RESEARCH ARTICLE

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The Clinical Significance of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography in Patients with Occupational Cholangiocarcinoma

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Abstract

Objective: The present study aimed to identify the clinical significance of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) imaging in patients with occupational cholangiocarcinoma. **Methods:** This study included 10 men with occupational cholangiocarcinoma who were former or current workers at a printing company in Osaka, Japan. Of the 10 patients, 2 had 2 main tumors and 1 had 3 main tumors. Twelve FDG-PET imaging findings in the 10 patients could be analyzed. We evaluated the relationships between FDG-PET imaging parameters and clinicopathological findings of occupational cholangiocarcinoma. **Results:** Abnormal FDG uptake was observed in 8 of the 14 main tumors, with maximum standardized uptake values ranging from 2.9 to 11.0, and the sensitivity was 57.1%. Four patients had lymph node metastases, and abnormal marrow uptake was detected in all these patients. Although precancerous lesions, such as biliary intraepithelial neoplasia (BilIN) and intraductal papillary neoplasm of the bile duct (IPNB) without any invasion, were not detected, abnormal FDG uptake was demonstrated in 2 of 4 patients with IPNB having an associated invasive carcinoma.**Conclusions:** Although FDG-PET may be useful for assessing tumor progression factors, such as lymph node metastasis, it cannot accurately detect precancerous lesions, such as BilIN and IPNB without invasive carcinoma.

Keywords: Occupational cholangiocarcinoma- lymph node metastasis- biliary intraepithelial neoplasia

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Introduction

Studies recently reported an outbreak of cholangiocarcinoma among young workers in printing companies in Japan (Kumagai et al., 2013, Kubo et al., 2014; Kubo et al., 2014). Such an occurrence of cholangiocarcinoma was recognized as an occupational disease by the Japanese Ministry of Health, Labour and Welfare in 2013, and 38 patients have been recognized as occupational cholangiocarcinoma in Japan until the endo of 2017. It has been reported that 1,2-dichloropropane (DCP) and dichloromethane (DCM) play important roles in the development of this type of cholangiocarcinoma (Kumagai et al., 2013, Japanese Ministry of Health, Labour and Welfare, 2013, Kubo et al., 2014; Kubo et al., 2014). In June 2014, the International Agency for Research on Cancer decided to classify DCP as a group 1 (carcinogenic to humans) and DCM as a group 2A (probably carcinogenic to humans) (Benbrahim-Tallaa et al., 2014). Although the number of patients with occupational cholangiocarcinoma is still limited, our previous studies showed that in addition to the main tumor, chronic bile duct injuries, such as fibrosis of the bile duct wall and periductal tissue, and precancerous lesions, such as biliary intraepithelial neoplasia (BilIN) and intraductal papillary neoplasm of the bile duct (IPNB), were observed at various sites of the large bile ducts in patients with occupational cholangiocarcinoma (Kubo et al., 2014;

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Kubo et al., 2014; Kinoshita et al., 2016). Therefore, in patients with occupational cholangiocarcinoma, various other parts of the bile ducts also have a high potential for the development of cholangiocarcinoma. Moreover, such pathological findings reflected characteristic radiological changes on diagnostic imaging, such as regional dilatation of the bile ducts without tumor-induced obstruction, and biliary findings similar to those indicating the presence of primary sclerosing cholangitis (PSC), such as multiple strictures of the bile ducts with or without fusiform dilatation (Kinoshita et al., 2016; Koyama et al., 2017).

It is important to make an accurate diagnosis with diagnostic imaging before and after treatments, because it is necessary to perform appropriate treatment and close follow-up for recurrence owing to a high potential for the development of cholangiocarcinoma (Kubo et al., 2016). Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) has been proven to be useful in the evaluation of different malignancies (Keidar et al., 2004; Votrubova et al., 2006; Albazaz et al., 2013; Jiang et al., 2016); however, the usefulness of FDG-PET is still unclear in patients with occupational cholangiocarcinoma. Therefore, this retrospective study aimed to investigate the clinical significance of FDG-PET, which has the potential to facilitate accurate diagnosis, in patients with occupational cholangiocarcinoma.

Materials and Methods

This retrospective study included 10 men with occupational cholangiocarcinoma who were former or current workers at a printing company in Osaka, Japan. In the 10 patients, FDG-PET was performed before treatment. In 1 patient (patient no. 9), FDG-PET was performed before the first operation and the second and third operations for recurrent tumors. In total, 12 FDG-PET imaging findings from 10 patients could be analyzed. Among the 10 patients, 8 underwent a total of 10 surgical procedures (patient nos. 1, 2, 3, 5, 7, 8, 9, and 10; 3 procedures in patient no. 9, as described above). Chemotherapy alone was performed in 2 patients (patient nos. 4 and 6). In another 2 patients (patient nos. 2 and 5), additional extrahepatic cholangiocarcinomas, which had not been detected before the operation, were diagnosed on macroscopic and microscopic examinations of the operative specimens. Patient no. 2 had 2 main tumors (tumor nos. 2a and 2b), and patient no. 5 had 2 main tumors (tumor nos. 5a and 5b). Patient no. 9 had 3 main tumors (primary tumor, tumor no. 9a; the first recurrent tumor, 9b; and the second recurrent tumor, 9c). The longest diameters of the tumors were measured according to macroscopic findings in patients with operative specimens and according to diagnostic imaging in patients who did not undergo surgery. In 2 tumors (tumor nos. 5a and 10), the diameter could not be measured because intraepithelial cancerous spread (without mass formation) could not be determined on macroscopic examination. The liver anatomy and operative methods were classified according to Brisbane 2000 terminology (Pang, 2000).

Pathological examinations of surgical specimens were performed in 8 patients (10 operations) (patient nos. 1–3, 5, 7, 8, 9 [3 operations], and 10) (Table 1). We evaluated clinicopathological characteristics, including the presence of BilIN or IPNB, in non-cancerous hepatic tissues. The pathological findings were evaluated by pathologists (Y.N. and Y.S.) according to the World Health Organization classification for intrahepatic cholangiocarcinoma (ICC) (Nakanuma et al., 2010). ICC was grossly classified as a mass-forming, periductal infiltrating, or intraductal growth. Extrahepatic cholangiocarcinoma (perihilar and distal cholangiocarcinoma; ECC) was grossly classified as a papillary, nodular, scirrhous constricting, or diffusely infiltrating tumor. Pre or early neoplastic lesions of the bile ducts were classified as BilIN or IPNB. BilIN lesions were histologically classified according to their cellular and structural features as BilIN-1 (mild atypia), BilIN-2 (moderate atypia), or BilIN-3 (severe atypia corresponding to in situ carcinoma). In this study, we mainly assessed BilIN-2 and BilIN-3 lesions because it was unclear whether BilIN-1 lesions included reactive hyperplastic changes. IPNB was characterized by dilated intrahepatic and extrahepatic bile ducts filled with papillary or villous biliary neoplasms that covered delicate fibrovascular stalks. The dilated bile ducts were fusiform or cystic (unilobular or multilobular), and the height of such lesions usually exceeded 10 mm, but papillary lesions <10 mm but >5 mm showing similar histologies were also occasionally encountered. IPNB was not infrequently associated with focal and minimal invasion (invasive IPNB).

We investigated abnormal marrow uptake on FDG-PET imaging, including the maximum standardized uptake value (SUVmax), through medical records and reports of radiologists. In addition, we evaluated the relationships between FDG-PET imaging parameters and clinicopathological findings of occupational cholangiocarcinomas, including main lesions and lymph node metastases in all patients, and precancerous lesions, such as BilIN-2/3 and IPNB, on pathological examination in patients who underwent surgery. The presence of lymph node metastasis was defined as follows: i) in patients who underwent surgery with lymph node dissection, the presence of metastasis was diagnosed by pathological examination; ii) in patients who underwent surgery without lymph node dissection, the presence of metastasis was assessed by intraoperative macroscopic findings first, and if any enlarged lymph nodes were not detected on diagnostic imaging for 1 year after surgery, the patients were assumed to not have lymph node metastasis; iii) in patients who did not undergo surgery, if some enlarged lymph nodes were detected on diagnostic imaging and the diameter or number of the lymph nodes increased subsequently, the patients were assumed to have lymph node metastasis.

This study was approved by the ethics committee of Osaka City University (No. 2368), and all of the participants or their legally authorized representatives (for decreased patients) provided written informed consent. This multicenter occupational cholangiocarcinoma study

involved investigators at 5 institutions.

Results

Clinicopathological findings of the 10 study patients

The age of the patients at diagnosis ranged from 31 to 48 years, and all patients were men (Table 1). Nine main tumors (tumor nos. 1, 2a, 3, 4, 5a, 7, 8, 9a, and 9c) were diagnosed as ICC, and 5 main tumors (tumor nos. 2b, 5b, 6, 9b, and, 10) were diagnosed as ECC, including distal and perihilar cholangiocarcinoma. Two patients (patient nos. 2 and 5) had both ICCs (tumor nos. 2a and 5a) and ECCs (tumor nos. 2b and 5b). Six ICCs (tumor nos. 1, 2a, 3, 4, 8, and 9c) were classified as mass-forming type and 3 ICCs (tumor no. 5a, 7, and 9a) were classified as intraductal growth type. Three ECCs (tumor nos. 2b, 9b, and 10) were located at the distal side of the common bile duct, and 2 ECCs (tumor nos. 5b and 6) were located at the perihilar bile duct. Three ECCs (tumor nos. 2b, 5b, and 9b) were classified as papillary type, 1 ECC (tumor no. 6) was classified as nodular type, and 1 ECC (tumor no. 10) was classified as diffusely infiltrating type. The longest diameters of 4 tumors (tumor nos. 2b, 6, 7, and 9b) were less than 1 cm, and the longest diameters of 8 other tumors ranged from 1 cm to 17 cm. The diameters of 2 tumors (tumor nos. 5a and 10) could not be measured, as described above. Liver resection alone was performed in 4 patients (5 operations) (patient nos. 1, 3, 7, and 9 [the first and third operations]), liver resection with resection of the extrahepatic bile duct was performed in 2 patients (patient nos. 5 and 8), resection of the extrahepatic bile duct was performed in 1 patient (patient no. 9 [the second operation]), liver resection and pancreaticoduodenectomy were performed in 1 patient (patient no. 2), and pancreaticoduodenectomy alone was performed in 1 patient (patient no. 10) (Table 1).

Pathological examination showed that the main lesions in 10 surgical specimens (patient nos. 1, 2, 3, 5, 7, 8, 9 [all 3 operations], and 10) were tubular or papillary adenocarcinomas. Four main lesions (tumor nos. 5a, 7, 9a, and 9b) were diagnosed as invasive IPNB by pathological examination. BilIN-2/3 lesions were observed in 9 surgical specimens (patient nos. 1–3, 5, 7, 8, and 9 [all 3 operations]) (Table 1). In patient no. 10, the presence of BilIN-2/3 could not be evaluated sufficiently because of the presence of small numbers of non-cancerous large bile ducts. IPNB without any invasion was observed in 5 surgical specimens (patient nos. 2, 5, 7, 8, and 9 [the first and second

Table 1 . Clinicopathological Findings of Patints with Occupational Cholangiocarcinoma

Patient no.	Age	Sex	Location, type, and longest diameter of cholangiocarcinoma (tumor no.)	Treatment	Pathological diagnosis of the main lesion (tumor no .)	BilIN-2/3	IPNB without any invasion	Lymph node metastasis
1	34	M	ICC, mass-forming, 17cm (1)	Right trisectionectomy	Poorly differentiated papillary adenocarcinoma (1)	Yes	No	No
2	40	M	ICC, mass-for ing,1.7 cm (2a) Distal ECC, papillary, <1cm (2b)	Right hepatectomy, pancreaticoduodenectomy	Well-differntiated tubular adenocarcinoma (2a) moderately diferntiated tubularadenocarcinoma (2b)"	Yes	Yes	No
3	38	M	ICC, mass-forming, 2.5 cm (3)	Segmentectomy 8	Well-differntiated tubular adenocarcinoma (3)	Yes	ND	Yes
4	39	M	ICC, mass-forming, 10 cm (4)	Chemotherapy	-	-	-	Yes
5	39	M	ICC, intraductal growth, 1.5 cm (5a) perihilar ECC, papillary, NM (5b)	Left hepatectomy, resection of extra hepatic bile duct	Invasive IPNB (5a), Well-differntiated tubular adenocarcinoma (5b)	Yes	Yes	No
6	37	M	Perihilar ECC, nodular,<1cm (6)	Chemotherapy	-	-	-	Yes
7	39	M	ICC, intraductal growth, <1 cm (7)	Left hepatectomy, segmentectomy 7	Invasive IPNB (7)	Yes	Yes	No
8	31	M	ICC, mass-forming, 2.1 cm (8)	Right hepatectomy, resection of extra hepatic bile duct	Moderately differntiated papillary adenocarcinoma (8)	Yes	Yes	Yes
9_1	34	M	ICC, intraductal growth, 1.5 cm (9a)	Extended left hepatectomy	Invasive IPNB (9a)	Yes	Yes	No
9_2	36	M	Distal ECC, papillaru, <1 cm (9b)	Resection of extra hepatic bile duct S8 partial hepatectomy"	Invasive IPNB (9b)	Yes	Yes	No
9_3	37	M	ICC, mass-forming, 2.5 cm (9c)	S6 and S7 partial hepatectomy	Moderately differntiated tubular adenocarcinoma (9c)	Yes	ND	No
10	48	M	Distal ECC, diffusely infiltrating, NM (10)	Pancreaticodusodenetomy	Moderately differntiated tubular adenocarcinoma (10)	ND	ND	Yes

ICC, intrahepatic cholangiocarcinoma; ECC, extrahepatic cholangiocarcinoma; <1 cm, diameter less than 1 cm; NM, diameter could not be determined because intraepithelial cancerous spread could not be measured on macroscopic examination; BilIN, biliary intraepithelial neoplasia; IPNB, intraductal papillary neoplasm of the bile duct; ND, not determined. Patient no. 9 is classified and defined as follows, 9-1) at the first surgery, 9-2) at the second surgery, and 9-3) at the third surgery.

Table 2. Abnormal Marrow Uptake on Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography Imaging in Patients with Occupational Cholangiocarcinoma

Patient no.	Turmor no.	Main lesion (SUVmax)	Metastatic lymph nodes (SUVmax)	BilIN-2/3 (SUVmax)	IPNB without any invasion (SUVmax)
1	1	Positive (11)	-	Negative	-
2	2a 2b	Negative Negative	-	Negative	Negative
3	3	Positive (5.8)	-	Negative	NA
4	4	Positive (4.0)	Positive(5.0)	NA	NA
5	5a 5b	Positive (4.1) Negative	-	Negative	Negative
6	6	Negative	Positive(14.2)	NA	NA
7	7	Negative	-	Negative	Negative
8	8	Positive (2.9)	Positive(3.8)	Negative	Negative
9_1	9a	Positive (3.8)	-	Negative	Negative
9_2	9b	Negative	-	Negative	Negative
9_3	9c	Positive (5.8)	-	Negative	NA
10	10	Positive (4.8)	Positive(4.7)	NA	NA

SUVmax, maximum standardized uptake value; NA, not available; (-), not present; BiLLN, biliary intaepithelial neoplasia; IPNB, intraductal papillary neoplasm of the bile duct. patient no. 9 is classified and defined as follows, 9-1) at the first surgery, 9-2) at the second surgery, and 9-3) at the third surgery

Table 3. Sensitivity and Specificity of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography Imaging in Patients with Occupational Cholangiocarcinoma

	Main lesion	Lymph node metastasis	BilIN-2/3	IPNB without any invasion
Sensitivity	53.1%	100%	0%	0%
Specificity	93.3%	100%	100%	100%

BilIN, biliary intraepithelial neoplasia; IPNB, intraductal papillary neoplasm of the bile duct

operations]). In 3 surgical specimens (patient nos. 3, 9 [the third operation], and 10), the presence of IPNB could not be evaluated sufficiently because of the presence of small numbers of non-cancerous large bile ducts. Of the 4 patients, lymph node metastasis in the hepatoduodenal ligament and/or peripancreatic region was diagnosed by pathological examination in 2 (patient nos. 3 and 8) and by diagnostic imaging alone in 2 (patient nos. 4 and 6).

Findings of FDG-PET imaging

Abnormal FDG uptake was observed in 8 main tumors (tumor nos. 1, 3, 4, 5a, 8, 9a, 9c, and 10) among the 14 main lesions (Table 2, Figure 1a). The SUVmax values ranged from 2.9 to 11.0 (Table 3). Of 6 tumors that were not detected on FDG-PET (false negative), 4 (tumor nos. 2b, 6, 7, and 9b) showed a longest diameter of less than 1 cm, 1 (tumor no. 2a) showed a longest diameter of 1.7 cm, and 1 (tumor no. 5b) showed intraepithelial cancerous spread without mass formation. Thus, the sensitivity was 57.1% (Table 3). On the other hand, in patient no. 9 at the third surgery, although

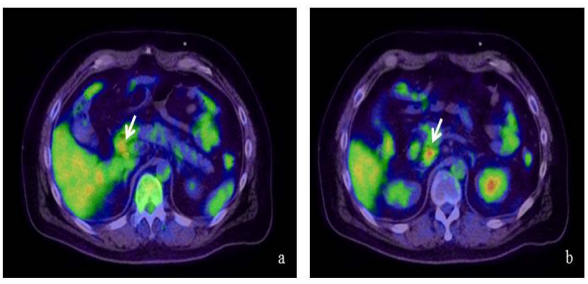

Figure 1. Distal Side of an Extrahepatic Cholangiocarcinoma and Lymph Node Metastasis in Patient no. 10. In patient no. 10, the distal side of an extrahepatic cholangiocarcinoma (tumor no. 10) (a, arrow) and lymph node metastasis (b, arrow) show abnormal marrow uptake on fluorine-18 fluorodeoxyglucose positron emission tomography.

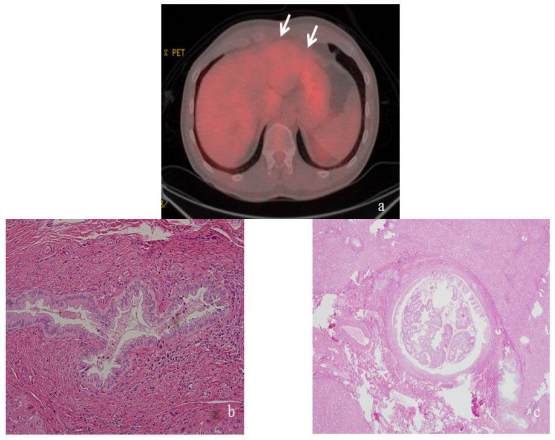

Figure 2. Biliary Intraepithelial Neoplasia (BilIN) and Intraductal Papillary Neoplasm of the Bile Duct (IPNB) in Patient no. 7. In patient no. 7, BilIN-3 (b) (Kinoshita et al., 2016) and IPNB lesions without any invasion (c) (Kinoshita et al., 2016) in the lateral segment of the liver are not detected on fluorine-18 fluorodeoxyglucose positron emission tomography imaging (a, arrow).

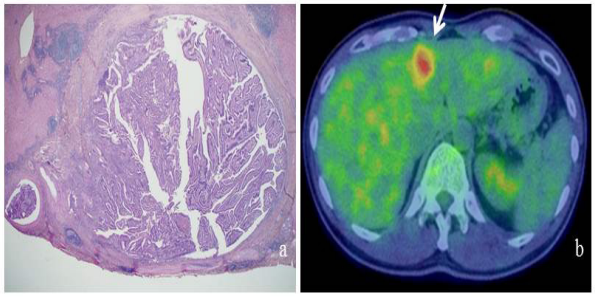

Figure 3. Invasive Intraductal Papillary Neoplasm of the Bile Duct (IPNB) in Patient no. 9. In patient no. 9 at the first operation, an invasive IPNB (a) (Kinoshita et al., 2016) in segment 4 (tumor no. 9a) is detected with abnormal marrow uptake on fluorine-18 fluorodeoxyglucose positron emission tomography (b, arrow).

abnormal FDG uptake was detected at a lesion located in S7, the pathological diagnosis was inflammatory pseudo tumor. Thus, the specificity was calculated as 93.3% (Table 3). In all 4 patients who had lymph node metastasis, abnormal FDG uptake was observed in each metastatic lymph node with high SUVmax values ranging from 3.8 to 14.2 (Table 2, Figure 1b), and the sensitivity and specificity were both 100% (Table 3). All of the BilIN-2/3 lesions were not found to have abnormal marrow uptake on FDG-PET imaging (Table 2, Figure. 2a, 2b). IPNB lesions without any invasion in 5 surgical specimens (patient nos. 2, 5, 7, 8, and 9 [the first and second operations]) were not detected on FDG-PET imaging (Table 2, Figure 2a, 2c). However, 2 (tumor nos. 5a and 9a) of 4 tumors with invasive IPNB as the main lesion showed abnormal marrow uptake on FDG-PET imaging (SUVmax 4.1 and 3.8, respectively) (Table 2, Figure 3a, 3b).

Discussion

Our previous studies reported that elevated serum gamma-glutamyl transpeptidase activities, regional dilatation of the intrahepatic bile ducts without tumor-induced obstruction and biliary findings similar to those indicating the appearance of PSC (Vitellas et al., 2000) on diagnostic imaging, a papillary proliferating tumor, presence of precancerous or early cancerous lesions, such as BilIN and IPNB, and non-specific bile duct injuries, such as fibrosis, are characteristics of patients with occupational cholangiocarcinoma (Kubo et al., 2014; Kubo et al., 2014; Kinoshita et al., 2016). Furthermore, a carcinogenic process consisting of chronic bile duct injury with DNA damage within various sites in the large bile ducts, the induction of pre or early cancerous lesions, such as BilIN and IPNB, and the development of invasive carcinoma with high frequency of somatic mutations, has been proposed (Kinoshita et al., 2016; Mimaki et al., 2016). Although it is sometimes difficult to perform curative resection for such multicentric carcinogenesis of occupational cholangiocarcinoma, aggressive treatment, including repeated resections, may be considered as effective through analyses of postoperative outcomes (Kubo et al., 2016). Therefore, accurate and efficient diagnostic imaging and the evaluation of the extent of carcinoma are important for treatment.

Although normal hepatic tissues displayed a relatively high glucose uptake, there was usually an intense FDG uptake in ICCs, indicating high metabolic activity with a consequently much greater tumor-to-normal liver tissue ratio (Kim et al., 2003; Lee et al., 2008; Jiang et al., 2016). However, the present study showed that the sensitivity of FDG-PET for occupational cholangiocarcinoma was not high (57.1%). A previous study suggested that the ICC size was significantly correlated with FDG uptake, and perihilar cholangiocarcinoma tended to lower FDG uptake because of symptoms involving the obstruction of the large bile duct by small tumors (Jiang et al., 2016). Actually, in the present study, all tumors less than 1 cm in the longest diameter and 1 of 2 lesions showing intraepithelial cancerous spread (without mass formation) were not found to have abnormal marrow uptake on FDG-PET. In patients with occupational cholangiocarcinoma, cholangiocarcinoma was detected by further examination after the identification of abnormal findings in a regular health examination (Kubo et al., 2014; Kubo et al., 2014; Kubo et al., 2016), and the main tumor was detected to be small without any symptoms. In addition, small carcinomas were sometimes detected through macroscopic and microscopic examinations of operative specimens because a multicentric carcinogenic process was noted at various sites of the bile ducts (Kubo et al., 2014; Kubo et al., 2014; Kinoshita et al., 2016). Because of these reasons, although FDG-PET is generally useful for the diagnosis of main lesions in patients with occupational cholangiocarcinoma, accurate detection of the carcinoma may be sometimes difficult with FDG-PET, especially when the tumor is small. On the other hand, all of the lymph node metastases showed abnormal FDG uptake on FDG-PET imaging. Some previous studies reported that FDG-PET has higher specificity (91.7-100%) and similar or superior sensitivity (43-70%) in the detection of lymph node metastases for patients with cholangiocarcinoma compared with computed tomography or magnetic resonance imaging (Itatsu et al., 2007; Jiang et al., 2016). In this study, the sensitivity and the specificity were 100% in the detection of lymph node metastases. Although the sensitivity of FDG-PET seemed to be higher in patients with occupational cholangiocarcinoma than in those with non-occupational cholangiocarcinoma, it was difficult to compare the usefulness of FDG-PET in the detection of lymph node metastases in patients with occupational cholangiocarcinoma because of a small number of patients with occupational cholangiocarcinoma. The distribution of the metastatic lymph nodes were similar in both patients with occupational cholangiocarcinoma and with non-occupational cholangiocarcinoma.

BilIN and IPNB are currently regarded as precancerous or early cancerous lesions according to the World Health Organization's classification of cholangiocarcinoma (Nakanuma et al., 2010), and they are considered to be involved in the multistep carcinogenesis of cholangiocarcinoma in patients with hepatolithiasis or PSC (Chen et al., 2001; Itatsu et al., 2007; Zen et al., 2007; Nakanuma et al.,

2014). Papillary or invasive carcinoma, precancerous or early cancerous lesions, such as BilIN and IPNB, and non-specific bile duct injuries, such as fibrosis, are reportedly pathological characteristics of occupational cholangiocarcinoma (Kubo et al., 2014; Kubo et al., 2014; Kubo et al., 2014; Hamano et al., 2016). In addition, high frequency of BilIN and/or IPNB and wide distribution of such lesions were considered to be characteristics of patients with occupational cholangiocarcinoma in comparison to patients with hepatolithiasis or PSC (Kinoshita et al., 2016). There are no reports about FDG-PET of BilIN lesions. Our present study showed that BilIN-2/3 lesions were not detected on FDG-PET in patients with occupational cholangiocarcinoma. Thus, the diagnosis and surveillance of BilIN lesions may be difficult with FDG-PET. On the other hand, FDG-PET findings of IPNB have been rarely reported, including case reports (Takanami et al., 2010; Takanami et al., 2011; Dong et al., 2012; Watanabe et al., 2013). These previous reports showed that an invasive IPNB with a large mural nodule may show increased FDG uptake and that FDG uptake was higher for a larger IPNB with high-grade dysplasia than for a small IPNB with low-grade dysplasia (Takanami et al., 2010; Takanami et al., 2011; Dong et al., 2012; Watanabe et al., 2013). In this study, although invasive IPNB was detected as abnormal marrow uptake on FDG-PET imaging with a sensitivity of 50%, IPNB without any invasion was not detected. Thus, although an invasive IPNB may be detected on FDG-PET, this approach is not an efficient diagnostic tool for IPNB without invasion.

This study has some limitations. This study included a few subjects because the number of patients with occupational cholangiocarcinoma is originally small. The pathological examination was performed using surgical specimens in 8 patients and it was impossible to examine pathologically using the whole liver. However, the results in this study provide an important information for the diagnosis of occupational cholangiocarcinoma.

In conclusion, although FDG-PET may be useful for assessing tumor progression, including progression of main tumors and lymph node metastasis, it cannot accurately detect precancerous lesions such as BilIN and IPNB without invasive carcinoma.

Author contribution

Study design: M. Kinoshita and SK designed the study

Acquisition of data: M. Kinoshita, YN, YS, S. Takemura, S. Tanaka, GH, TI, M. Koda, TA, SN, AA, TY, HT, and SK. Pathological aspect of the study: YN and YS analyzed pathological findings. Data analysis: M. Kinoshita, S. Takemura, S. Tanaka, GH, TI, M. Koda, TA, TM, and SK. Manuscript drafted by MK and SK. All authors reviewed the manuscript.

Conflicts of interest

No potential conflicts of interest were disclosed.

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