG PET/CT is valuable in lymph node staging and in the detection of distant metastasis. In a prospective study by Kim and colleagues 2008,[33] 123 patients with suspected cholangiocarcinoma underwent work-up with conventional imaging, including CT, chest radiography, and MR imaging/MRCP with MR imaging angiography. These

Table 1
PET/CT in the staging of pancreas cancer

Study	N	Metastasis	Accuracy	SN (%)	SP (%)	% Change in Management	Description
Kauhanen et al,[21] 2009	38	Distant	—	85	94	29	SN and SP for ^{18}F-FDG PET/CT compared with MDCT and MR imaging. SN/SP for MDCT and MR imaging: 85%/67% and 85%/72% ^{18}F-FDG PET/CT is more sensitive in diagnosing distant metastasis.
Heinrich et al,[26] 2005	59	Distant	—	81	100	16	^{18}F-FDG PET/CT is important in staging.
Casneuf et al,[22] 2007	46	Locoregional	85.3	90	—	—	^{18}F-FDG PET/CT has higher accuracy and SN for locoregional staging compared with CT alone.
Topkan et al,[27] 2013	71	Distant and locoregional	—	—	—	36.6	^{18}F-FDG PET/CT has value in restaging of M0 patients with advanced pancreatic carcinoma.
Asagi et al,[28] 2013	31	Locoregional Distant	42 94	—	—	—	^{18}F-FDG PET/CT compared with CECT. CECT performed worse with accuracy of 35% for N staging.

Table 2
PET and PET/CT in patient prognosis and outcome in pancreatic cancer

Study	N	Study Type	Patients, Treatments	Description
Xu et al,[29] 2014	122	Retrospective	Resectable pancreatic ductal carcinoma	MTV and TLG are independent risk factors. Doubling of the MTV on ^{18}F-FDG PET/CT led to an increase in the hazard ratio of OS by 1.27 times, and a decrease in RFS by 1.25 times.
Lee et al,[30] 2014	87	Retrospective	Pancreatic carcinoma with surgical resection	TLG and MTV can help predict OS and RFS in patients with pancreatic cancer (P<.05).
Schellenberg et al,[31] 2010	55	Retrospective	Unresectable pancreatic cancer undergoing SBRT	SUVs and MTB from PET scans are independent prognostic factors for both OS and PFS.
Moon et al,[32] 2013	21	Retrospective	Metastatic pancreatic cancer prior to and after chemotherapy	Pretreatment SUVmax on ^{18}F-FDG PET/CT is a good prognostic factor of PFS postpalliative chemotherapy (P = .046)

patients also underwent ^{18}F-FDG PET/CT scanning, with the aim of comparing the 2 in both staging and management change. ^{18}F-FDG PET/CT was found to have a higher SP and accuracy in detecting lymph node metastasis compared with CT alone. The investigators calculated an SP and accuracy of 88.2% and 75.9%, respectively compared with 64.7% and 60.9%, respectively, for CT. The SN for ^{18}F-FDG PET/CT was lower, however, at 31.6% compared with 47.4%. In

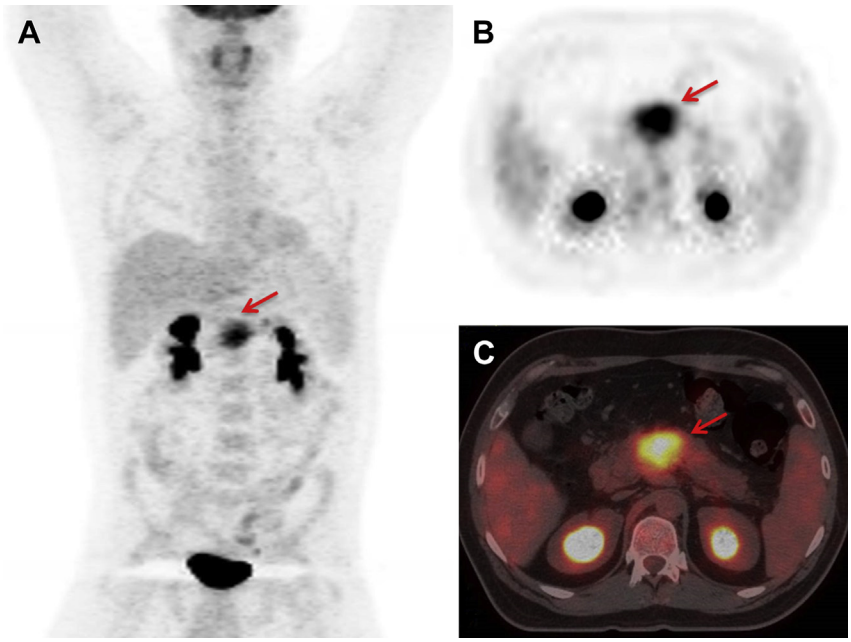

Fig. 4. Pancreas cancer—prognosis: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of a 35-year-old man with newly diagnosed pancreatic adenocarcinoma. The study demonstrates an intensely ^{18}F-FDG avid (SUVmax 8.6, MTV 27.11 mL, TLG 134.41) pancreatic mass (*red arrows*). Despite aggressive treatment with chemoradiation, the disease progressed ending in death 18 months after the study.

regard to detection of distant metastasis, ^{18}F-FDG PET/CT was found superior. The calculated SN, SP, and accuracy for ^{18}F-FDG PET/CT were 58.3%, 92.7%, and 88.3%, respectively, compared with 0%, 90.2%, and 78.7%, respectively, for CT alone. PET/CT was, therefore, able to change management in 22.3% of patients (21 of 123). Seven patients (5.7%) were up-staged with treatment changing from curative to palliative and 8 patients (6.5%) were down-staged with treatment changing to surgical resection. In a study of 18 patients with pretreatment intrahepatic cholangiocarcinoma by Park and colleagues 2014,[34] ^{18}F-FDG PET/CT was found to have an SN and SP of 80% and 92.3%, respectively, in the detection of lymph node metastasis. In contrast, CT alone had an SN and SP of only 20% and 86.4%, respectively (**Fig. 5**).

Over the course of more than a decade, ^{18}F-FDG PET alone has shown to provide additional benefit in the staging of cholangiocarcinoma. In a study of 18 patients by Kluge and colleagues 2001,[35] ^{18}F-FDG PET was found to detect distant metastasis in 7 of the 10 cases (70%) of biopsy-proved cholangiocarcinoma, although ^{18}F-FDG PET was not suitable in detecting lymph node metastasis. In another study of 35 patients with intrahepatic cholangiocarcinoma, however, Seo and colleagues[36] found that ^{18}F-FDG PET was superior to CT and MR imaging in detecting lymph node metastasis. The accuracy, SN, and SP for detection of lymph node metastasis with ^{18}F-FDG PET were calculated as 86%, 43%, and 100%, respectively. The accuracy, SN, and SP for CT and MR imaging were 68%, 43% and 76%, respectively and 57%, 43% and 64% respectively.

Likewise, ^{18}F-FDG PET and ^{18}F-FDG PET/CT may play a valuable role in the staging of gallbladder cancer, thus affecting treatment management. Studies, however, are scarce at this time. Conventional work-up for staging of gallbladder cancer includes CT, MR imaging, ultrasound, exploratory laparoscopy, and ^{18}F-FDG PET. ^{18}F-FDG PET alone remains, however, somewhat controversial, due to a lack of studies. A study by Leung and colleagues[37] in 2014 sought to identify the value of ^{18}F-FDG PET in staging patients with gallbladder cancer. In 63 with incidental gallbladder cancer postcholecystectomy, additional PET imaging to CT benefited 5 patients (8%). Of those 5 patients, PET imaging changed management to surgical resection in 3 patients and curative to palliative treatment in 2

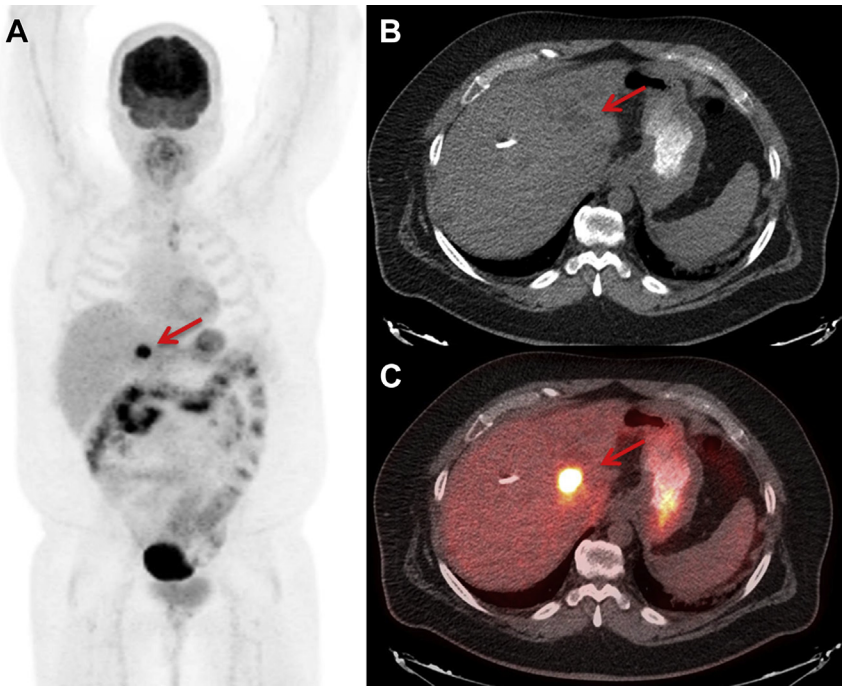

Fig. 5. Cholangiocarcinoma—staging and prognosis: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of a 55-year-old man with cholangiocarcinoma, who underwent a staging ^{18}F-FDG PET/CT study. The study demonstrated an ^{18}F-FDG–avid (SUVmax 8.55) in the liver hilum (*red arrows*). Despite aggressive treatment the disease progressed, ending in death 1 year after the study.

Table 3
PET and PET/CT in biliary tract cancer staging

Study	Patients	Metastasis	Accuracy (%)	SN (%)	SP (%)	% Change in Management	Description
Kim et al,[33] 2008	123 patients with suspected cholangiocarcinoma	Locoregional lymph node, Distant	75.9 88.3	31.6 58.3	88.2 92.7	22.3	SN and SP for ^{18}F-FDG PET/CT compared with CT alone. 5.7% up-staged and 6.5% down-staged with treatment changes.
Park et al,[34] 2014	18 patients with pretreatment intrahepatic cholangiocarcinoma	Locoregional	—	80	92.3	—	^{18}F-FDG PET/CT detecting lymph nodes compared with CT alone with an SN and SP of 20% and 86.4%, respectively.
Kluge et al,[35] 2001	18 patients with biopsy-proved cholangiocarcinoma	Distant	70	—	—	—	^{18}F-FDG PET in detection of distant metastasis.
Seo et al,[36] 2008	35 patients with intrahepatic cholangiocarcinoma	Locoregional	86	43	100	—	^{18}F-FDG PET found superior to CT and MR imaging in detecting lymph nodes.

Table 4
PET and PET/CT in gallbladder cancer staging

Study	Patients	Metastasis	Accuracy (%)	SN (%)	SP (%)	% Change in Management	Description
Leung et al,[37] 2014	63 patients with incidental gallbladder carcinoma post cholecystectomy	Locoregional	—	56	94	8	^{18}F-FDG PET with correlation to CT/MR imaging scans. ^{18}F-FDG PET has added value as an addition to CT, and helps confirm suspicious nodal disease.
Butte et al,[38] 2009	32 patients with incidental gallbladder carcinoma	Locoregional, distant (disseminated)	—	—	—	38	^{18}F-FDG PET/CT superior in detecting lymph nodes compared with CT alone. ^{18}F-FDG PET/CT has value in staging in patients with T1b or greater.
Ramos-Font et al,[39] 2014	49 patients suspicious for gallbladder cancer	Locoregional Distant	85.7 95.9	—	—	22.4	^{18}F-FDG PET/CT has high diagnostic accuracy for staging using pathology report as reference standard.
Petrowsky et al,[40] 2006	14 patients with gallbladder carcinoma + 14 patients with cholangiocarcinoma	Locoregional Distant	—	12 100	96 100	—	^{18}F-FDG PET/CT found superior to CT alone in identifying distant metastasis. ^{18}F-FDG PET/CT showed no benefit in regional lymph node metastasis.

patients. An additional 12 patients had confirmation of equivocal CT findings with PET. ^{18}F-FDG PET alone, however, contributed to false-positive readings in 3% of patients. The investigators concluded that ^{18}F-FDG PET may be used as an adjunct to conventional CT, and its use is particularly valuable in patients with suspected nodal disease or other suspicious findings. Butte and colleagues,[38] in 2009, studied 32 patients with incidental gallbladder carcinoma and noted that ^{18}F-FDG PET/CT has value in staging and thus changing the management in patients with gallbladder cancer postcholecystectomy, specifically in patients with stage T1b cancer or greater. ^{18}F-FDG PET/CT was able to uncover both local and disseminated disease (either systemic disease or regional lymph node involvement) in the interaortacaval and paraaortic bed. Ten of 32 (31%) patients were found to have disseminated disease, altering surgical management in 25% of patients (8 of 32). Overall, ^{18}F-FDG PET/CT altered the pretest staging in 12 out of 32 patients (38%). In a recent study of 49 patients suspicious for gallbladder cancer by Ramos-Font and colleagues in 2014,[39] the investigators found that ^{18}F-FDG PET/CT had a diagnostic accuracy of 85.7% for lymph node detection and 95.9% for metastatic disease using pathology reports as the reference standard. ^{18}F-FDG PET/CT changed the management in 22.4% of patients. Moreover, in a study of 14 patients with gallbladder carcinoma, 14 patients with intrahepatic cholangiocarcinoma, and 33 patients with extrahepatic cholangiocarcinoma by Petrowsky and colleagues[40] 2006, the investigators concluded that ^{18}F-FDG PET/CT plays an important role in identifying distant metastasis from cholangiocarcinoma and gallbladder cancer. PET/CT was found to have an SN and SP of 100% and 100%, respectively compared with 25% and 100%, respectively, for CECT alone (P = .001). Therefore, PET/CT was able to detect every patient with distant metastasis. CECT failed to detect 9 patients with distant metastasis. This study, however, did not show a benefit in detection of regional lymph node metastasis. PET/CT was found to have an SN and SP of 12% and 96%, respectively, compared with 24% and 86% for CT alone. Larger multicenter prospective studies are indicated at this time to determine the benefit of ^{18}F-FDG PET/CT in detecting nodal and distant metastasis in gallbladder cancer. A summary of studies evaluating the role of ^{18}F-FDG PET and PET/CT in biliary tract cancer and gall bladder cancer staging has been described in **Tables 3** and **4**.

Cholangiocarcinoma: Patient Outcome and Prognosis

^{18}F-FDG PET/CT may play a role in the prognosis of patients with cholangiocarcinoma but has not been established. There are a few studies identifying the value of ^{18}F-FDG PET/CT in patient outcome, length of both OS, and PFS. Park and colleagues[34] evaluated 18 patients with intrahepatic cholangiocarcinoma and sought to determine the value of PET/CT to predict recurrence after surgical resection. The investigators found a positive correlation between PET/CT detection of lymph node metastasis and a 1-year recurrence of carcinoma (P = .02). In a study by Seo and colleagues,[36] the investigators compared SUVmax data to disease-free survival. Patients with high SUVmax had significantly lower disease-free survival compared with patients with low SUVmax (P = .04). OS was also statistically different when patients were stratified by detection of lymph node metastasis with ^{18}F-FDG PET. The investigators concluded that SUV data and lymph node metastasis detection from ^{18}F-FDG PET might be prognostic factors in cholangiocarcinoma for postoperative recurrence and disease-free survival (**Fig. 6**).

Gall Bladder Cancer: Patient Outcome and Prognosis

^{18}F-FDG PET/CT may also play a role in the prognosis of patients with gallbladder cancer. Currently, pathologic staging is the best predictive factor for survival in patients with gallbladder cancer.[41,42] In contrast to cholangiocarcinoma, several studies have now established the role of ^{18}F-FDG PET/CT in patient outcome. In a 2014 study of 50 patients with gallbladder cancer who underwent ^{18}F-FDG PET/CT imaging post-treatment by Hwang and colleagues,[43] the investigators concluded that SUVmax data from PET/CT imaging was prognostic and an independent predictor for OS. In the univariate analysis, a SUVmax cutoff of 6.0 was chosen. Patients with SUVmax greater than 6.0 had a median survival of 203 days versus 405 days in patients with SUVmax less than 6.0 (P = .04). In the multivariate analysis, SUVmax was found to have a hazard ratio of 3.05 with a P-value of .04. In a study of 44 patients with gallbladder cancer by Yoo and colleagues,[41] the investigators concluded that TLG, a volume-based metabolic parameter in ^{18}F-FDG PET/CT, was predictive of OS, superior to both MTV and SUV. In the univariate analysis, the mean OS was statistically significantly different with a TLG cutoff of 7090 g. The mean OS with a TLG greater than 7090 g was 36 months, whereas patients with a TLG less than or equal to 7090 g had

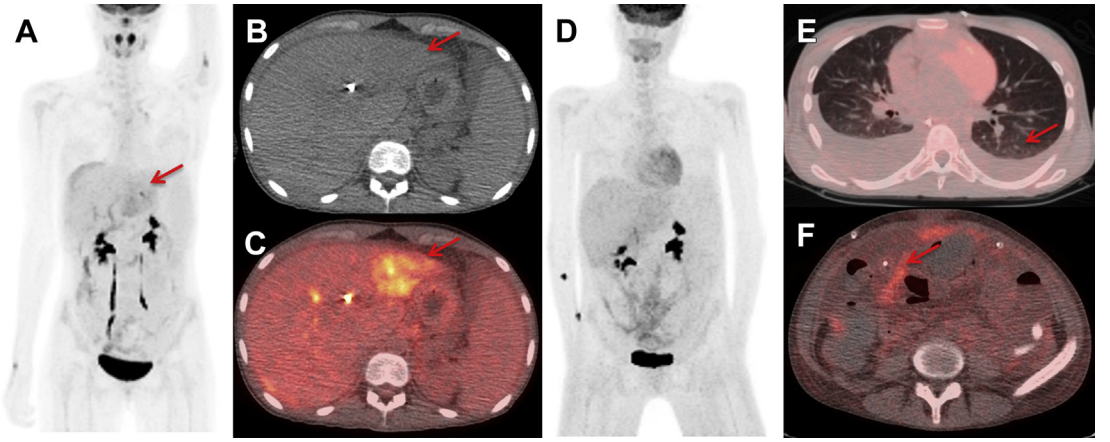

Fig. 6. Cholangiocarcinoma—restaging and prognosis: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of 17-year-old woman with a recent diagnosis of cholangiocarcinoma who underwent a staging ^{18}F-FDG PET/CT study. The study demonstrates a moderately ^{18}F-FDG–avid (SUVmax 3.01) mass in the left lobe of liver (*red arrow*). The patient underwent chemotherapy. Anterior maximum intensity projection (*D*), axial CT (*E*), and axial fused PET/CT (*F*) of the restaging ^{18}F-FDG PET/CT study performed 2 months after the previous study demonstrates progressive disease involving the lungs and extensive omental/peritoneal involvement (*red arrow*). Despite aggressive treatment, the patient died 4 months after the study.

a mean OS of 8 months ($P = .014$). In the multivariate analysis, the hazard ratio for TLG was calculated to be 2.93 with a *P*-value of less than .05. In a study by Butte and colleagues,[38] the investigators concluded that ^{18}F-FDG PET/CT helps offer prognostic information. In 32 patients with incidental gallbladder carcinoma status postcholecystectomy, the findings on ^{18}F-FDG PET/CT correlated with median survival. In patients with a positive ^{18}F-FDG PET/CT showing disseminated disease, the median survival was approximately 4.9 months, whereas patients with a negative ^{18}F-FDG PET/CT had a median survival of 13.5 months. In a study by Redondo and colleagues,[44] the investigators also concluded that ^{18}F-FDG PET/CT holds valuable prognostic information. In 69 patients with incidental gallbladder carcinoma, the median survival in patients with a negative ^{18}F-FDG PET/CT was on average 115.3 months, whereas the medial survival for patients with a positive ^{18}F-FDG PET/CT was 35.3 months. Studies like these help establish ^{18}F-FDG PET/CT as a valuable tool in determining prognosis and survival in patients with gallbladder cancer.[38,41,43,44]

FLUDEOXYGLUCOSE F 18 PET/COMPUTED TOMOGRAPHY IN STAGING AND THERAPY PLANNING OF HEPATOCELLULAR CARCINOMA

Current work-up for diagnosis and staging of HCC includes CT, MR imaging, chest CT, and bone scintigraphy, if clinically indicated.[7] Although several staging systems exist, such as the Okuda system and Barcelona Clinic Liver Cancer classification,[45,46] the AJCC TNM staging remains the most widely accepted system. Over the course of a decade, ^{18}F-FDG PET/CT has shown promise in the staging of liver malignancies by detecting extrahepatic metastasis. ^{18}F-FDG PET alone has been found to offer additional value to CT in identifying regional and distant metastasis, thereby changing therapy planning. In a study of 91 patients diagnosed with HCC by Wudel and colleagues,[47] ^{18}F-FDG PET detected distant metastasis in 5 patients. Ultimately, ^{18}F-FDG PET had an impact in the management plan in 26 of 91 patients with HCC. In a 2007 study of 18 patients with HCC by Yoon and colleagues,[48] ^{18}F-FDG PET detected all extrahepatic metastasis from HCC, including 19 lymph nodes, 12 lung, and 11 bone. ^{18}F-FDG PET was found superior to conventional imaging. Four lymph node metastases and 6 bone metastases were detected by ^{18}F-FDG PET that were not found on CT or MR imaging. Furthermore, ^{18}F-FDG PET changed management in 4 patients. With the addition of CT to provide anatomic localization, ^{18}F-FDG PET/CT has shown useful in detecting extrahepatic disease in patients with HCC. Lee and colleagues[49] found that ^{18}F-FDG PET/CT was more sensitive and specific for bone metastases compared with bone scans. Of the 11 patients with bone metastasis, ^{18}F-FDG PET/CT was found to have an accuracy, SN, and SP of 100%, 100% and 100%, respectively. Conversely, bone scan was found to have an accuracy, SN, and SP of 94.1%, 63.6%, and 96.8%, respectively. ^{18}F-FDG PET/CT was also found valuable in detecting lung

metastasis greater than 1 cm in size. Kawaoka and colleagues[50] also found higher SN with ^{18}F-FDG PET/CT in the detection of bone metastasis compared with both bone scan and MDCT. The sensitivities for ^{18}F-FDG PET/CT, MDCT, and bone scan were 83.3%, 41.6%, and 52.7%, respectively. ^{18}F-FDG PET/CT also had higher SN and SP in the detection of lymph node metastasis: 66.7% and 91.7% for ^{18}F-FDG PET/CT compared with 62.5% and 79.2% for MDCT. Lin and colleagues[51] performed a meta-analysis of 8 studies and concluded that ^{18}F-FDG PET/CT helps rule in extrahepatic metastasis in patients with primary HCC. The investigators calculated pooled SN and SP of 76.6% and 98%, respectively. The positive likelihood ratio was calculated at 14.08 (**Fig. 7**).

Hepatocellular Carcinoma and Colorectal Liver Metastasis: Patient Outcome and Prognosis

^{18}F-FDG PET/CT plays an important role in the prognosis of patients with HCC. Studies have found that the use of ^{18}F-FDG PET/CT can help predict patient OS.[52–55] Xia and colleagues[53] determined that lymph node metastasis detected with ^{18}F-FDG PET/CT was the most important factor for OS. The median survival time for patients with lymph node metastasis was 5 months compared with 12 months for patients without lymph node metastasis (P = .036). In a recent study of 75 patients with cirrhosis and HCC by Sims and colleagues[52] the investigators also found that ^{18}F-FDG PET/CT is a predictor for OS in patients with HCC. In patients with positive ^{18}F-FDG uptake prior to treatment, the median survival was calculated to be 1038 days compared with 387 days in patients with negative ^{18}F-FDG uptake (P = .0079). Park and colleagues[54] studied 68 patients with resectable HCC and found that preoperative PET/CT markers, SUVmax, and tumor to background normal tissue ratios of SUVmax (TNR), were prognostic factors in OS. Increased SUVmax and TNR correlated with decreased OS with P values of .012 and .0005, respectively. Other studies have shown the prognostic value in terms of either OS or RFS of ^{18}F-FDG PET/CT after either radiation therapy or embolization.[56–58]

^{18}F-FDG PET/CT also may play an important role in predicting prognosis and survival in patients with CRLM.[1] Abbadi and colleagues,[59] in a retrospective study, found that staging CRLM by ^{18}F-FDG PET/CT improved OS compared with staging with CT. Survival rates for patients staged with ^{18}F-FDG PET/CT were 79.8% at 3 years and 54.1% at 5 years. Conversely, survival rates for patients staged with CT alone were 54.1% at

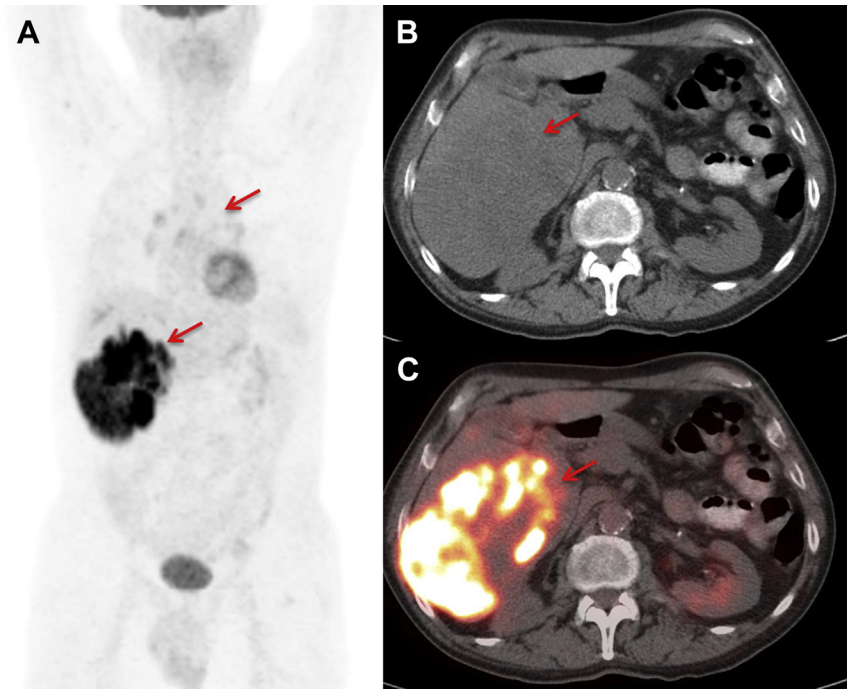

Fig. 7. HCC—staging: anterior maximum intensity projection (*A*), axial CT (*B*), and axial fused PET/CT (*C*) of a 76-year-old man with HCC who underwent a staging ^{18}F-FDG PET/CT study. The study demonstrates a large ^{18}F-FDG–avid (SUVmax 30.1) mass in the right lobe of liver (*red arrows*) with satellite lesions with multiple, moderately ^{18}F-FDG–avid, metastatic mediastinal lymphadenopathy.

Table 5
PET and PET/CT in prognosis and patient outcome in cholangiocarcinoma, gallbladder cancer, hepatocellular carcinoma, and colorectal liver metastasis

Study	N	Study Type	Patients, Treatments	Description
Park et al,[34] 2014	18	Retrospective	Intrahepatic cholangiocarcinoma status post–surgical resection	Positive correlation between PET/CT detection of lymph node metastasis and a 1-y recurrence of carcinoma (P = .02).
Seo et al,[36] 2008	35	Retrospective	Cholangiocarcinoma	Patients with high SUVmax had significantly lower disease-free survival compared with patients with low SUVmax (P = .04). SUV data and lymph node metastasis detection from ^{18}F-FDG PET might be prognostic factors in cholangiocarcinoma for postoperative RFS and disease-free survival.
Hwang et al,[43] 2014	50	Retrospective	Gallbladder cancer postcurative or palliative treatment	SUVmax data from PET/CT imaging was prognostic and an independent predictor for OS. Patients with SUVmax >6.0 had a median survival of 203 d vs 405 d in patients with SUVmax <6.0 (P = .04).
Yoo et al,[41] 2012	44	Retrospective	Gallbladder carcinoma	TLG, a volume-based metabolic parameter in ^{18}F-FDG PET/CT, was predictive of OS, superior to both MTV and SUV. Mean clinical follow-up was 22.2 mo. The mean OS with a TLG >7090 g was 36 mo, whereas patients with a TLG less than or equal to 7090 g had a mean OS of 8 mo (P = .014).
Butte et al,[38] 2009	32	Retrospective	Incidental gallbladder carcinoma status postcholecystectomy	In patients with a positive ^{18}F-FDG PET/CT showing disseminated disease, the median survival was approximately 4.9 mo, whereas patients with a negative ^{18}F-FDG PET/CT had a median survival of 13.5 mo.
Redondo et al,[44] 2012	69	Retrospective	Incidental gallbladder carcinoma	The median survival in patients with a negative ^{18}F-FDG PET/CT was on average 115.3 mo, whereas the medial survival for patients with a positive ^{18}F-FDG PET/CT was 35.3 mo
Xia et al,[53] 2014	132	Retrospective	HCC with extrahepatic metastasis	Lymph node metastasis detected with ^{18}F-FDG PET/CT was the most important factor for OS. The median survival time for patients with lymph node metastasis was 5 mo, compared with 12 mo for patients without lymph node metastasis (P = .036).
Sims et al,[52] 2014	75	Retrospective	HCC and cirrhosis	^{18}F-FDG PET/CT is a predictor for OS in patients with HCC. In patients with positive ^{18}F-FDG uptake prior to treatment, the median survival was calculated to be 1038 d compared with 387 d in patients with negative ^{18}F-FDG uptake (P = .0079).
Abbadi et al,[59] 2014	131	Retrospective	CRLM undergoing hepatectomy	Staging CRLM by ^{18}F-FDG PET/CT improved OS compared with staging with CT. Survival rates for patients staged with ^{18}F-FDG PET/CT were 79.8% at 3 y and 54.1% at 5 y. Conversely, survival rates for patients staged with CT alone were 54.1% at 3 y and 37.3% at 5 y.

3 years and 37.3% at 5 years. Median survival lengths in years were calculated as 6.4 years for PET/CT and 3.9 years for CT alone (P = .018). A few large studies evaluating the value of PET and PET/CT in the prognosis and patient outcome in cholangiocarcinoma, gallbladder cancer, HCC, and CRLM are summarized in **Table 5**.

SUMMARY

Although ^{18}F-FDG PET/CT has not been shown to offer additional benefit in the initial diagnosis of pancreatic cancer, studies show benefit of ^{18}F-FDG PET/CT in staging, particularly in the detection of distant metastasis, and patient prognosis. Likewise, there is good evidence for ^{18}F-FDG PET and ^{18}F-FDG PET/CT in the staging and prognosis of both cholangiocarcinoma and gallbladder cancer. ^{18}F-FDG PET/CT has shown promise in the staging of liver malignancies by detecting extrahepatic metastasis. There is good evidence supporting the ability of PET/CT in predicting prognosis in patients with HCC. There is evolving evidence for ^{18}F-FDG PET/CTs role in predicting prognosis and survival in patients with CRLM.

REFERENCES

1. American Cancer Society. Cancer facts & figures 2014. Atlanta (GA): American Cancer Society; 2014.
2. Michl P, Pauls S, Gress TM. Evidence-based diagnosis and staging of pancreatic cancer. Best Pract Res Clin Gastroenterol 2006;20(2):227–51.
3. Dibble EH, Karantanis D, Mercier G, et al. PET/CT of cancer patients: part 1, pancreatic neoplasms. AJR Am J Roentgenol 2012;199(5):952–67.
4. Marsh Rde W, Hagler KT, Carag HR, et al. Pancreatic panniculitis. Eur J Surg Oncol 2005;31:1213–5.
5. Krejs GJ. Pancreatic cancer: epidemiology and risk factors. Dig Dis 2010;28(2):355–8.
6. National comprehensive cancer network website. NCCN guidelines version 1.2014: pancreatic adenocarcinoma. Available at: www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed July 14, 2014.
7. Hennedige T, Venkatesh SK. Imaging of hepatocellular carcinoma: diagnosis, staging and treatment monitoring. Cancer Imaging 2013;12:530–47.
8. Sacks A, Peller PJ, Surasi DS, et al. Value of PET/CT in the management of liver metastases, part 1. AJR Am J Roentgenol 2011;197:W256–9.
9. Sacks A, Peller PJ, Surasi DS, et al. Value of PET/CT in the management of primary hepatobiliary tumors, part 2. AJR Am J Roentgenol 2011;197:W260–5.
10. Ismaili N. Treatment of colorectal liver metastases. World J Surg Oncol 2011;9:154.
11. Bragazzi MC, Cardinale V, Carpino G, et al. Cholangiocarcinoma: epidemiology and risk factors. Transl Gastrointest Cancer 2012;1:21–32.
12. Davison J, Mercier G, Russo G, et al. PET-based primary tumor volumetric parameters and survival of patients with non-small cell lung carcinoma. AJR Am J Roentgenol 2013;200(3):635–40.
13. Agarwal A, Chirindel A, Shah BA, et al. Evolving role of FDG PET/CT in multiple myeloma imaging and management. AJR Am J Roentgenol 2013;200(4):884–90.
14. Jackson T, Chung MK, Mercier G, et al. FDG PET/CT interobserver agreement in head and neck cancer: FDG and CT measurements of the primary tumor site. Nucl Med Commun 2012;33(3):305–12.
15. Paidpally V, Chirindel A, Lam S, et al. FDG-PET/CT imaging biomarkers in head and neck squamous cell carcinoma. Imaging Med 2012;4(6):633–47.
16. Hadiprodjo D, Ryan T, Truong MT, et al. Parotid gland tumors: preliminary data for the value of FDG PET/CT diagnostic parameters. AJR Am J Roentgenol 2012;198:W185–90.
17. Antoniou AJ, Marcus C, Tahari AK, et al. Follow-up or surveillance 18F-FDG PET/CT and survival outcome in lung cancer patients. J Nucl Med 2014;55(7):1062–8.
18. Karantanis D, Kalkanis D, Czernin J, et al. Perceived misinterpretation rates in oncologic 18F-FDG PET/CT studies: a survey of referring physicians. J Nucl Med 2014;55(12):1925–9.
19. Sridhar P, Mercier G, Tan J, et al. FDG PET metabolic tumor volume segmentation and pathologic volume of primary human solid tumors. AJR Am J Roentgenol 2014;202(5):1114–9.
20. Rijkers AP, Valkema R, Duivenvoorden HJ, et al. Usefulness of F-18-fluorodeoxyglucose positron emission tomography to confirm suspected pancreatic cancer: a meta-analysis. Eur J Surg Oncol 2014;40(7):794–804.
21. Kauhanen SP, Komar G, Seppänen MP, et al. A prospective diagnostic accuracy study of 18F-fluorodeoxyglucose positron emission tomography/computed tomography, multidetector row computed tomography, and magnetic resonance imaging in primary diagnosis and staging of pancreatic cancer. Ann Surg 2009;250(6):957–63.
22. Casneuf V, Delrue L, Kelles A, et al. Is combined 18F-fluorodeoxyglucose-positron emission tomography/computed tomography superior to positron emission tomography or computed tomography alone for diagnosis, staging and restaging of pancreatic lesions? Acta Gastroenterol Belg 2007;70(4):331–8.
23. Lee TY, Kim MH, Park do H, et al. Utility of 18F-FDG PET/CT for differentiation of autoimmune pancreatitis with atypical pancreatic imaging findings from pancreatic cancer. AJR Am J Roentgenol 2009;193(2):343–8.

24. Nakamoto Y, Higashi T, Sakahara H, et al. Delayed (18)F-fluoro-2-deoxy-D-glucose positron emission tomography scan for differentiation between malignant and benign lesions in the pancreas. Cancer 2000;89(12):2547–54.
25. Saif MW, Cornfeld D, Modarresifar H, et al. 18F-FDG positron emission tomography CT (FDG PET-CT) in the management of pancreatic cancer: initial experience in 12 patients. J Gastrointestin Liver Dis 2008; 17(2):173–8.
26. Heinrich S, Goerres GW, Schäfer M, et al. Positron emission tomography/computed tomography influences on the management of resectable pancreatic cancer and its cost-effectiveness. Ann Surg 2005; 242(2):235–43.
27. Topkan E, Parlak C, Yapar AF. FDG-PET/CT-based restaging may alter initial management decisions and clinical outcomes in patients with locally advanced pancreatic carcinoma planned to undergo chemoradiotherapy. Cancer Imaging 2013;13(3):423–8.
28. Asagi A, Ohta K, Nasu J, et al. Utility of contrast-enhanced FDG-PET/CT in the clinical management of pancreatic cancer: impact on diagnosis, staging, evaluation of treatment response, and detection of recurrence. Pancreas 2013;42(1):11–9.
29. Xu HX, Chen T, Wang WQ, et al. Metabolic tumour burden assessed by (1)(8)F-FDG PET/CT associated with serum CA19-9 predicts pancreatic cancer outcome after resection. Eur J Nucl Med Mol Imaging 2014;41(6):1093–102.
30. Lee JW, Kang CM, Choi HJ, et al. Prognostic value of metabolic tumor volume and total lesion glycolysis on preoperative 18F-FDG PET/CT in patients with pancreatic cancer. J Nucl Med 2014;55(6):898–904.
31. Schellenberg D, Quon A, Minn AY, et al. 18Fluorodeoxyglucose PET is prognostic of progression-free and overall survival in locally advanced pancreas cancer treated with stereotactic radiotherapy. Int J Radiat Oncol Biol Phys 2010;77(5): 1420–5.
32. Moon SY, Joo KR, So YR, et al. Predictive value of maximum standardized uptake value (SUVmax) on 18F-FDG PET/CT in patients with locally advanced or metastatic pancreatic cancer. Clin Nucl Med 2013;38(10):778–83.
33. Kim JY, Kim MH, Lee TY, et al. Clinical role of 18F-FDG PET-CT in suspected and potentially operable cholangiocarcinoma: a prospective study compared with conventional imaging. Am J Gastroenterol 2008;103(5):1145–51.
34. Park TG, Schmidt F, Caca K, et al. Implication of lymph node metastasis detected on 18F-FDG PET/CT for surgical planning in patients with peripheral intrahepatic cholangiocarcinoma. Clin Nucl Med 2014;39(1):1–7.
35. Kluge R, Schmidt F, Caca K, et al. Positron emission tomography with [(18)F]fluoro-2-deoxy-D-glucose for diagnosis and staging of bile duct cancer. Hepatology 2001;33(5):1029–35.
36. Seo S, Hatano E, Higashi T, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography predicts lymph node metastasis, P-glycoprotein expression, and recurrence after resection in mass-forming intrahepatic cholangiocarcinoma. Surgery 2008;143(6): 769–77.
37. Leung U, Pandit-Taskar N, Corvera CU, et al. Impact of pre-operative positron emission tomography in gallbladder cancer. HPB (Oxford) 2014;16:1023–30.
38. Butte JM, Redondo F, Waugh E, et al. The role of PET-CT in patients with incidental gallbladder cancer. HPB (Oxford) 2009;11(7):585–91.
39. Ramos-Font C, Gómez-Rio M, Rodríguez-Fernández A, et al. Ability of FDG-PET/CT in the detection of gallbladder cancer. J Surg Oncol 2014;109(3):218–24.
40. Petrowsky H, Wildbrett P, Husarik DB, et al. Impact of integrated positron emission tomography and computed tomography on staging and management of gallbladder cancer and cholangiocarcinoma. J Hepatol 2006;45(1):43–50.
41. Yoo J, Choi JY, Lee KT, et al. Prognostic significance of volume-based metabolic parameters by (18)F-FDG PET/CT in gallbladder carcinoma. Nucl Med Mol Imaging 2012;46(3):201–6.
42. Donohue JH. Present status of the diagnosis and treatment of gallbladder carcinoma. J Hepatobiliary Pancreat Surg 2001;8(6):530–4.
43. Hwang JP, Lim I, Na II, et al. Prognostic value of suvmax measured by fluorine-18 fluorodeoxyglucose positron emission tomography with computed tomography in patients with gallbladder cancer. Nucl Med Mol Imaging 2014;48(2):114–20.
44. Redondo F, Butte J, Lavados H, et al. 18F-FDG PET/CT performance and prognostic value in patients with incidental gallbladder carcinoma. J Nucl Med 2012;53(515):515.
45. Okuda K, Ohtsuki T, Obata H, et al. Natural history of hepatocellular carcinoma and prognosis in relation to treatment. Study of 850 patients. Cancer 1985; 56(4):918–28.
46. Llovet JM, Fuster J, Bruix J, et al. The Barcelona approach: diagnosis, staging, and treatment of hepatocellular carcinoma. Liver Transpl 2004;10(2 Suppl 1):S115–20.
47. Wudel LJ Jr, Delbeke D, Morris D, et al. The role of [18F]fluorodeoxyglucose positron emission tomography imaging in the evaluation of hepatocellular carcinoma. Am Surg 2003;69(2):117–24 [discussion: 124–6].
48. Yoon KT, Kim JK, Kim do Y, et al. Role of 18F-fluorodeoxyglucose positron emission tomography in detecting extrahepatic metastasis in pretreatment staging of hepatocellular carcinoma. Oncology 2007;72:104–10.

49. Lee JE, Jang JY, Jeong SW, et al. Diagnostic value for extrahepatic metastases of hepatocellular carcinoma in positron emission tomography/computed tomography scan. World J Gastroenterol 2012;18(23): 2979–87.
50. Kawaoka T, Aikata H, Takaki S, et al. FDG positron emission tomography/computed tomography for the detection of extrahepatic metastases from hepatocellular carcinoma. Hepatol Res 2009;39(2): 134–42.
51. Lin CY, Chen JH, Liang JA, et al. 18F-FDG PET or PET/CT for detecting extrahepatic metastases or recurrent hepatocellular carcinoma: a systematic review and meta-analysis. Eur J Radiol 2012;81(9): 2417–22.
52. Sims J, Tann M, Baskin M. FDG PET/CT predicts overall survival in patiens with hepatocellular carcinoma. J Nucl Med 2014;54(Supplement 2):1478.
53. Xia F, Wu L, Lau WY, et al. Positive lymph node metastasis has a marked impact on the long-term survival of patients with hepatocellular carcinoma with extrahepatic metastasis. PLoS One 2014;9: e95889.
54. Park J, Lim I, Cho E, et al. Preoperative 18F-FDG PET/CT predicts the overall survival of patients with resectable hepatocellular carcinoma. J Nucl Med 2013;54(Supplement 2):574.
55. Pant V, Sen IB, Soin AS. Role of (1)(8)F-FDG PET CT as an independent prognostic indicator in patients with hepatocellular carcinoma. Nucl Med Commun 2013;34(8):749–57.
56. Sabet A, Ahmadzadehfar H, Bruhman J, et al. Survival in patients with hepatocellular carcinoma treated with 90Y-microsphere radioembolization. Prediction by 18F-FDG PET. Nuklearmedizin 2014; 53(2):39–45.
57. Kucuk ON, Soydal C, Araz M, et al. Prognostic importance of 18F-FDG uptake pattern of hepatocellular cancer patients who received SIRT. Clin Nucl Med 2013;38:e283–9.
58. Huang WY, Kao CH, Huang WS, et al. 18F-FDG PET and combined 18F-FDG-contrast CT parameters as predictors of tumor control for hepatocellular carcinoma after stereotactic ablative radiotherapy. J Nucl Med 2013;54(10):1710–6.
59. Abbadi RA, Sadat U, Jah A, et al. Improved long-term survival after resection of colorectal liver metastases following staging with FDG positron emission tomography. J Surg Oncol 2014;110(3):313–9.