World J Surg (2018) 42:823–834
DOI 10.1007/s00268-017-4192-3

ORIGINAL SCIENTIFIC REPORT

Diagnostic and Prognostic Role of 18-FDG PET/CT in the Management of Resectable Biliary Tract Cancer

Ka Wing Ma[1] · Tan To Cheung[1] · Wong Hoi She[1] · Kenneth Siu Ho Chok[1] · Albert Chi Yan Chan[1] · Wing Chiu Dai[1] · Wan Hang Chiu[3] · Chung Mau Lo[1,2]

Published online: 13 September 2017

Abstract

Objectives Role of 18-FDG PET/CT had been well established in other more prevalent malignancies such as colorectal and lung cancer; however, this is not as well defined in cholangiocarcinoma. Literature focusing on the prognostic values of preoperative PET/CT for resectable cholangiocarcinoma is scarce.

Method This is a retrospective cohort of 66 consecutive patients who had received curative resection for cholangiocarcinoma from 2010 to 2015. All patients had preoperative 18-FDG PET/CT performed. Accuracy of metastatic lymph node detection of PET/CT and the prognostic value of maximum standard uptake value (SUV-max) was explored.

Results There were 38 male and 28 female recruited, and the median age was 66. Intrahepatic cholangiocarcinoma (ICC) constituted the majority (59.1%) of the cases, followed by hilar cholangiocarcinoma (22.8%), gallbladder cancer (13.6%) and common bile duct cancer (4.5%). The 3-year disease-free survival (DFS) and overall survival (OS) of the whole population were 27.1 and 39.2%, respectively. The median follow-up duration was 27 months. The accuracy of PET/CT in metastatic lymph node detection was 72.7% ($P = 0.005$, 95% CI 0.583–0.871) and 81.8% ($P = 0.011$, 95% CI 0.635–0.990) in whole population and ICC subgroup analysis, respectively. SUV-max was shown by multivariate analysis to be an independent factor for DFS ($P = 0.007$ OR 1.16, 95% CI 1.04–1.29) and OS ($P = 0.012$ OR 1.145, 95% CI 1.030–1.273) after resection. SUV-max of 8 was shown to be a discriminant cut-off for poor oncological outcomes in patients with early cholangiocarcinoma (TNM stage I or II) after curative resection (3-year DFS: 21.2 vs. 63.2%, $P = 0.004$, and 3-year OS: 29 vs. 74% $P = 0.048$, respectively).

Conclusion PET/CT is a reliable imaging modality for metastatic lymph node detection in cholangiocarcinoma. Tumour SUV-max is an independent factor for oncological outcomes in patients with resectable disease. For patients who have TNM stage I or II cholangiocarcinoma, tumour SUV-max over 8 is associated with significantly inferior disease-free and overall survival even after curative resection.

Introduction

Cholangiocarcinoma is an uncommon but fatal malignancy of the biliary tract. Over 90% of them were adenocarcinoma. Cholangiocarcinoma can be classified histologically into mass-forming, periductal infiltrative and intraductal growth type [1], and by tumour location, it can be classified into intrahepatic and extrahepatic cholangiocarcinoma. Regardless of the type and location, the prognosis of these tumours remains poor; the 5-year overall survivals are in

✉ Tan To Cheung
tantocheung@hotmail.com

[1] Department of Surgery, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, China

[2] State Key Laboratory for Liver Research, The University of Hong Kong, 102 Pokfulam Road, Hong Kong, China

[3] Department of Radiology, The University of Hong Kong, 102 Pokfulam Road, Hong Kong, China

the order of 30–40% in most series [2–6]. Resection is the only hope of cure; margin status and presence of metastatic lymph node are the two main determinants for recurrence and survival. Preoperative recurrence risk stratification is essential for individualized surgical planning and oncological treatments; however, method for such purpose is scarce. Carcinoembryonic antigen (CEA) [7] and carbohydrate antigen (CA) 19-9 [8–10] were found to be independent factors associated with survival after resection. However, these markers lack specificity as elevation of markers is commonly seen in benign conditions, while it remains normal even in patients with advanced cholangiocarcinoma [11, 12]. Recent research has been focusing on the role of PET/CT in the management of cholangiocarcinoma. It has been shown that PET/CT is superior to CT scan in detecting distant metastasis in cholangiocarcinoma [13]; however, the reported accuracy of PET/CT in metastatic lymph node detection was variable [14–16]. In addition, evidence about the prognostic value of PET/CT in patients with resectable cholangiocarcinoma is limited [17, 18]. This retrospective study served to further elucidate the accuracy of PET/CT in metastatic lymph node detection and the implication of maximum standardized uptake value in the prognosis of resectable cholangiocarcinoma.

Method

Consecutive patient with hepatectomy performed for cholangiocarcinoma with curative intent from January 2010 to March 2015 in Queen Mary Hospital was recruited. In our centre, working diagnosis and management plan of patients with resectable cholangiocarcinoma were made in a multidisciplinary meeting. In this study, all diagnoses were confirmed by experienced pathologist through identification cholangiocarcinoma with or without special immunohistochemical staining (i.e. cytokeratin-7, cytokeratin 20 and TTF-1) in the surgical specimen. Cholangiohepatocellular carcinoma, metastatic adenocarcinoma, carcinoma of the ampulla of Vater, carcinoma of distal common bile duct and pancreatic cancer were excluded from the study. Demographic, biochemical, radiological and operative data of patients were extracted from our

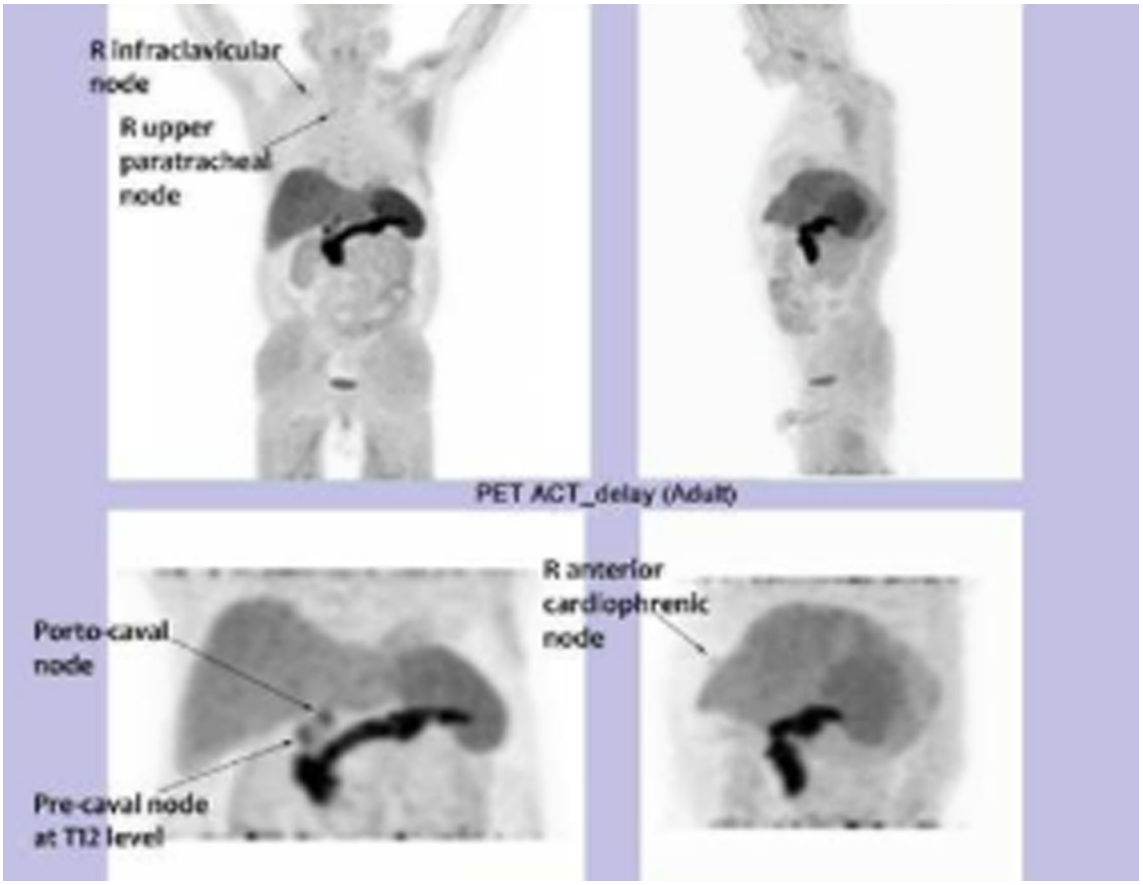

Fig. 1 Regional and distant lymph node detected by PET scan

prospectively maintained database. PET/CT report of each patient was reviewed; data such as the presence of hypermetabolic lymph node (Fig. 1), SUV-max (maximal standard uptake value) (Fig. 2) and metabolic size of the primary tumour were retrieved.

PET/CT predicted lymph node status was correlated with final pathological results; sensitivity, specificity, positive and negative predictive values of PET lymph node prediction were then calculated. Accuracy of the PET/CT in the detection of metastatic regional lymph node and the correlation between SUV-max and oncological outcomes were determined by the area under the receiver operator characteristic (ROC) curve. Cut-off value of SUV-max was determined by the point on ROC curve which corresponds to the highest value of sensitivity and specificity. Continuous variables including SUV-max, CEA, CA19-9, alanine aminotransferase (SGOT) and tumour size were analysed using Mann–Whitney U test or independent *t* test wherever appropriate, while categorical parameter including the presence of PET-positive node, pathological lymph node status and presence of lymphovascular permeation was analysed with Chi-square test/Fisher's exact test whenever appropriate. Factors found to have a significant association (P value <0.05) in univariate analysis were put into multivariate analysis for the identification of independent factors. Kaplan–Meier analysis was used for survival calculation, and the difference of survival was compared using log-rank test. All data were presented as median with a given range unless otherwise specified. P value of <0.05 was considered statistically significant, and all P values were two tails in this article. Statistical Package for the Social Sciences (SPSS) version 20.0 was used for the analytical work.

The PET/CT imaging protocol

Patients in this study had undergone a PET/CT examination within 2 months of hepatectomy. The PET/CT protocol had been previously described [19]. In brief, patients would be kept fast for 6 h before examination. After normoglycemia checked, 18-F FDG with the dosage of 6.3 MBq/kg of body weight (330–520 MBq) was injected. Limited whole body PET/CT (from skull base to mid-thigh) was performed at 60 min after injection of 18-F FDG. Data acquisition with an integrated in-line PET/CT scanner (Biograph LSO or Biograph 16 LSO HI-REZ; Siemens) started with non-contrast CT scanning (130 kV, 110–115 mA, 2-mm pitch and 1-s tube rotation) followed by PET of a 2-min emission acquisition time and a 16.2-cm axial field of view per position. All PET/CT images were interpreted and reported by radiologists with extensive experience in the field of nuclear medicine. SUV-max was compared with the baseline liver parenchymal and lymph node metabolic activity. The metabolic size of lesion and whether the metabolic activities of lymph nodes were up to a suspicious level rested on the reporting radiologist's discretion.

Technical aspect and follow-up of hepatectomy

The technical details of hepatectomy in our centre had been described in another report [20]. In short, all patients would have indocyanine green clearance (ICG) test and CT volumetric assessment before major liver resection. The maximum ICG-R15 (ICG retention in 15 min) for major liver resection was 22%, while the future liver remnant should be no less than 25% of the estimated standard liver volume by HKU formula in usual circumstances [21]. Major hepatectomy referred to resection of more than 3 Couinaud's liver segments. Frozen section would be taken at resection margin of bile duct whenever possible, until clear margin status is achieved. Margin status is classified into three categories according to pathologist comments (R0 margin width over 1 mm or above, R1 margin width less than 1 mm, R2 margin involved by tumour). Patient

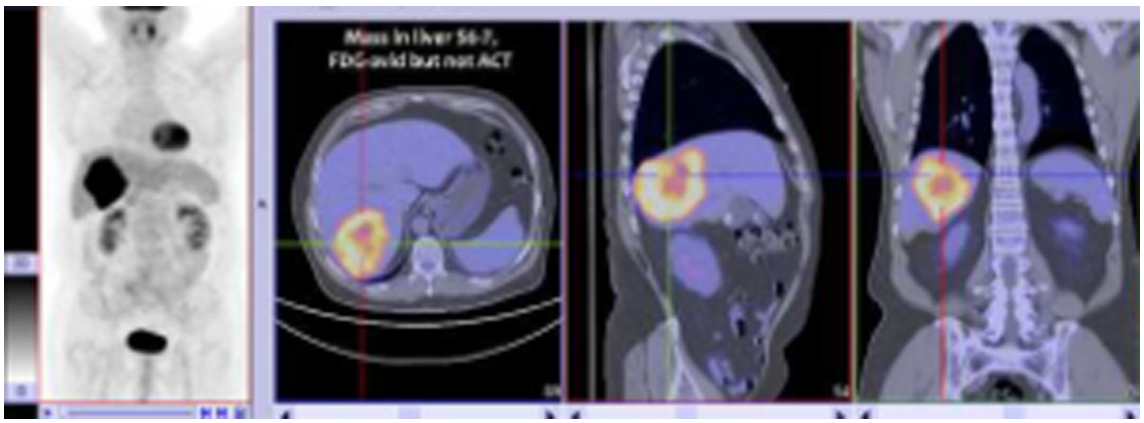

Fig. 2 Intrahepatic cholangiocarcinoma appears as hypermetabolic lesion on PET scan

Table 1 Baseline demographic and biochemical characteristics of the whole study population

Total number of patients (n)	66
Age (year)	66 (35–84)
Sex (M:F)	38:28
Presence of comorbidity (%)	37 (56.1%)
Hepatitis B carrier	13 (19.7%)
Child–pugh score	5 (5–8)
Haemoglobin (g/dl)	12.4 (7.6–15.5)
White cell count ($\times 10^6$)	6.5 (1.3–21.7)
Bilirubin (umol/l)	10 (3–94)
Albumin (g/l)	40 (24–47)
Alkaline phosphatase (u/l)	108 (38–897)
Aspartate aminotransferase (u/l)	32 (14–150)
Prothrombin time (s)	11.5 (10–14.7)
Carcinoma embryonic antigen, CEA (ng/ml)	3.2 (0.5–145)
Cancer antigen, CA 19.9 (ng/ml)	82.5 (2–4070)
Metabolic tumour size (mm)	42 (22–130)
Maximum standard uptake value (SUV-max)	7.8 (2.5–20.5)
Nodal metastasis on PET/CT	22 (33.3%)

Table 2 Operative findings and outcomes

Total number of patient (n)	66
Operation duration (min)	468.5 (144–1026)
Blood loss (ml)	887 (50–2700)
Operative procedure	
Right hepatectomy	22
Left hepatectomy	13
Extended left hepatectomy	3
Right trisectionectomy	3
Left trisectionectomy	2
Left lateral sectionectomy	1
Hepaticopancreaticoduodenectomy	1
Others	11
Hospital mortality	4 (6%)
Hospital length of stay (day)	12 (4–85)

could be discharged home around 1–2 weeks depending on individual progress of recovery. Outpatient follow-up would be scheduled at 2 weeks after discharge, then 1 month later and 3 monthly thereafter. Biochemical tests including liver function test, CEA and CA 19-9 would be monitored, and contrasted cross-sectional imaging was arranged 3 months and then every half yearly after operation. Recurrence is defined histologically by liver or lymph node biopsy or radiologically by the presence of intrahepatic or extrahepatic tumour.

Table 3 Tumour characteristics after pathological examination

Diagnosis (total)	66
Intrahepatic cholangiocarcinoma	39
Hilar cholangiocarcinoma	15
Carcinoma of common bile duct	9
Carcinoma of gallbladder	3
Tumour size (cm)	4.5 (1.2–13)
Lymphovascular permeation	29 (43.9%)
Margin (mm)	4 (0–25)
Margin status	
R0	78.8%
R1	3
R2	18.2%
Degree of tumour differentiation	
Well differentiated	7 (10.6%)
Moderately differentiated	43 (65.2%)
Poorly differentiated	12 (18.2%)
Metastatic lymph node (%)	21 (31.8%)
TNM staging (7th edition)	
I	25 (37.9%)
II	19 (28.8%)
III	1 (1.5%)
IV	19 (28.8%)

Results

There were 66 patients (39 intrahepatic cholangiocarcinoma, 15 hilar cholangiocarcinoma, 9 gallbladder cancer and 3 carcinoma of common bile duct) eligible for the study. In this series, 28 patients were female and 38 were male; the median age was 66 year old. In total, 37 (56.1%) of them had one or more medical comorbidities before hepatectomy. Hepatitis B status was positive in thirteen patients, and one patient was a hepatitis C carrier. Majority of the patients were non-cirrhotic, and the median preoperative haemoglobin, bilirubin, albumin and CEA level was 12.4 g/dl, 10 μmol/l, 40 g/l and 3.2 ng/ml, respectively (Table 1).

Operative findings and tumour characteristics

Majority of patients underwent right hepatectomy, followed by left hepatectomy (Table 2). The median operation time and blood loss were 469 min and 887 ml, respectively. None of the patient required intraoperative blood transfusion. The median hospital length of stay was 13 days. There were four hospital mortalities (6.1%). The median tumour size was 5 cm. R0 resection was achieved in 78.8%, while R2 and R1 resection was found in 18.2 and 3% of the patient, respectively. Lymphovascular permeation was found in more than half of our patients (43.9%).

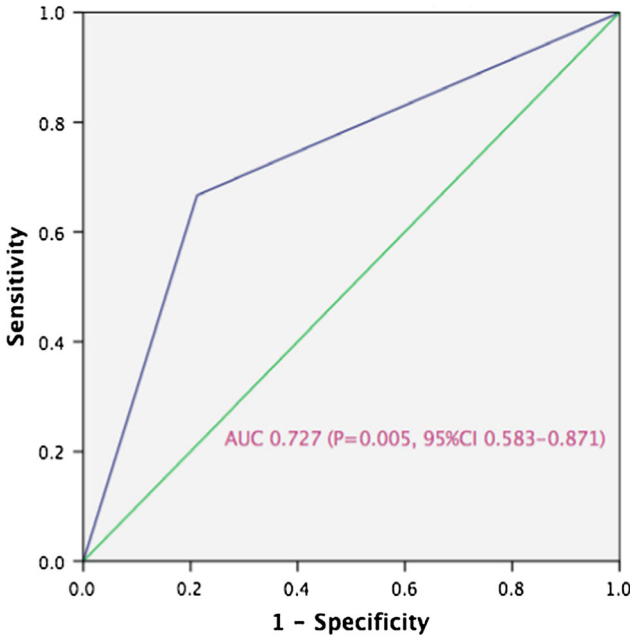

Fig. 3 Receiver operating characteristic curve showing the predictive value of PET/CT for metastatic lymph node

	Pathological positive LN	Pathological negative LN
PET positive LN met	14	7
PET negative LN met	7	26

Sensitivity	Specificity	Positive predictive value	Negative predictive value
66.7%	78.8%	66.7%	78.8%

Out of the 54 patients with pathological lymph node examination, metastatic adenocarcinoma was detected in 21 patients (31.8%). Most of our patients had either TNM stage I or II disease (Table 3), and 29 patients were given adjuvant chemotherapy after the operation. In total, 38 patients developed recurrence upon the date of analysis. The 1- and 3-year disease-free survival was 47.2 and 27.1%, respectively, while the 1- and 3-year overall survival was 67.4 and 39.2%, respectively. The median follow-up time was 27 months.

Diagnostic and prognostic ability of PET/CT

The median metabolic size of tumour was 42 mm (2.2–130). In total, 22 patients were suggested to have metastatic lymph node on PET/CT, and the rest of them had either "reactive" lymph nodes or "no metastatic lymph node". Pathological examination of lymph node was performed in 54 patients, and the pathological assessment of lymph node was correlated with preoperative PET findings. The sensitivity, specificity, positive predictive value and negative predictive value were 66.7, 78.8, 66.7 and 78.8%, respectively ($P = 0.001$). The area under receiver operating characteristic (ROC) curve for metastatic LN prediction was 0.727 ($P = 0.005$, 95% CI 0.583–0.871) (Fig. 3). When the analysis was repeated in intrahepatic cholangiocarcinoma subgroup, the accuracy of metastatic LN prediction increased to 81.3% ($P = 0.011$, 95% CI 0.635–0.990) (Fig. 4).

Prognostic significance of primary tumour SUV-max in cholangiocarcinoma patient

The median SUV-max of the primary tumour was 7.8 (2.5–20.5). Univariate analysis showed that white cell count ($P = 0.006$), albumin ($P = 0.02$), carcinoembryonic antigen ($P = 0.037$), lymphovascular invasion ($P = 0.042$), pathological lymph node status, TNM staging ($P = 0.003$) and SUV-max ($P = 0.016$) were factors associated with

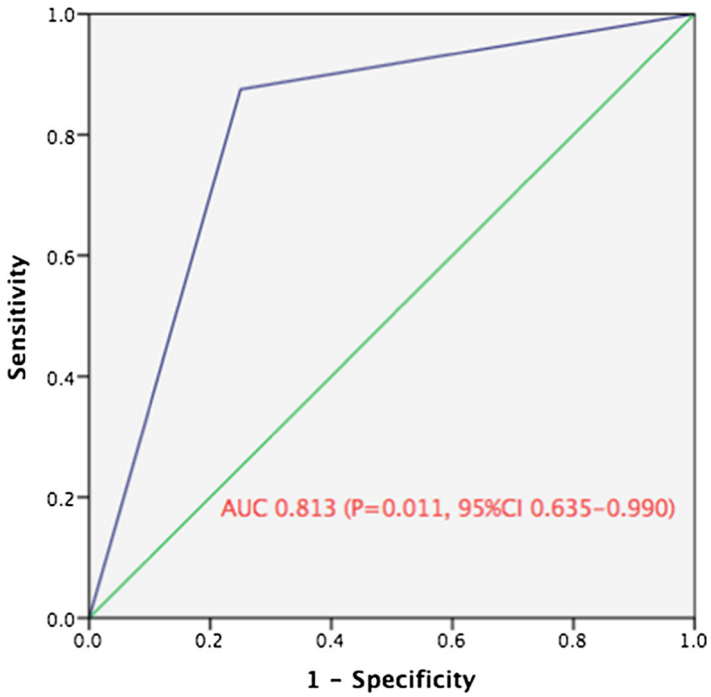

Fig. 4 Receiver operating characteristic curve showing the predictive value of metastatic lymph node in intrahepatic cholangiocarcinoma

	Pathological positive LN	Pathological negative LN
PET positive LN met	7	5
PET negative LN met	1	15

Sensitivity	Specificity	Positive predictive value	Negative predictive value
87.5%	75.0%	58.3%	93.8%

disease-free survival. In multivariate analysis, TNM staging ($P < 0.001$ OR 1.881, 95% CI 1.318–2.685) and SUV-max of tumour ($P = 0.007$ OR 1.16, 95% CI 1.04–1.29) were the only independent factors of disease recurrence (Table 4). Concerning overall survival, SUV-max ($P = 0.001$), leucocyte count ($P = 0.003$), albumin ($P = 0.001$), aspartate transaminase ($P = 0.025$), CEA ($P = 0.006$), metabolic tumour size ($P = 0.019$), pathological tumour size ($P = 0.017$), presence of nodal metastasis ($P = 0.035$) and TNM staging ($P = 0.006$) showed association in univariate analysis; multivariate analysis revealed that presence of metastatic lymph node ($P = 0.037$ OR 3.211 95% CI 1.070–9.634) and SUV-max of tumour ($P = 0.012$ OR 1.145, 95% CI 1.030–1.273) were independent preoperative factors for overall survival (Table 5).

Prognostic cut-off value of SUV-max of primary tumour and subgroup analysis

Statistically significant association between disease-free, overall survival and SUV-max value was demonstrated in the whole population analysis (AUC 0.66.9, $P = 0.022$ 95% CI 0.538–0.800, and AUC 0.698, $P = 0.006$ 95% CI 0.571–0.826, respectively) (Fig. 5a, b). In subgroup analysis of patients with early disease, i.e. TNM stage I or II, SUV-max was shown to have high predictive value for disease-free and overall survival (AUC 0.747, $P = 0.006$ 95% CI 0.600–0.894, and AUC 0.741, $P = 0.012$ 95% CI 0.590–0.892, respectively) (Fig. 6a, b). SUV-max cut-off of 8 was determined with ROC curve, and we found that this SUV-max cut-off had a high predictive accuracy for disease-free survival (AUC 0.723, $P = 0.013$ 95% CI 0.567–0.879) and overall survival (AUC 0.721, $P = 0.018$ 95% CI

Table 4 Univariate and multivariate analysis for factors associated with disease-free survival

Factors	Univariate analysis	Multivariate (cox regression)
SUV-max	0.001	0.025 (OR 1.089, 95% CI 1.011–1.174)
White cell count	0.006	NS
Bilirubin	0.458	NS
Albumin	0.020	NS
SGOT	0.051	NS
Prothrombin time	0.060	NS
CEA	0.037	NS
CA19-9	0.594	NS
Tumour size (PET)	0.151	NS
Actual tumour size	0.150	NS
Tumour differentiation	0.700	NS
Margin status	0.348	NS
Margin width	0.069	NS
Lymphovascular permeation	0.042	NS
Pathological LN	0.016	NS
TNM staging	0.003	<0.001 (OR 1.881, 95% CI 1.318–2.685)
Adjuvant treatment	0.353	NS

Table 5 Univariate and multivariate analysis for factors associated with overall survival

Factors	Univariate analysis	Multivariate (cox regression)
SUV-max	0.001	0.012 (OR 1.145, 95% CI 1.030–1.273)
White cell count	0.003	NS
Bilirubin	0.318	NS
Albumin	0.001	NS
SGOT	0.025	NS
Prothrombin time	0.594	NS
CEA	0.006	NS
CA19-9	0.342	NS
PET functional size	0.019	NS
Tumour size	0.017	NS
Tumour differentiation	0.733	NS
Margin status	0.773	NS
Margin width	0.056	NS
Lymphovascular permeation	0.071	NS
Metastatic lymph node	0.035	0.037 (OR 3.211 95% CI 1.070–9.634)
TNM staging (7th ed.)	0.006	NS
Adjuvant treatment	0.217	NS

0.561–0.881) (Fig. 7a, b). Kaplan–Meier analysis showed that patients with primary tumour SUV-max value over 8 had significantly lower 3-year disease-free and overall survival (21.2 vs. 63.2%, $P = 0.004$, and 29 vs. 74% $P = 0.048$, respectively) (Fig. 8a, b).

Resectable ICC was defined as R0 or R1 resection margin in the final pathology. In the 32 patients with resectable ICC, the median SUV-max of this group was 9, and the median disease-free survival and overall survival were 9.5 and 14 months, respectively. ROC curve showed that the value of SUV-max of primary tumour predicts survival outcomes (Fig. 9a, b). Patients with primary tumour SUV-max less than 8 were shown to have significantly better 3-year disease-free survival (55.6 vs. 13.4%) and a tendency of better 3-year overall survival (67.7 vs. 34.8%) (Fig. 10a, b).

Discussion

This study conveyed two important messages about the role of PET/CT in management of cholangiocarcinoma; firstly, it is an accurate imaging modality to predict the presence of metastatic lymph node in patients with cholangiocarcinoma, and the predictability is even higher in patients with intrahepatic cholangiocarcinoma. In a small series of intrahepatic cholangiocarcinoma, Park et al. found that the sensitivity and specificity of PET/CT in detecting metastatic lymphadenopathy were 80 and 92%, respectively [16]; in contrast, Kluge R et al. doubted this role as only 2 out of the 15 node-positive cholangiocarcinoma patients were detected by PET/CT in their series [15]. There seemed to be an intrinsic metabolic difference between the metastatic lymph node from intrahepatic and extrahepatic cholangiocarcinoma. Secondly, SUV-max value of the primary tumour is an independent factor for survival outcomes in all cholangiocarcinoma patients, and SUV-max cut-off of 8 is a prognostic indicator for patients with early disease (TNM stage I and II). These findings are useful in the perioperative management planning. Although conflicting is the role of neoadjuvant therapy in the management of cholangiocarcinoma in terms of local disease control and long-term survival benefits [22, 23], it should be considered in patients who have high primary tumour SUV-max (cut-off > 8) and presence of PET-positive lymph nodes. In case of intrahepatic cholangiocarcinoma where lymphadenectomy is not a routine procedure, the presence of PET-positive regional lymph node should indicate lymph node dissection so as to facilitate pathological staging and reduce the local recurrence rate in case of genuine nodal disease [24, 25]. For patients with low

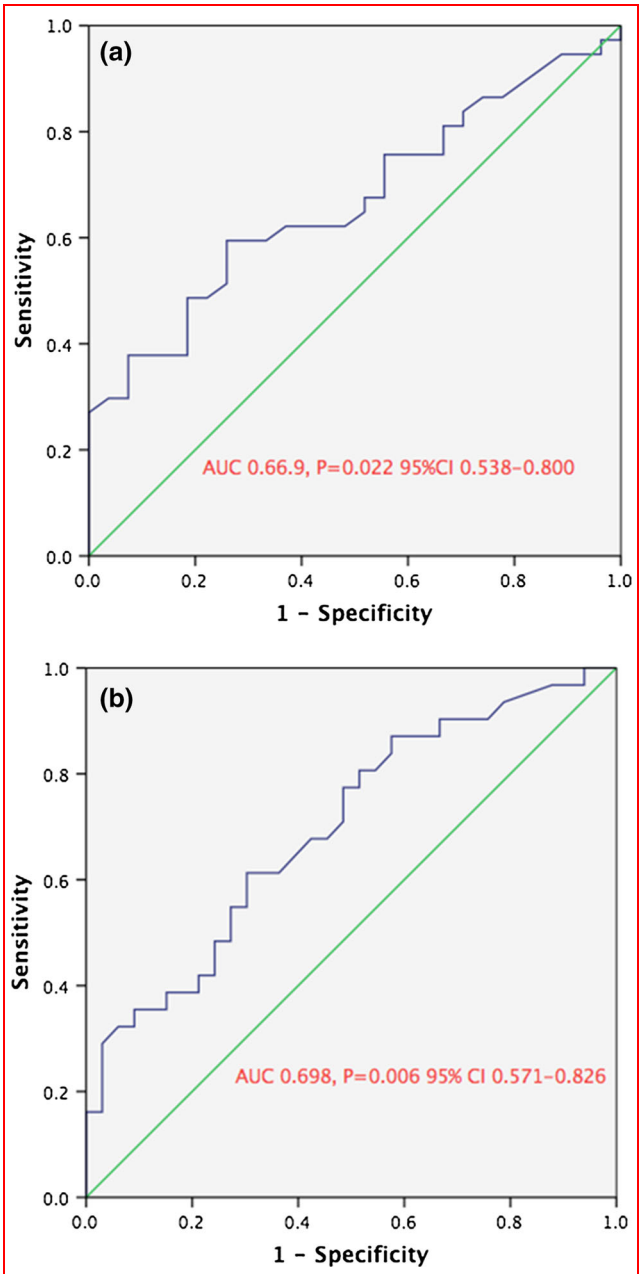

Fig. 5 **a** Receiver operating characteristic curve showing the predictive value of tumour SUV-max to disease-free survival. **b** Receiver operating characteristic curve showing the predictive value of tumour SUV-max to overall survival

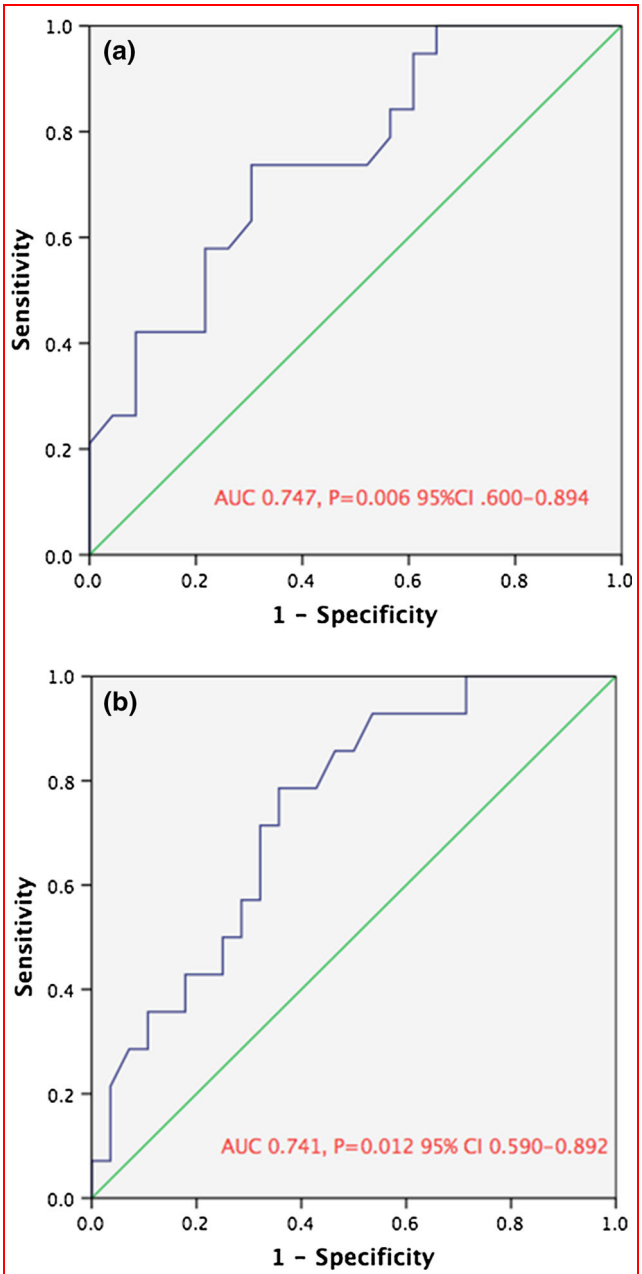

Fig. 6 **a** Receiver operating characteristic curve showing the predictive value of tumour SUV-max to disease-free survival in patients with stage I or II disease. **b** Receiver operating characteristic curve showing the predictive value of tumour SUV-max to overall survival in patients with stage I or II disease

SUV-max and absence of suspicious hypermetabolic lymph node on PET/CT, aggressive surgery to obtain R0 resection and a wider negative margin (over 1 cm) could benefit survival particularly in patients with intrahepatic cholangiocarcinoma [26]. Furthermore, aggressive hepatic operation with radical lymphadenectomy is less justified in patients who have high primary tumour SUV-max, predicted distant lymph node spread and marginal physiological reserve. Despite the fact that the role of adjuvant treatment in resectable cholangiocarcinoma remains to be defined [27–29], SUV-max can serve as an extra point of consideration, in addition to the conventional tumour characteristics, before contemplating adjuvant treatment.

Apart from SUV-max, metabolic tumour volume (MTV) and total lesion glycolysis (TLG) are the two more

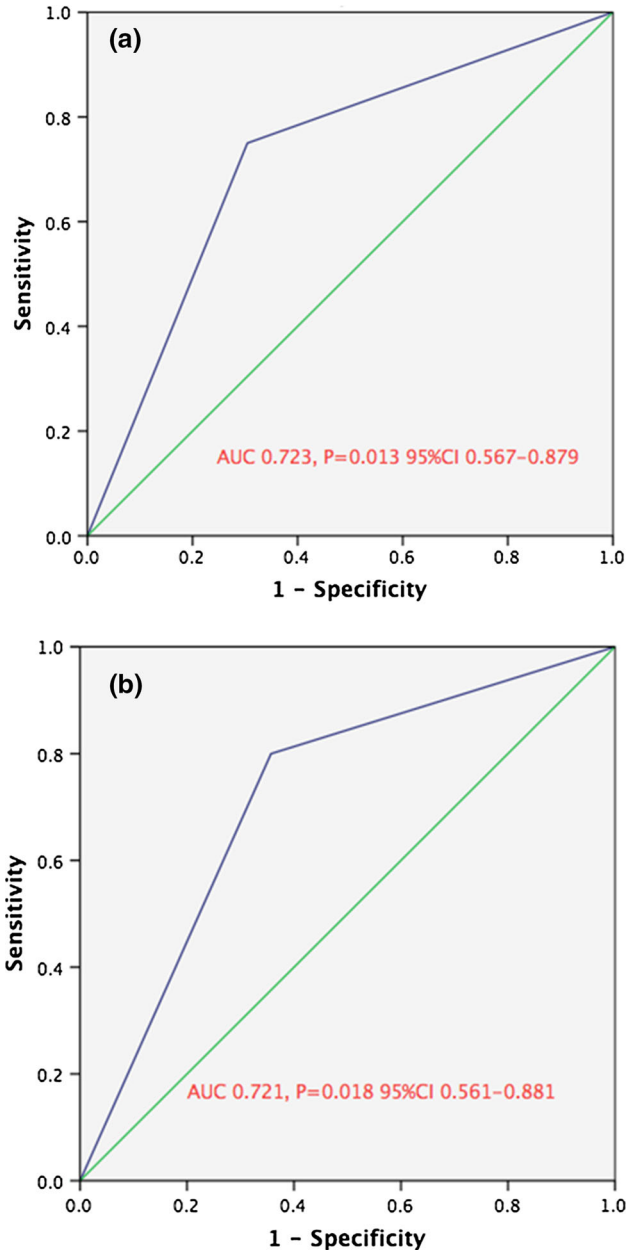

Fig. 7 **a** Receiver operating characteristic curve showing the predictive value of tumour SUV-max over 8 with respect to disease-free survival. **b** Receiver operating characteristic curve showing the predictive value of SUV-max over 8 with respect to overall survival

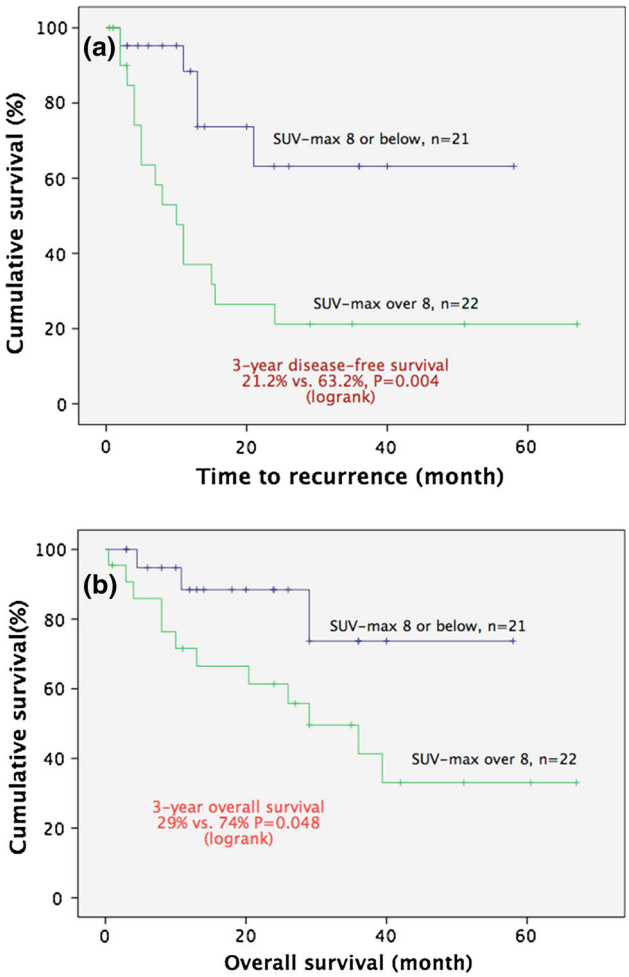

Fig. 8 **a** Kaplan–Meier curve showing the disease-free survival in patients with stage I or II cholangiocarcinoma. **b** Kaplan–Meier curve showing the overall survival of patients with stage I or II cholangiocarcinoma

sophisticated PET parameters that were shown to reflect viable tumour bulk [30]. In pancreatic cancer, it had been reported that MTV and TLG are superior prognostic parameters when compared to cancer antigen 19.9 (CA 19.9), tumour size and SUV-max [31]. However, these calculations are not routinely performed as MTV and TLG require manual tumour mapping and that could tedious and time-consuming. Use of automated volumetric study and the adaptive threshold for SUV-max calculation (tumour to background metabolic gradient) were suggested solutions for such drawbacks [32]. Nonetheless, the role of MTV and TLG in the management of cholangiocarcinoma remains to be elucidated as there is very limited study in this context [33].

There are a few weaknesses in the present study. Firstly, retrospective nature of the analysis inevitably confounded by selection bias and missing data. Consecutive patient recruitment and use of multivariate analysis in this study would have alleviated this inherent weakness of retrospective study; secondly, low incidence of cholangiocarcinoma limited the case volume of study, and this is the Achilles heel in the study of uncommon disease. Furthermore, inter-observer variability in the PET interpretation and SUV calculation could not be excluded. It has been reported that scanner calibration, synchronization between

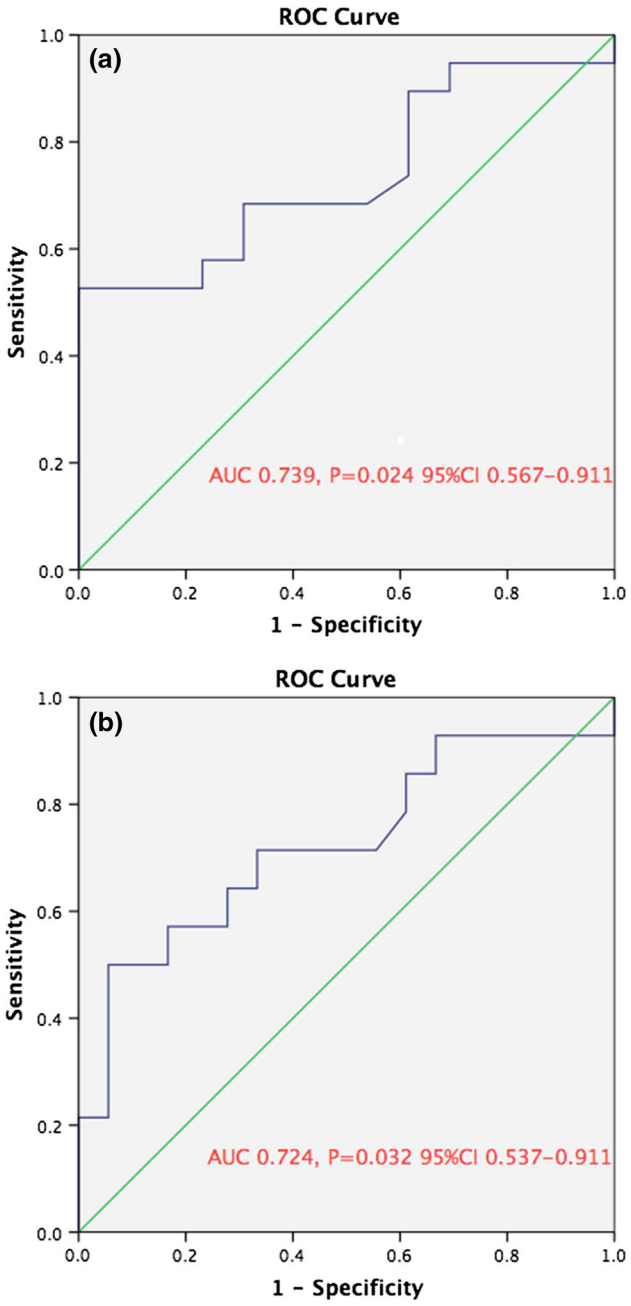

Fig. 9 **a** Receiver operating characteristic curve showing the predictive value of SUV-max to recurrence in patients with resectable ICC. **b** Receiver operating characteristic curve showing the predictive value of SUV-max to overall survival in patients with resectable ICC

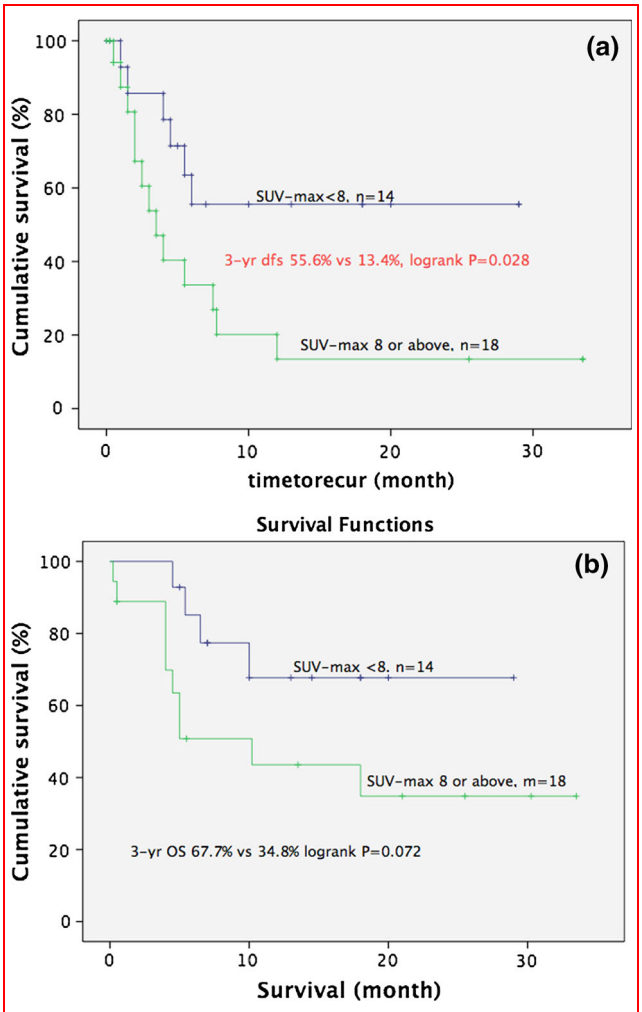

Fig. 10 **a** Kaplan–Meier curve showing the difference in disease-free survival of ICC patients with SUV-max cut-off of 8. **b** Kaplan–Meier curve showing the difference in overall survival of ICC patients with SUV-max cut-off at 8

machine and injector, partial volume effect, imaging reformation protocol, patient body weight and serum glucose level, image acquisition time and definition of region of interest can all influence the precision of SUV-max [33–35]. Nonetheless, the findings of the current study provide important information to future multicenter study or meta-analysis on the area of PET and cholangiocarcinoma.

Conclusion

PET/CT is a reliable imaging modality for metastatic lymph node detection in cholangiocarcinoma. Tumour SUV-max is an independent factor for oncological outcomes in patients with resectable disease. For patients who have TNM stage I or II cholangiocarcinoma, tumour SUV-max over 8 is associated with significantly inferior disease-free and overall survival even after curative resection.

Compliance with ethical standards

Conflict of interest There is no conflict of interest of disclosures.

References

1. Lim JH (2003) Cholangiocarcinoma: morphologic classification according to growth pattern and imaging findings. Am J Roentgenol 181(3):819–827
2. Akamatsu N, Sugawara Y, Hashimoto D (2011) Surgical strategy for bile duct cancer: advances and current limitations. World J Clin Oncol 2(2):94–107
3. Shimada K, Sano T, Nara S, Esaki M, Sakamoto Y, Kosuge T et al (2009) Therapeutic value of lymph node dissection during hepatectomy in patients with intrahepatic cholangiocellular carcinoma with negative lymph node involvement. Surgery 145(4):411–416
4. Choi S-B, Kim K-S, Choi J-Y, Park S-W, Choi J-S, Lee W-J et al (2009) The prognosis and survival outcome of intrahepatic cholangiocarcinoma following surgical resection: association of lymph node metastasis and lymph node dissection with survival. Ann Surg Oncol 16(11):3048
5. Nakagohri T, Kinoshita T, Konishi M, Takahashi S, Gotohda N (2008) Surgical outcome and prognostic factors in intrahepatic cholangiocarcinoma. World J Surg 32(12):2675–2680. doi:10.1007/s00268-008-9778-3
6. Paik KY, Jung JC, Heo JS, Choi SH, Choi DW, Kim YI (2008) What prognostic factors are important for resected intrahepatic cholangiocarcinoma? J Gastroenterol Hepatol 23(5):766–770
7. Yi B, Zhang B-H, Zhang Y-J, Jiang X-Q, Zhang B-H, Yu W-L et al (2004) Surgical procedure and prognosis of hilar cholangiocarcinoma. Hepatobiliary Pancreat Dis Int HBPD INT 3(3):453–457
8. Huang JL, Biehl TR, Lee FT, Zimmer PW, Ryan JA (2004) Outcomes after resection of cholangiocellular carcinoma. Am J Surg 187(5):612–617
9. Ohtsuka M, Ito H, Kimura F, Shimizu H, Togawa A, Yoshidome H et al (2002) Results of surgical treatment for intrahepatic cholangiocarcinoma and clinicopathological factors influencing survival. Br J Surg 89(12):1525–1531
10. Heimbach JK, Gores GJ, Haddock MG, Alberts SR, Pedersen R, Kremers W et al (2006) Predictors of disease recurrence following neoadjuvant chemoradiotherapy and liver transplantation for unresectable perihilar cholangiocarcinoma. Transplantation 82(12):1703–1707
11. Miwa S, Miyagawa S, Kobayashi A, Akahane Y, Nakata T, Mihara M et al (2006) Predictive factors for intrahepatic cholangiocarcinoma recurrence in the liver following surgery. J Gastroenterol 41(9):893–900
12. Sirica AE, Dumur CI, Campbell DJ, Almenara JA, Ogunwobi OO, Dewitt JL (2009) Intrahepatic cholangiocarcinoma progression: prognostic factors and basic mechanisms. Clin Gastroenterol Hepatol 7(11):S68–S78
13. Kim JY, Kim M-H, Lee TY, Hwang CY, Kim JS, Yun S-C et al (2008) Clinical role of 18F-FDG PET-CT in suspected and potentially operable cholangiocarcinoma: a prospective study compared with conventional imaging. Am J Gastroenterol 103(5):1145–1151
14. Moon CM, Bang S, Chung JB, Park SW, Song SY, Yun M et al (2008) Usefulness of 18F-fluorodeoxyglucose positron emission tomography in differential diagnosis and staging of cholangiocarcinomas. J Gastroenterol Hepatol 23(5):759–765
15. Kluge R, Schmidt F, Caca K, Barthel H, Hesse S, Georgi P et al (2001) Positron emission tomography with [18F] fluoro-2-deoxy-D-glucose for diagnosis and staging of bile duct cancer. Hepatology (Baltimore, MD) 33(5):1029–1035
16. Park TG, Yu Y-D, Park BJ, Cheon GJ, Oh SY, Kim D-S et al (2014) Implication of lymph node metastasis detected on 18F-FDG PET/CT for surgical planning in patients with peripheral intrahepatic cholangiocarcinoma. Clin Nucl Med 39(1):1–7
17. Lee EJ, Chang S-H, Lee TY, Yoon SY, Cheon YK, Shim CS et al (2015) Prognostic value of FDG-PET/CT total lesion glycolysis for patients with resectable distal bile duct adenocarcinoma. Anticancer Res 35(12):6985–6991
18. Lee Y, Yoo IR, Boo SH, Kim H, Park HL (2017) The role of F-18 FDG PET/CT in intrahepatic cholangiocarcinoma. Nucl Med Mol Imaging 51(1):69–78
19. Cheung TT, Ho CL, Lo CM, Chen S, Chan SC, Chok KS et al (2013) 11C-acetate and 18F-FDG PET/CT for clinical staging and selection of patients with hepatocellular carcinoma for liver transplantation on the basis of Milan criteria: surgeon's perspective. J Nucl Med 54(2):192–200
20. Fan S-T, Lo C-M, Liu C-L, Lam C-M, Yuen W-K, Yeung C et al (1999) Hepatectomy for hepatocellular carcinoma: toward zero hospital deaths. Ann Surg 229(3):322
21. Chan SC, Liu CL, Lo CM, Lam BK, Lee EW, Wong Y et al (2006) Estimating liver weight of adults by body weight and gender. World J Gastroenterol WJG 12(14):2217
22. Nelson JW, Ghafoori AP, Willett CG, Tyler DS, Pappas TN, Clary BM et al (2009) Concurrent chemoradiotherapy in resected extrahepatic cholangiocarcinoma. Int J Radiat Oncol Biol Phys 73(1):148–153
23. Nathan H, Pawlik TM, Wolfgang CL, Choti MA, Cameron JL, Schulick RD (2007) Trends in survival after surgery for cholangiocarcinoma: a 30-year population-based SEER database analysis. J Gastrointest Surg Off J Soc Surg Aliment Tract 11(11):1488–1496 **discussion 96–97**
24. Nguyen KT, Steel J, Vanounou T, Tsung A, Marsh JW, Geller DA et al (2009) Initial presentation and management of hilar and peripheral cholangiocarcinoma: is a node-positive status or potential margin-positive result a contraindication to resection? Ann Surg Oncol 16(12):3308–3315
25. de Jong MC, Nathan H, Sotiropoulos GC, Paul A, Alexandrescu S, Marques H et al (2011) Intrahepatic cholangiocarcinoma: an international multi-institutional analysis of prognostic factors and lymph node assessment. J Clin Oncol Off J Am So Clin Oncol 29(23):3140–3145
26. Farges O, Fuks D, Boleslawski E, Le Treut YP, Castaing D, Laurent A et al (2011) Influence of surgical margins on outcome in patients with intrahepatic cholangiocarcinoma: a multicenter study by the AFC-IHCC-2009 study group. Ann Surg 254(5):824–829 **discussion 30**
27. Cereda S, Belli C, Reni M (2012) Adjuvant treatment in biliary tract cancer: to treat or not to treat? World J Gastroenterol 18(21):2591–2596
28. Mavros MN, Economopoulos KP, Alexiou VG, Pawlik TM (2014) Treatment and prognosis for patients with intrahepatic cholangiocarcinoma: systematic review and meta-analysis. JAMA Surg 149(6):565–574
29. Sur MD, In H, Sharpe SM, Baker MS, Weichselbaum RR, Talamonti MS et al (2015) Defining the benefit of adjuvant therapy following resection for intrahepatic cholangiocarcinoma. Ann Surg Oncol 22(7):2209–2217
30. Tylski P, Stute S, Grotus N, Doyeux K, Hapdey S, Gardin I et al (2010) Comparative assessment of methods for estimating tumor volume and standardized uptake value in 18F-FDG PET. J Nucl Med 51(2):268–276

31. Xu H-X, Chen T, Wang W-Q, Wu C-T, Liu C, Long J et al (2014) Metabolic tumour burden assessed by 18F-FDG PET/CT associated with serum CA19-9 predicts pancreatic cancer outcome after resection. Eur J Nucl Med Mol Imaging 41(6):1093–1102
32. Obara P, Pu Y (2013) Prognostic value of metabolic tumor burden in lung cancer. Chin J Cancer Res 25(6):615–622
33. Gallamini A, Zwarthoed C, Borra A (2014) Positron emission tomography (PET) in oncology. Cancers 6(4):1821–1889
34. Adebonojo SA, Bowser AN, Moritz DM, Corcoran PC (1999) Impact of revised stage classification of lung cancer on survival: a military experience. CHEST J 115(6):1507–1513
35. Mountain CF (1997) Revisions in the international system for staging lung cancer. Chest 111(6):1710–1717