Comparison of Computed Tomographic Finding of the Intraductal and Periductal Cholangiocarcinoma

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Objective: *To compare the CT findings of the intraductal and periductal cholangiocarcinoma (CCA) in Srinagarind Hospital.*
Material and Method: *The authors retrospectively reviewed the abdominal CT images (taken between January 2004 and December 2005) of 60 patients with pathological proof of CCA. There were 34 and 26 cases of the intraductal and periductal CCA, respectively. The bile duct dilatation, size and location of the intraductal and infiltrative extraductal masses, ductal wall enhancement and other associated findings (i.e., biliary stones, ascites, intra-abdominal lymphadenopathy and distant metastases) were compared and analyzed using the χ^2 and Fisher exact tests.*
Results: *All cases of the intraductal and periductal CCA showed bile duct dilatation. The intraductal mass was seen in all cases of the intraductal CCA but none in the periductal CCA (p = 0.00). All intraductal mass sizes were > 1 cm. Most (77%, n = 20/26) cases of the periductal CCA had an infiltrative extraductal mass, whereas none were found in the intraductal CCA (p = 0.00). Ductal wall enhancement was found in 73% (n = 19/26) of the periductal CCA and 26% (n = 9/34) of the intraductal CCA cases (p = 0.01). Only one case in each group presented with biliary stones. Half (50%, n = 13/26) and 12% (n = 3/26) of the periductal CCA cases demonstrated with intra-abdominal lymphadenopathy and ascites, respectively, vs. none in the intraductal CCA (p = 0.00 and 0.07, respectively). No distant metastasis was found in either group.*
Conclusion: *The CT findings that helped to differentiate the intraductal from periductal CCA include: the intraductal mass, an infiltrative extraductal mass, ductal wall enhancement and other associated findings such as intra-abdominal lymphadenopathy. Features of the intraductal CCA included the intraductal mass without intra-abdominal lymphadenopathy and ductal wall enhancement about 26% (9/34 cases).*

Keywords: *Computed tomography (CT), Cholangiocarcinoma, Periductal type, Intraductal type*

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Cholangiocarcinoma (CCA) is a primary malignant liver tumor arising from the epithelium of the bile duct[1]. Most common CCA are adenocarcinoma. It is a major public health problem in Thailand, especially in the Northeast where *Opisthorchis viverrini* is an endemic area[1]. The clinical manifestations of CCA include: malignant obstructive jaundice (70%), non-jaundice (30%), right upper quadrant abdominal mass (14%), acute acalculous cholecystitis (7%) and hydrop of gallbladder (6.7%)[1]. The average age at diagnosis is approximately 65 years[2]. This cancer occurs slightly more often in men than in women[2].

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According to the classification of primary liver cancer proposed by the Liver Cancer Study Group of Japan[3], CCA were classified into three types based on growth characteristic of the tumor: mass-forming or exophytic, periductal or infiltrative-growing and intraductal or papillary-growing types. In the intraductal or papillary-growing type, tumor cells are confined within the mucosal layer and do not invade deeply into the submucosal layer and the tumor spreads superficially along the mucosal layer. In the periductal or infiltrative-growing type, tumor cells arising from the mucosa of the bile ducts invade the wall and penetrate the serosa[3].

Jae Hoon Lim reported the typical findings of the periductal CCA included an ill-defined or infiltrative

extraductal mass, ductal wall enhancement and non-union of the dilated right and left hepatic ducts with or without a visible mass or thickened wall[3].

Regarding a study by Byung Ihn Choi et al in 51 cases of the periductal CCA found 40 cases (78%) and 4 cases (8%) revealed an ill-defined or infiltrative tumor and a polypoid intraluminal mass, respectively[4]. Besides, they also found that 10 cases had intra-abdominal lymphadenopathy[4].

According to the study by Philippe Soyer et al the preoperative detection of enlarged lymph nodes is correct in only 20% of cases[5].

Concerning the report by Joon Woo Lee et al the 53.3% of cases with intraductal CCA revealed the intraductal mass upon CT imaging[6]. They also found that CT cannot depict masses under 1 cm. In addition, they found no ascites, intra-abdominal lymphadenopathy or distant metastasis in the intraductal CCA[6]. JK Han and JM Lee also found that CT scan cannot depict tumor < 1 cm, whereas all tumors > 1 cm can be detected[7].

Recent reports have shown that the intraductal CCA has a better prognosis after surgical resection than other types of CCA[7-11]. Besides, surgical planning for a permanent cure outcome should be tailored depending on the morphologic type. In this regard, surgical planning for the intraductal CCA includes a liver resection with tumor-free margin, whereas surgical planning for the periductal CCA requires aggressive surgery including extensive liver and lymph node resections plus adjuvant chemotherapy[12].

Furthermore, many reports about the radiographic appearances of CCA have focused mainly on the more common mass-forming or exophytic type. In this regard, the precise CT findings of the intraductal and periductal CCA are helpful for the clinicians to allow the optimal surgical planning and to determine the prognosis of the patients. If the characteristic findings on CT imaging can help to differentiate the intraductal from periductal CCA, it would be a valuable diagnostic tool. The purpose of the present study was to compare the CT findings of the intraductal vs. periductal CCA.

Material and Method

The database at Srinagarind Hospital was searched for CCA patients treated between January 2004 and December 2005. Of the 322 patients, the authors selected the respective 34 and 26 cases that underwent surgery with pathologic proven intraductal and periductal CCA.

The data from the 34 cases of the intraductal CCA (27 males, 7 females, age range 41-74 years, mean 58) and 26 cases of the periductal CCA (25 males, 1 female, age range 31-70 years, mean 51) were analyzed for demographic data, presenting symptoms and radiographic findings.

A multi-detector CT scanner (Somatom Plus4 Volume zoom: Siemens, Forchheim, Germany) was used in all cases. The scan area included liver and both kidneys or the whole abdomen with 2.5 mm collimator, a pitch of 0.25 with 8 mm reconstruction. The scanning parameters were 120 kV and 120 mA. The scanning time was 0.5 seconds.

Each case received 100 mL of a water soluble nonionic contrast material through a 18-gauge angiographic catheter inserted into an antecubital vein. The contrast material was injected at a rate of 2.5-3.0 mL/sec by an automatic injector. Biphasic helical CT scans were obtained at 30 seconds delaying for arterial phase and 70 seconds delaying for portovenous phase after initiation of the contrast material injection.

The hard copies of the CT images of all proven cases were retrospectively and independently reviewed by two staff radiologists (NC and VL) not apprised of the clinical data or pathologic findings. If there was any disagreement, the final interpretation would be solved by consensus.

The images were analyzed to determine the bile duct dilatation, location and size of the intraductal and an infiltrative extraductal masses, ductal wall enhancement and other associated findings (*i.e.*, biliary stones, ascites, intra-abdominal lymphadenopathy and distant metastasis).

The bile duct dilatation was categorized as dilated or non-dilated ducts. The intraductal mass was classified as presence or absence. The sizes of the intraductal mass were sub-classified as < 1 cm, 1-3 cm or > 3 cm. The locations of the intraductal masses were also sub-classified as right and left intrahepatic bile duct, common hepatic duct, common bile duct or mixed locations.

The ductal wall enhancement and an infiltrative extraductal mass were divided as present or absent. The infiltrative extraductal mass sizes were sub-categorized as < 1 cm, 1-3 cm or > 3 cm. The locations of an infiltrative extraductal mass were sub-categorized as right lobe, left lobe, right and left lobes or extrahepatic regions. The other associated findings (*viz.*, biliary stones, ascites, intra-abdominal lymphadenopathy and distant metastasis) were divided as presence or absence.

The demographic data were demonstrated in number, percentage, mean and range.

The CT findings of the intraductal vs. periductal CCA were compared and analyzed by χ^2 and Fisher exact tests.

Results

There were totally 60 cases of CCA, including 34 cases in the intraductal group and 26 cases in the periductal group. The demographic data of all cases are presented in Table 1. Both the intraductal or periductal group occurred in males (79%, n = 27/34 of the intraductal group and 96%, n = 25/26 of the periductal group). The mean and range ages in the intraductal group were 58 and 41-74 years, respectively. The mean and range ages in the periductal group were 51 and 31-70 years, respectively.

The most common presenting symptom was jaundice (87%, n = 52/60) followed by weight loss (75%, n = 45/60), dyspepsia (67%, n = 40/60), fever of unknown origin (65%, n = 39/60), anorexia (55%, n = 33/60) and abdominal mass (47%, n = 28/60). Non-jaundice was the presenting symptom in ~13% (n = 8/60) of cases (Table 2).

Table 3 shows the CT findings among the intraductal and periductal groups. Bile duct dilatation was found in all cases of both groups (Fig. 1A, 1B, 2A, 2B). There was no significant difference in the frequency of bile duct dilatation between the 2 groups.

The intraductal mass was seen in all cases of the intraductal group, but none in the periductal group (Fig. 1A, 1B). The difference between the groups was statistic significance (p-value = 0.00). All detected intraductal mass were > 1 cm in diameter.

According to ductal wall enhancement, 26% (n = 9/34) of the intraductal group (Fig. 3) and 73%

Table 1. Number and age of the intraductal and periductal CCA cases

Group	Number of cases	Mean age (range) years
Intraductal CCA	Total 34	58 (41-74)
	Male 27	58 (41-74)
	Female 7	56 (44-67)
Periductal CCA	Total 26	51 (31-70)
	Male 25	51 (31-70)
	Female 1	55

CCA = cholangiocarcinoma

Table 2. The presenting symptoms among the intraductal and periductal CCA cases

Clinical presentations	Numbers	Percentage
Jaundice	52	87
Weight loss	45	75
Abdominal mass	28	47
Dyspepsia	40	67
Anorexia	33	55
Fever of unknown origin	39	65

The patient may had one or more clinical presentations
CCA = cholangiocarcinoma

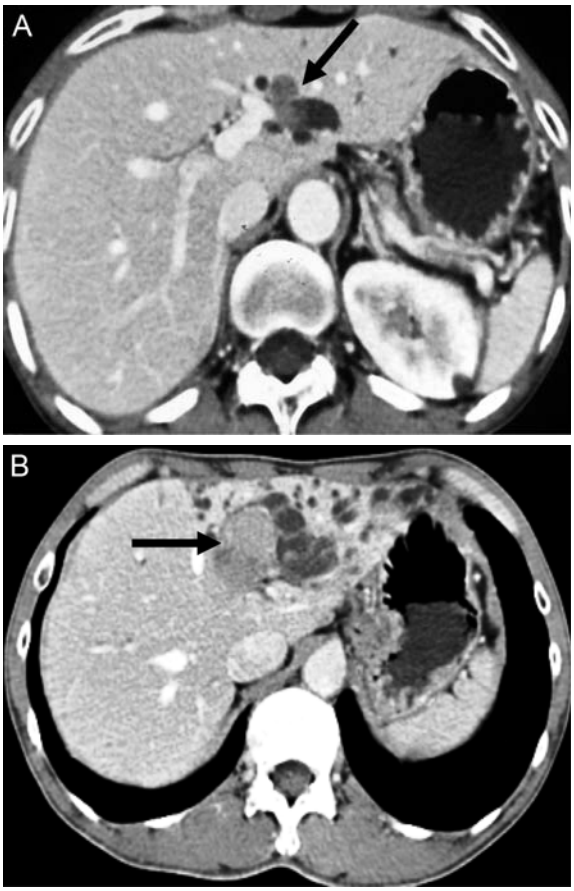

Fig. 1 A) A 72-year-old man with intraductal CCA. The image exhibits the intraductal mass within the dilated intrahepatic bile duct of left lobe liver (arrow). B) A 55-year-old man with intraductal CCA. The image shows a well-defined enhancing mass, measuring ~2.5 cm, within the dilated intrahepatic bile duct of left liver lobe (arrow)

(n = 19/26) of the periductal group (Fig. 2A, 2B) had ductal wall enhancement. The difference between the 2 groups was statistically significant (p-value = 0.01).

An infiltrative extraductal mass was characteristic of ~77% (n = 20/26) of the periductal group over against the intraductal group (Fig. 4). There was statistically significant difference between the 2 groups (p-value = 0.00).

About 65% (n = 17/26) of the periductal group and 3% (n = 1/34) of the intraductal group had other associated findings. The difference between the groups was statistically significant (p-value = 0.01). Only one case in each group presented with biliary stones (Fig. 5A, 5B) and 12% (3/26) of the periductal group demonstrated ascites vs. none in the intraductal group (Fig. 5B). There was no significant difference in the frequency of biliary stones and ascites between the 2 groups (p-value = 1.00 and 0.07, respectively). Half (50%, n = 13/26) of the periductal group showed intra-abdominal lymphadenopathy vs. none in the intraductal group (Fig. 6A, 6B). The difference between the 2 groups was statistic significance

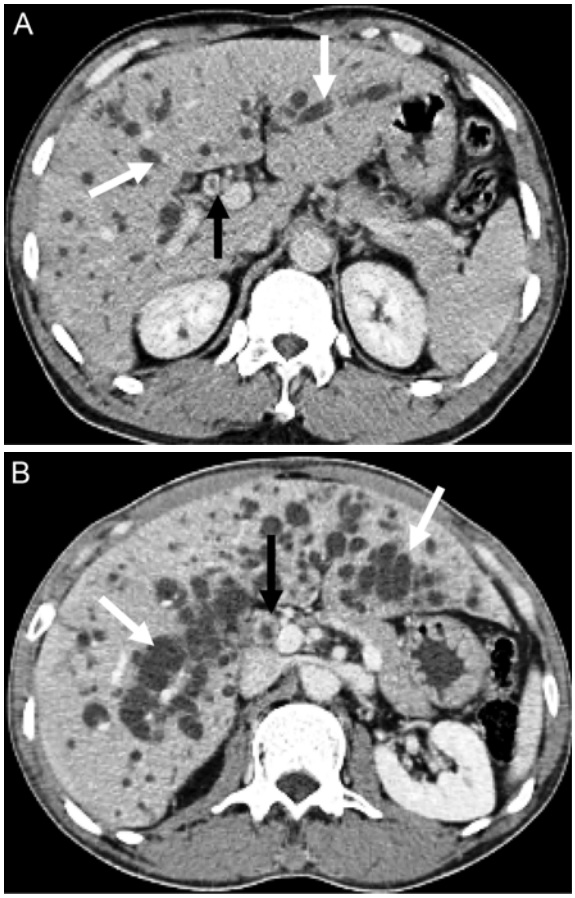

Fig. 2 A) A 52-year-old man with periductal CCA. The image shows concentric ductal wall enhancement without any definite mass of the common hepatic duct (black arrow). Note dilated intrahepatic bile duct of both lobes of the liver (white arrow). B) A 53-year-old man with periductal CCA. The image shows circumferential ductal wall enhancement of the dilated common hepatic duct (black arrow). Note dilated intrahepatic bile ducts of both lobes of the liver (white arrow)

Fig. 3 A 67-year-old woman with intraductal CCA. The image reveals circumferential ductal wall enhancement of the common bile duct (arrow)

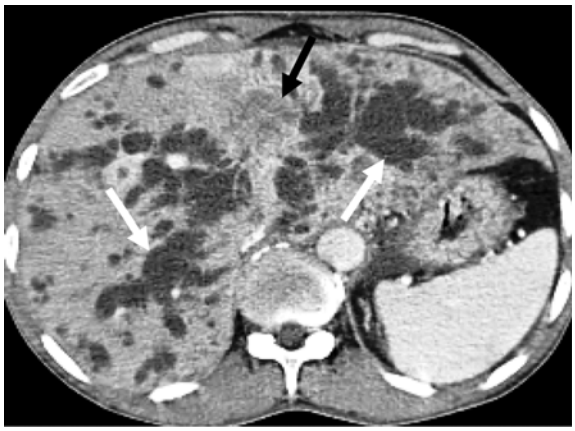

Fig. 4 A 58-year-old man with periductal CCA. The image shows an infiltrative heterogenous enhancing extraductal mass, measuring ~3.5 cm, at segment 4 (black arrow). No demonstrated intraductal mass is shown. Note dilated intrahepatic bile duct of both lobes of the liver (white arrow)

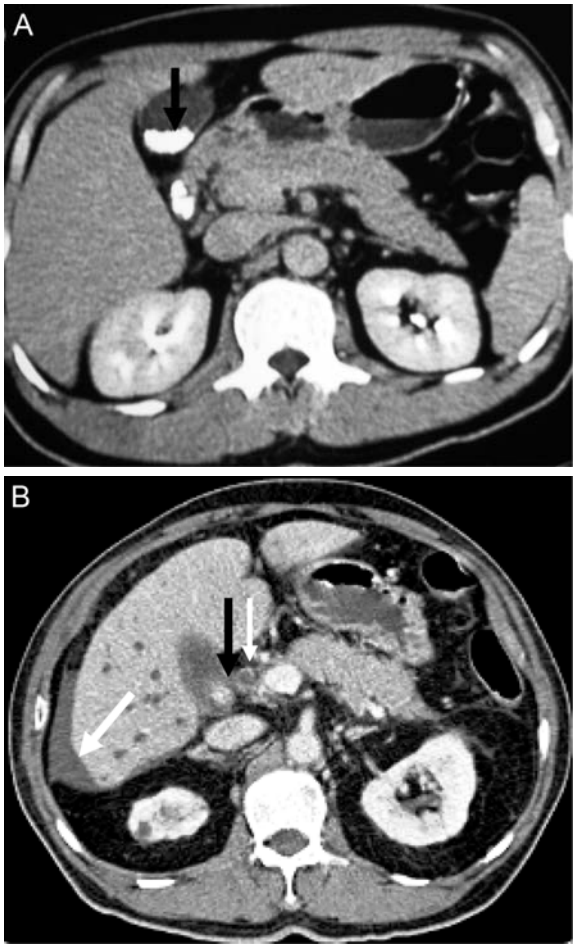

Fig. 5 A) A 47-year-old man with intraductal CCA. The image demonstrates an associated gallstone (arrow). B) A 66-year-old man with periductal CCA. The image reveals concentric ductal wall enhancement of the common bile duct (white small arrow). Note ascites at right subphrenic region (white large arrow) and gallstone (black arrow)

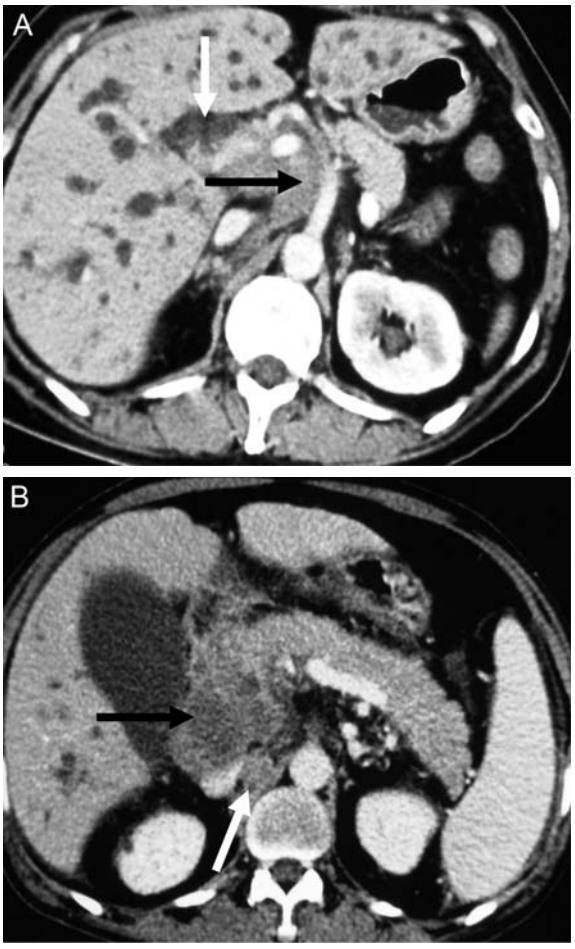

Fig. 6 A) A 55-year-old woman with periductal CCA. The image exhibits tumor metastases along the hepatoduodenal ligament (white arrow) and celiac trunk (black arrow). B) A 52-year-old man with periductal CCA. The image reveals portocaval (black arrow) and aortocaval lymph node metastases (white arrow)

(p-value = 0.00). No distant metastasis was found in either group (Table 3).

Discussion

In the present study, the intraductal CCA commonly demonstrates the intraductal mass, whereas the periductal CCA usually reveals ductal wall enhancement, an infiltrative extraductal mass and other associated findings (*i.e.*, intra-abdominal lymphadenopathy). The types of presentation were statistically significantly different between the 2 groups. (p-value < 0.05). Jae Hoon Lim found that ductal wall enhancement and an ill-defined or infiltrative extraductal mass are typical findings of the periductal CCA[3]. Regarding the study by Byung Ihn Choi et al, 78% of cases of the periductal CCA revealed an ill-defined or infiltrative tumor[4]. The authors had similar results of ductal wall enhancement and an infiltrative extraductal mass upon CT imaging in the periductal CCA. However, they also found that 8% of the periductal CCA demonstrated a polypoid intraluminal mass[4], which is not found in the present study.

Byung Ihn Choi et al reported that 10 of 51 patients of the periductal CCA had intra-abdominal lymphadenopathy[4]. In addition, Philippe Soyer et al

Table 3. Comparison of the CT findings of the intraductal and periductal CCA

CT findings		Intraductal (n = 34)		Periductal (n = 26)		p-value
		No.	%	No.	%	
Bile duct dilatation	Non-dilated	0	0	0	0	a
	Dilated	34	100	26	100	
Intraductal mass	Absent	0	0	26	100	0.00
	Present	34	100	0	0	
Intraductal mass features						
Size	< 1 cm	0	0	0	0	-
	1-3 cms	32	94	0	0	
	> 3 cms	2	6	0	0	
Location	Right IHD	10	29	0	0	-
	Left IHD	9	26	0	0	
	Right and left IHD	3	9	0	0	
	CHD	3	9	0	0	
	CBD	0	0	0	0	
	Right IHD and CHD	3	9	0	0	
	Right IHD and CBD	1	3	0	0	
	Left IHD and CHD	3	9	0	0	
	Left IHD and CBD	0	0	0	0	
	CHD and CBD	2	6	0	0	
Ductal wall enhancement	Absent	25	74	7	27	0.01
	Present	9	26	19	73	
An infiltrative extraductal mass	Absent	34	100	6	23	0.00
	Present	0	0	20	77	
An infiltrative extraductal mass features						
Size	< 1 cm	0	0	0	0	-
	1-3 cms	0	0	15	75	
	> 3 cms	0	0	5	25	
Location	Right lobe	0	0	6	30	-
	Left lobe	0	0	14	70	
	Right and left lobes	0	0	0	0	
	Extrahepatic	0	0	0	0	
Other associated findings	Absent	33	97	9	35	0.01
	Present	1	3	17	65	
Presented other associated findings	Biliary stone	1	100	1	3	1.00
	Ascites	0	0	3	12	0.07
	Intraabdominal lymphadenopathy	0	0	13	50	0.00
	Distant metastasis	0	0	0	0	-

CCA = cholangiocarcinoma; IHD = intrahepatic bile duct; CHD = common hepatic duct; CBD = common bile duct
a = No statistics are computed because bile duct is a constant

showed that ~ 20% of the periductal CCA cases had intra-abdominal lymphadenopathy[5].

By comparison, the authors found a higher frequency (*i.e.*, 50%) of intra-abdominal lymphadenopathy in the periductal CCA.

In the present study, ~12% of the periductal CCA cases revealed ascites which is not statistically significantly different compared to the intraductal CCA.

According to the study by Joon Woo Lee et al 53.3% of the intraductal CCA cases revealed the intraductal mass upon CT imaging and all > 1 cm intraductal masses could be detected by CT scan[6]. In addition, JK Han and JM Lee showed that the detection of obstructing tumor depends on the size of the tumor and CT scan cannot depict tumors which are < 1 cm, whereas all > 1 cm tumors can be detected[7].

By comparison, the authors found a higher frequency (*i.e.*, 100%) of the intraductal mass in the intraductal CCA. Besides, the authors also found the potential of the spiral or helical CT scan can detect the intraductal mass with the minimum size of 1 cm.

Regarding ascites, intra-abdominal lymphadenopathy and distant metastasis, Joon Woo Lee et al did not find these findings in the intraductal CCA[6] and the authors did not either.

Because the authors utilized multi-detector CT scanner in all cases, the authors found that high efficacy of detecting intraductal mass and intra-abdominal lymphadenopathy detections.

A limitation of the present study could be the purative small sample size because Northeast Thailand is an endemic area of CCA, the number of cases in the present study is not too small, compared to previous studies, which were case reports[3]. In fact, the number of cases in the present study had sufficient statistical power. Because of the authors' using retrospective data collection, it can result in a subjective bias.

Recent reports have shown that the intraductal CCA has a better prognosis after surgical resection than other types of CCA[7-11]. However, the present study did not focus on the prognosis of disease. Further analysis and comparison of the prognosis among the types of CCA is therefore recommended.

Nevertheless, the significant findings of the present study support the indication of a method to confidently distinguish the intraductal from periductal CCA using CT imaging.

Conclusion

In conclusion, the CT findings that helped to differentiate the intraductal from periductal CCA include: the intraductal mass, ductal wall enhancement, an infiltrative extraductal mass and intra-abdominal lymphadenopathy. While the intraductal mass without ductal wall enhancement or intra-abdominal lymphadenopathy tend to indicate the intraductal CCA, ductal wall enhancement, an infiltrative extraductal mass or intra-abdominal lymphadenopathy indicate the periductal CCA.

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การศึกษาเปรียบเทียบลักษณะภาพเอกซเรย์คอมพิวเตอร์ระหว่าง intraductal และ periductal cholangiocarcinoma

นิตยา ฉมาดล, วัลลภ เหล่าไพบูลย์, จีรพงษ์ แก้วระดี, ณรงค์ ขันตีแก้ว, วัชรพงศ์ พุทธิสวัสดิ์, ชวลิต ไพโรจน์กุล

วัตถุประสงค์*: เพื่อศึกษาเปรียบเทียบลักษณะภาพเอกซเรย์คอมพิวเตอร์ ระหว่าง intraductal และ periductal choliocarcinoma ในโรงพยาบาลศรีนครินทร์*

รูปแบบการศึกษา*: แบบสังเกตการณ์เปรียบเทียบ (Observation: analytical study)*

วัสดุและวิธีการ*: เป็นการศึกษาลักษณะภาพเอกซเรย์ขอมพิวเตอร์ย้อนหลังในผู้ป่วย จำนวน 60 ราย ระหว่างเดือนมกราคม พ.ศ. 2547 ถึงเดือน ธันวาคม พ.ศ. 2548 ที่ผลทางพยาธิเป็น CCA เป็น intraductal CCA 34 ราย และเป็น periductal CCA 26 ราย ศึกษาเปรียบเทียบ การขยายของท่อน้ำดี ขนาด ตำแหน่งของพยาธิสภาพ ลักษณะ ductal wall enhancement และลักษณะอื่น ๆ เช่นนิ่ว น้ำในท้อง ต่อมน้ำเหลืองและการกระจายของมะเร็งใช้สถิติ Chi-square และ Fisher exact test*

ผลการศึกษา*: ในผู้ป่วย intraduxtal CCA และ periductal CCA ทุกรายมีการขยายของท่อน้ำดี ในผู้ป่วย intraductal CCA พบ intraductal mass ทุกรายแต่ไม่พบในผู้ป่วย periductal CCA (p = 0.00) intraductal mass ทุกรายขนาดใหญ่กว่า 1 ซม. ใน periductal CCA พบ infiltrative extraductal mass 77% (20/26) แต่ไม่พบใน intraductal CCA (p = 0.00). ลักษณะ ductal wall enhancement พบใน periductal CCA 73% (19/26) และพบใน intraductal CCA 26% (9/34) (p = 0.01) แต่ละกลุ่มพบ นิ่วกลุ่มละ 1 ราย ใน periductal CCA พบ ต่อมน้ำเหลืองในช่องท้องโต 50% (13/26) พบน้ำในช่องท้อง 12% (3/26) แต่ใน intraductal CCA ไม่พบต่อมน้ำเหลืองในช่องท้องโต และน้ำในช่องท้อง (p = 0.00 and 0.07) ทั้งสองกลุ่มไม่พบ distance metastases*

สรุป*: ลักษณะภาพเอกซเรย์คอมพิวเตอร์ที่ช่วยวินิจฉัยแยกโรคระหว่าง intraductal และ periductal CCA ได้แก่ intraductal mass, infiltrative extraductal mass, ductal wall enhancement ลักษณะอื่น ๆ เช่น ต่อมน้ำเหลืองในช่องท้องโตลักษณะของ intraductal CCA ประกอบด้วย intraductal mass ไม่มี ductal wall enhancement หรือต่อมน้ำเหลืองในช่องท้องโต*