PET/CT in Gall Bladder and Biliary Tract Malignancies

8

Archi Agrawal, Nilendu Purandare, Sneha Shah, Ameya Puranik, and Venkatesh Rangarajan

Contents

8.1 Gall Bladder Cancer 75
8.2 Conventional Imaging Modalities for Diagnosis and Staging of Gall Bladder Cancer 76
8.3 Role of FDG PET/CT in the Evaluation of Gall Bladder Malignancies 76
8.4 Role of FDG PET/CT in Prognostication 79
8.5 Cholangiocarcinoma 80
8.6 Role of Conventional Imaging Modalities 80
8.7 Role of ^{18}F–FDG PET in Diagnosis of the Primary Lesion 80
8.8 Role of ^{18}F–FDG PET in Detection of Lymph Nodal Metastases 82
8.9 Role of ^{18}F–FDG PET in Detection of Distant Metastases 82
References 83

In this chapter we shall discuss the role of positron emission tomography (PET/CT) in biliary tract malignancies—i.e., gall bladder cancer (GBC) and cholangiocarcinoma (CCA). Though carcinoma of ampulla of Vater could also be included here, it will be discussed separately in pancreatic malignancies.

8.1 Gall Bladder Cancer

Gall bladder cancer (GBC) is an aggressive and lethal malignancy and has a very poor outcome. It has a propensity to invade the hepatic parenchyma and the biliary tree resulting in high mortality rate with 5-year survival of less than 5%. It

A. Agrawal (✉) • N. Purandare • S. Shah • A. Puranik • V. Rangarajan
Tata Memorial Hospital, Mumbai, Maharashtra, India
e-mail: drarchi23@gmail.com

© Springer International Publishing AG 2018

N. Purandare, S. Shah (eds.), *PET/CT in Hepatobiliary and Pancreatic Malignancies*, Clinicians' Guides to Radionuclide Hybrid Imaging,
DOI 10.1007/978-3-319-60507-4_8

metastasizes to the lymph nodes, causes peritoneal implants, and also spreads hematogenously. The diagnosis is often delayed due to nonspecific symptoms which are common to benign conditions like cholecystitis and cholelithiasis [1–3]. Most often GBC is discovered incidentally after surgical exploration for suspected benign gall bladder disease. It has been reported that approximately 1% of elective cholecystectomies harbor GBC [3]. More than 98% of GBC are of epithelial origin, and approximately more than 90% are adenocarcinomas. The commonest site within the GB is the fundus (approximately 60%), followed by the body (30%) and the neck (10%) [1].

8.2 Conventional Imaging Modalities for Diagnosis and Staging of Gall Bladder Cancer

Though ultrasonography (USG) is the first and commonest modality used for the detection of GB masses, CT definitely is a better modality for assessment of GB wall thickness and mucosal irregularities [1]. Contract-enhanced CT (CECT) also gives critical information regarding resectability of GB tumors, i.e., local, vascular and organ invasion, and the presence of lymph node metastases. But MRI is more accurate in differentiating benign from malignant GB masses. Magnetic resonance cholangiopancreatography (MRCP) and MR angiography help in diagnosing vascular and biliary invasion which are essential for deciding upon the resectability of GB tumors.

8.3 Role of FDG PET/CT in the Evaluation of Gall Bladder Malignancies

There is paucity of data regarding the use of ^{18}F–fluorodeoxyglucose (FDG) PET/CT in the evaluation of GBC. GBC concentrates FDG avidly and hence appears to have a potential role in staging [4]. FDG PET combined with diagnostic CECT helps in evaluation of the primary mass [Fig. 8.1], in evaluation of adjacent organ invasion (Fig. 8.2), and in detection of regional and metastatic nodal disease and peritoneal and distant metastases (Fig. 8.3). PET/CT is also helpful in demonstrating benign changes like cholangitis (Fig. 8.4), which are commonly seen coexisting with biliary tract malignancy. Ramos-Font et al., in a recent prospective study,

Fig. 8.2 ^{18}F–FDG PET/CT study of a 62-year-old lady showing hypermetabolic GB mass with loss of fat planes with the hepatic flexure of the colon (*arrow* in **a**–**c**) suggesting colonic infiltration

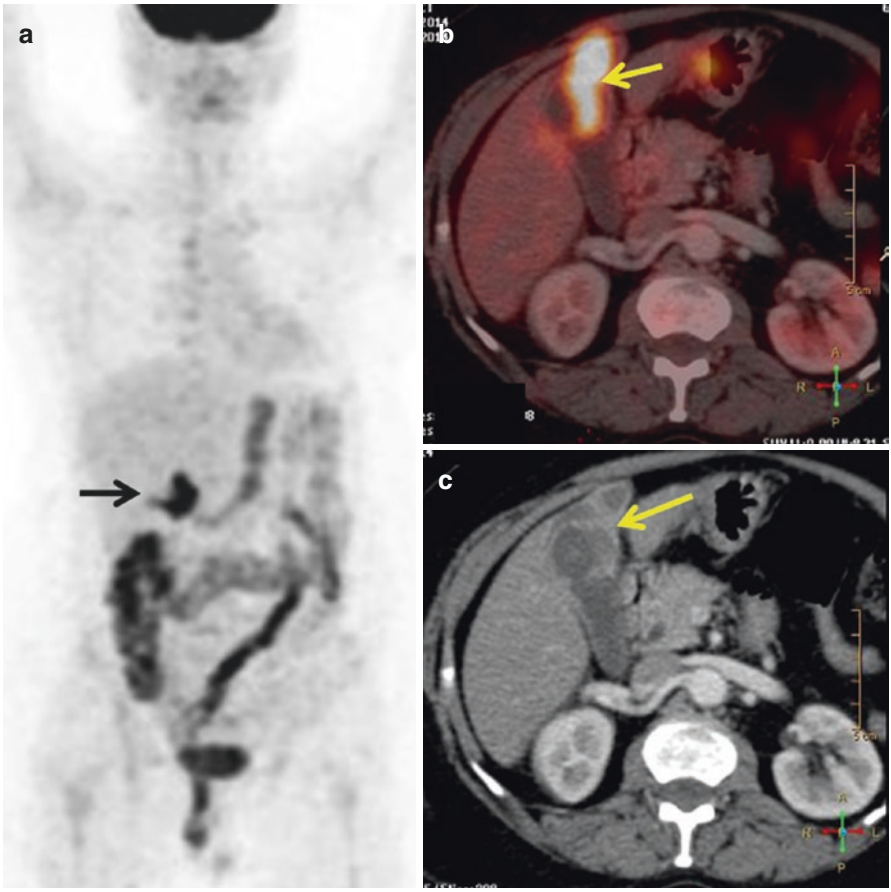
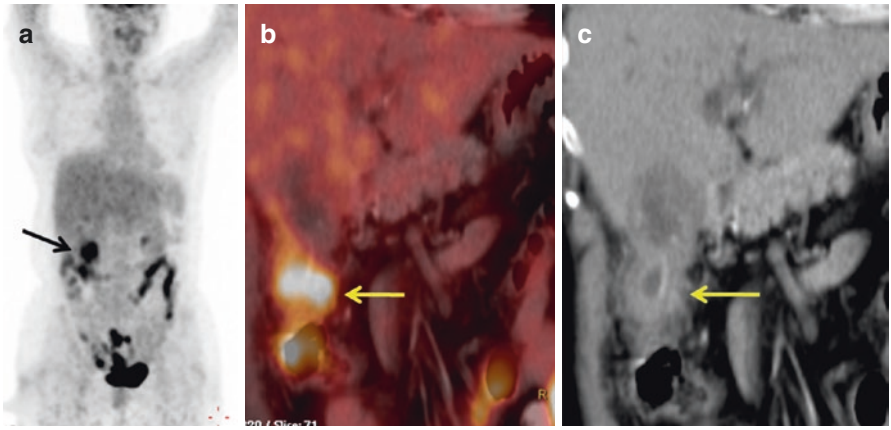


Fig. 8.1 51-year-old lady with suspected gall bladder cancer. ^{18}F–FDG PET/CT shows hypermetabolic mass with maxSUV 13.4 involving the fundus and body of the gall bladder (*arrow* in **a**–**c**). Histopathology post-radical cholecystectomy was adenocarcinoma of the GB



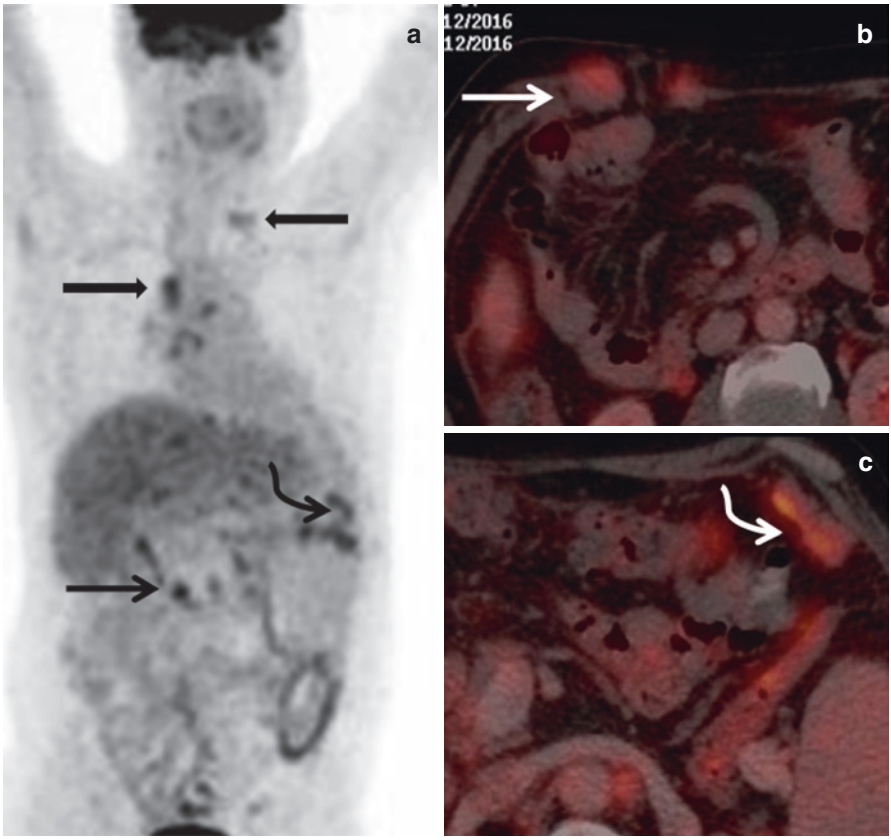


Fig. 8.3 55-year-old male, a case of GB carcinoma post-cholecystectomy. ^{18}F–FDG PET/CT shows hypermetabolic metastatic supraclavicular, mediastinal nodes (*block arrows* in **a**), anterior abdominal wall deposits (*arrow* in **a**, **b**), and peritoneal deposits (*curved arrow* in **a**, **c**)

showed an overall diagnostic accuracy of ^{18}F–FDG PET/CT, of 95.9% for the primary, 85.7% for lymph nodal metastases, and 95.9% for metastatic disease. In the restaging setting, the accuracy was 100%. FDG PET/CT led to change in management in 22.4% of patients [5]. In another study by Leung et al. done on 63 patients with incidental GBC postcholecystectomy, the sensitivity was 56% and specificity was 94%. It led to management change in 8% of patients [6]. PET/CT has also been used to stratify patients with incidentally detected GBC, to the most appropriate treatment depending on the presence or absence of distant metastatic disease [7]. A recent meta-analysis comprising of 13 studies demonstrated a sensitivity of 87% and specificity of 78% with area under curve (AUC) of 0.88 [8].

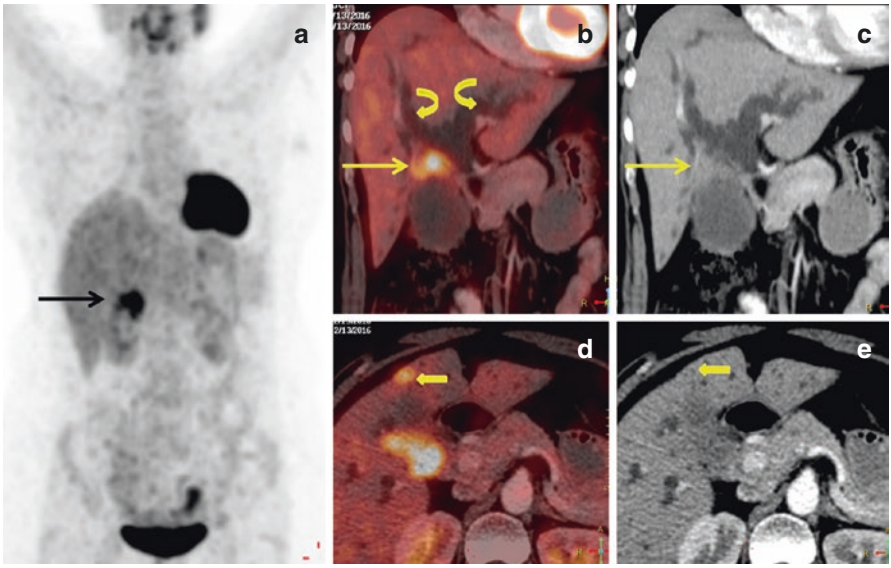


Fig. 8.4 ^{18}F–FDG PET/CT study of a 52-year-old lady with GB cancer. The study shows a hypermetabolic soft tissue mass (maxSUV 9.4) in the neck of the gall bladder (*arrow* in **a**–**c**) with bilateral intrahepatic biliary radical dilatation (*curved arrow* in **b**). The block arrow in **d**, **e** shows a focal hypermetabolic area in segment IVB, which was along the biliary radicals suggesting focal cholangitis (*block arrow*)

8.4 Role of FDG PET/CT in Prognostication

^{18}F–FDG PET/CT has a potential role in prognostication of patients with GBC. It has the ability to gauge the aggressiveness of a tumor based on increased glucose uptake in cancer cells. Hwang et al. demonstrated that maximum SUV (maxSUV) values were prognostic and were an independent predictor of overall survival (OS). They showed that patients with maxSUV <6 had longer survival as compared to patients with maxSUV >6. Also in multivariate analysis, patients with lower maxSUV in the pretreatment study and nonmetastatic disease survived longer [9]. Volume-based metabolic parameters like metabolic tumor volume (MTV) and total lesion glycolysis (TLG) are also prognostic in GBC. In a study by Yoo et al., TLG of the primary GB mass was an independent prognosticator for OS [10]. Also patients with positive FDG PET/CT have a shorter median survival as compared to those with a negative PET/CT study [11].

8.5 Cholangiocarcinoma

Cholangiocarcinomas (CCA) are rare adenocarcinomas (>90%) arising from intrahepatic bile ducts, at the bifurcation of the hepatic ducts or from the distal common bile duct. The commonest form is that which arises from the bifurcation of the hepatic ducts (70%) and is called the Klatskin tumor. They are usually classified as intrahepatic or extrahepatic tumors. Intrahepatic can be further divided into mass forming, periductal, or intraductal based on the pattern of growth [12]. The patient usually is symptomless till an advanced stage is reached, and thus these are often diagnosed in late stage of the disease.

8.6 Role of Conventional Imaging Modalities

USG, CT, and MRI are the imaging modalities of choice for diagnosis and staging. These imaging modalities help in determining the size and extent of the tumor, biliary ductal dilatation, and involvement of regional lymph nodes [13–15]. Endoscopic retrograde cholangiopancreatography (ERCP) helps in obtaining brush cytology and biopsy.

8.7 Role of ^{18}F–FDG PET in Diagnosis of the Primary Lesion

^{18}F–FDG PET/CT has no advantage over these conventional imaging modalities in the diagnosis of CCA [16, 17]. The ability of PET/CT to detect a lesion depends on the location of the lesion. Studies have shown the highest sensitivity in the range of 91–95% and specificity ranging from 80 to 100% for intrahepatic bile duct lesions [18, 19]. This could be due to large tumor size of intrahepatic cholangiocarcinoma as compared to extrahepatic lesions. Another possibility is more accumulation of FDG in the malignant lesion as compared to the surrounding normal hepatocytes, where the turnover of ^{18}F–FDG is faster [20].

The ability of FDG PET to detect cholangiocarcinoma also depends upon the pattern of growth of the lesion—whether mass forming or infiltrative. The sensitivity for detection of a lesion is highest for mass-forming/nodular lesion as compared to periductal or infiltrating lesions [21, 23, 24]. In a study by Anderson et al., they found a sensitivity of 85% for nodular lesions and only 18% for infiltrative lesions [21]. Hilar CCA are well demonstrated on FDG PET/CT and also help in demonstrating intrahepatic biliary dilatation (Figs. 8.5 and 8.6).

In patients with benign inflammatory conditions like primary sclerosing cholangitis, abscesses, and granulomatous diseases, the results of FDG PET/CT should be reported cautiously; these conditions are potential mimics of cholangiocarcinoma. The ability of PET to detect CCA in patients with primary sclerosing cholangitis is debatable [20–22].

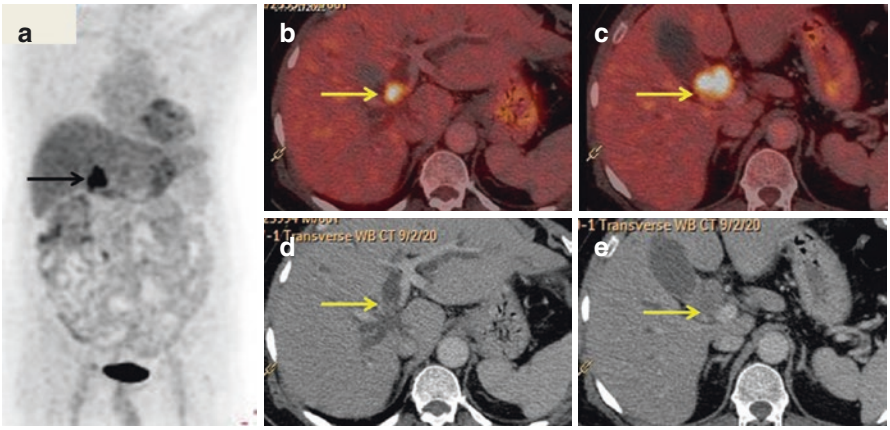


Fig. 8.5 ^{18}F–FDG PET/CT study of a 61-year-old male, diagnosed case of hilar cholangiocarcinoma. The study shows hypermetabolic mass at the confluence of right and left hepatic ducts (*arrow* in **a**–**e**) (maxSUV 13.51) with bilateral IHBR dilatation

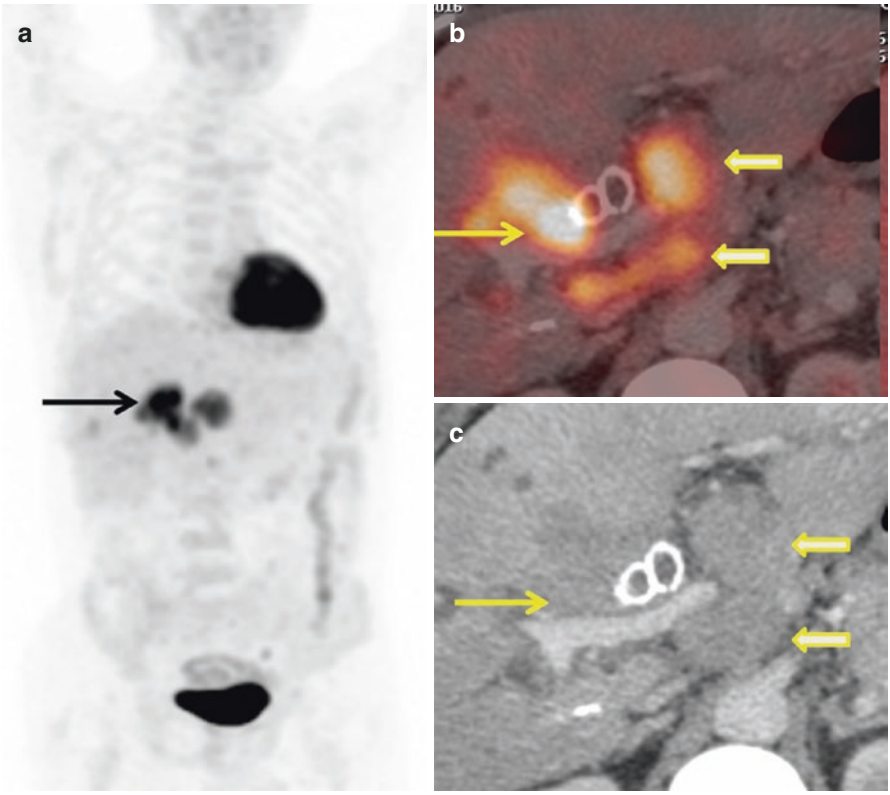


Fig. 8.6 ^{18}F–FDG PET/CT study of a male patient, 57 years, a case of cholangiocarcinoma. Hypermetabolic mass is seen at the hilar confluence (*arrow* **a**–**c**) (maxSUV 10.38) with multiple enlarged periportal lymph nodes (*block arrow*) (maxSUV 8.1)

8.8 Role of ^{18}F–FDG PET in Detection of Lymph Nodal Metastases

PET has a lower sensitivity (38–43%) and greater specificity (95–100%) in detection of involved nodes, as compared to CECT (SN 43–54%, SP 59–76%) [25, 26]. PET has an added advantage of detecting malignant nodes of less than 1 cm size, in contrast to conventional imaging, which is size dependent.

8.9 Role of ^{18}F–FDG PET in Detection of Distant Metastases

PET is highly accurate for the detection of suspected as well as unsuspected distant metastases. It has the ability to detect metastases not detected by conventional imaging modalities. It leads to change in management in up to 30% of patients by detection of distant metastatic lesions [21, 22].

The role of FDG PET/CT in the prediction of prognosis in CCA is not well established.

Key Points

Gall Bladder Cancer

- Gall bladder cancer concentrates FDG avidly and hence appears to have a potential role in staging.
- FDG PET combined with diagnostic CECT helps in evaluation of the primary mass, evaluation of adjacent organ invasion, and detection of regional and nodal and peritoneal and distant metastases.
- Diagnostic accuracy of ^{18}F–FDG PET/CT is 96% for the primary, 86% for lymph nodal metastases, and 96% for metastatic disease.
- ^{18}F–FDG PET/CT has a potential role in prognostication of patients with GBC.
- Maximum SUV (maxSUV) values are reported as an independent predictor of overall survival (OS). (Patients with maxSUV <6 had longer survival as compared to patients with maxSUV >6.)
- Patients with positive FDG PET/CT have a shorter median survival as compared to those with a negative PET/CT study.

Cholangiocarcinoma

- ^{18}F–FDG PET/CT has no advantage over conventional imaging modalities in diagnosis of CCA.

- In the detection of intrahepatic bile duct lesions, the sensitivity is in the range of 91–95% and specificity ranging from 80 to 100%.
- The ability of FDG PET to detect cholangiocarcinoma also depends upon the pattern of growth of the lesion—whether mass-forming or infiltrative.
- PET has a lower sensitivity (38–43%) and greater specificity (95–100%) in detection of involved nodes, as compared to CECT (SN 43–54%, SP 59–76%).
- PET is highly accurate for the detection of suspected as well as unsuspected distant metastases and leads to change in management in up to 30% of patients.
- The role of FDG PET/CT in the prediction of prognosis in CCA is not well established.

References

1. Levy AD, Murakata LA, Rohrmann CA Jr. Gallbladder carcinoma: radiologic-pathologic correlation. Radiographics 2001, 21:295–314.
2. Rodríguez-Fernández A, Gómez-Río M, Medina-Benítez A, Moral JV, Ramos-Font C, Ramia-Angel JM, Llamas-Elvira JM, Ferrón-Orihuela JA, Lardelli-Claret P. Application of modern imaging methods in diagnosis of gallbladder cancer. J Surg Oncol. 2006;93:650–64.
3. Duffy A, Capanu M, Abou-Alfa GK, Huitzil D, Jarnagin W, Fong Y, D'Angelica M, Dematteo RP, Blumgart LH, O'Reilly EM. Gallbladder cancer (GBC):10-year experience at Memorial Sloan-Kettering Cancer Centre (MSKCC). J Surg Oncol. 2008;98:485–9.
4. Agrawal A, Rangarajan V. Appropriateness criteria of FDG PET/CT in oncology. Indian J Radiol Imaging. 2015;25(2):88–101.
5. Ramos-Font C, 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.
6. 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.
7. Goel M, Tamhankar A, Rangarajan V, Patkar S, Ramadwar M, Shrikhande SV. Role of PET CT scan in redefining treatment of incidental gall bladder carcinoma. J Surg Oncol. 2016;113(6):652–8.
8. Annunziata S, Pizzuto DA, Caldarella C, Galiandro F, Sadeghi R, Treglia G. Diagnostic accuracy of fluorine-18-fluorodeoxyglucose positron emission tomography in gallbladder cancer: a meta-analysis. World J Gastroenterol. 2015;21(40):11481–8.
9. Hwang JP, Lim I, Na II, et al. Prognostic value of maxSUV 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.
10. Yoo J, Choi JY, Lee KT, et al. Prognostic significance of volume-based metabolic parameters by (18)FFDG PET/CT in gallbladder carcinoma. Nucl Med Mol Imaging. 2012;46(3):201–6.
11. 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.
12. Blechacz BR, Gores GJ. Cholangiocarcinoma. Clin Liver Dis. 2008;12:131e50.
13. De Groen PC, Gores GJ, LaRusso NF, Gunderson LL, Nagorney DM. Biliary tract cancers. N Engl J Med. 1999;341:1368e78.

14. Gores GJ. Early detection and treatment of cholangiocarcinoma. Liver Transpl. 2000;6:S30e4.
15. Zech CJ, Shoenberg SO, Reiser M, Helmberger T. Cross-sectional imaging of biliary tumors: current clinical status and future developments. Eur Radiol. 2004;14:1174e87.
16. 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;103:1145–51.
17. 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;45:43–50.
18. Moon CM, Bang S, Chung JB, Park SW, Song SY, Yun M, et al. Usefulness of 18F- fluorodeoxyglucose positron emission tomography in differential diagnosis and staging of cholangiocarcinomas. J Gastroenterol Hepatol. 2008;23:759e65.
19. Corvera CU, Blumgart LH, Akhurst T, DeMatteo RP, D'Angelica M, Fong Y, et al. 18F-fluorodeoxyglucose positron emission tomography influences management decisions in patients with biliary cancer. J Am Coll Surg. 2008;206:57e65.
20. Keiding S, Hansen SB, Rasmussen HH, Gee A, Kruse A, Roelsgaard K, et al. Detection of cholangiocarcinoma in primary sclerosing cholangitis by positron emission tomography. Hepatology. 1998;28:700e6.
21. Anderson CD, Rice MH, Pinson CW, Chapman WC, Chari RS, Delbeke D. Fluorodeoxyglucose PET imaging in the evaluation of gallbladder carcinoma and cholangiocarcinoma. J Gastrointest Surg. 2004;8:90–7.
22. Kluge R, Schmidt F, Caca K, Barthel H, Hesse S, Georgi P, et al. Positron emission tomography with [18F]fluoro-2-deoxy-D-glucose for diagnosis and staging of bile duct cancer. Hepatology. 2001;33:1029e35.
23. Nakeeb A, Pitt HA, Sohn TA, et al. Cholangiocarcinoma: a spectrum of intrahepatic, perihilar, and distal tumors. Ann Surg. 1996;224:463–473, discussion 473–475.
24. Jadvar H, Henderson RW, Conti PS. [F-18]Fluorodeoxyglucose positron emission tomography and positron emission tomography: computed tomography in recurrent and metastatic cholangiocarcinoma. J Comput Assist Tomogr. 2007;31:223–8.
25. Kato T, Tsukamoto E, Kuge Y, Katoh C, Nambu T, Nobuta A, et al. Clinical role of [18] F-FDG PET for initial staging of patients with extrahepatic bile duct cancer. Eur J Nucl Med. 2002;29:1047e54.
26. Seo S, Hatano E, Higashi T, Nakajima A, Nakamoto Y, Tada M, 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;143:769e77.