Original Article

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Evaluation of Cholangiocarcinoma on MDCT: Varying Imaging Patterns and Preoperative Assessment of Resectability

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Abstract

Background: The objectives of our study are to evaluate the various imaging appearances of cholangiocarcinoma and determine the resectability of the tumour on MDCT. **Subjects and Methods:** Our study is a retrospective study. A search of the case records using the keyword cholangiocarcinoma from the hospital information system yielded 62 patients of cholangiocarcinoma in a period of four years (January 2017 to December 2020). Twelve patients were excluded because of the unavailability of complete records. Study sample was formed by remaining 50 patients. **Results:** In our institute, hilar cholangiocarcinoma was the most frequent type accounting for 60% (30 patients) followed by distal cholangiocarcinoma accounting for 26% (13 patients) and intrahepatic cholangiocarcinoma was the less common type with 14% (7 patients). Out of 30 patients of hilar cholangiocarcinoma, 23.3% (7 patients) showed mass forming type, 70% (21 patients) showed periductal infiltrating type and 6.6% (2 patients) showed intraductal growing type. Intrahepatic biliary radical dilatation was seen in 92% (46 patients), all patients of hilar and distal cholangiocarcinoma, three patients of intrahepatic cholangiocarcinoma. Portal vein involvement was seen in 34 % (17 patients). Lobar atrophy was seen in 58% (29 patients). Involvement of adjacent liver parenchyma in hilar and distal cholangiocarcinoma was seen in 20% (6 out of 30 pCCA). Out of 21 cases that were taught to be resectable based on the findings of CT 12 cases underwent curative resection and the remaining 9 cases were found to have unresectable tumours giving a positive predictive value of 57.14%. **Conclusion:** Cholangiocarcinoma is a slow-growing malignant tumour arising from the bile duct epithelium. Most of the cases have poor diagnosis due to late presentation leading to delay in diagnosis and unresectability. Diagnosis of cholangiocarcinoma on imaging can be done by identifying their typical pattern. In our institute, hilar cholangiocarcinoma (periductal infiltrating) was the most frequent type.

Keywords: Cholangiocarcinoma, computed tomography, imaging patterns, preoperative resectability.

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Introduction

Cholangiocarcinoma (CCA) is a slow-growing malignant tumour that arises from the bile duct epithelium and can occur anywhere from peripheral terminal ductules to the ampulla of Vater.[1,2] The vast majority (95%) of CCA are adenocarcinomas which can be well, moderately, or poorly differentiated with a high proportion of fibrous stroma.[3] It is the second most common liver malignancy after hepatocellular carcinoma and the most frequent malignant tumour of the biliary tract, accounting for 10–20% of all primary liver tumours.[1–3] It is a rare disease and accounts for <2% of all human malignancies.[4] The prevalence of CCA shows geographic variations, with the highest prevalence in Southeast Asia.[5] The aetiology of CCA is not fully understood, but several risk factors like primary sclerosing cholangitis (PSC), hepatolithiasis, liver fluke infestations (Opisthorchis viverrini, Clonorchis sinensis), Thorotrast exposure, and choledochal cysts have been identified.[6]

CCAs can be divided into three subtypes depending on their anatomical site of origin [Figure 1]: intrahepatic CCA (iCCA) above the second-order bile ducts in the liver parenchyma, perihilar CCA (pCCA) between the second-order bile ducts and insertion of the cystic duct into common bile duct whereas distal CCA (dCCA) is confined to the common bile duct below the insertion of the cystic duct. pCCA is the most common group, accounting for approximately 50–60% of all CCAs, followed by dCCA (20–30%) and iCCA (10–20%).[7]

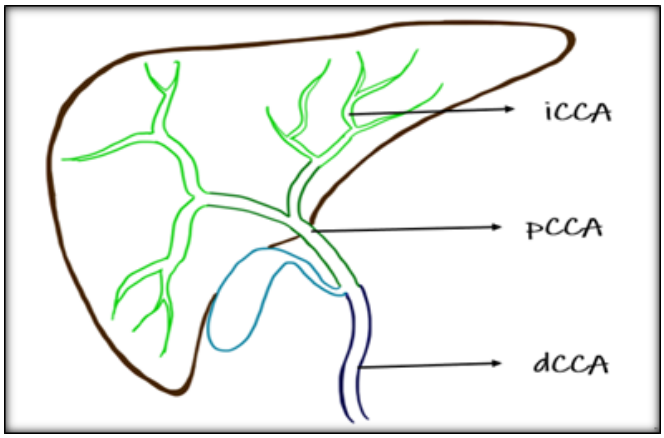

Figure 1: Anatomical subtypes of cholangiocarcinoma. iCCA - intrahepatic cholangiocarcinoma, pCCA - perihilar cholangiocarcinoma, dCCA - distal cholangiocarcinoma.

A tumour that arises from right or left hepatic ducts or their confluence is hilar cholangiocarcinoma (Klatskin tumour) categorized using Bismuth classification [Figure 2] into four types: Type I-Tumour below the confluence of the common hepatic duct.[8] Type II- Tumour involving the confluence; but not extending into the main right and left hepatic duct. Type III- Tumour extending into the right (IIIa) or the left (IIIb) hepatic duct. Type IV-Tumour extending into both right and left hepatic ducts.

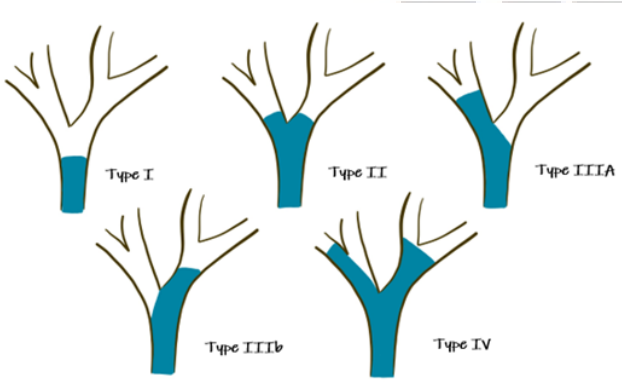

Figure 2: Bismuth corlette classification of hilar cholangiocarcinoma.

As per the morphologic classification system proposed by the Liver Cancer Study Group of Japan,[9] the growth pattern can be classified into mass-forming, periductal infiltrating, and intraductal growth types [Figure 3] each having its own characteristic imaging findings.[10–12] The periductal infiltrating type is more common in the pCCA and the mass forming type is most common in iCCA.[11,12] This classification is considered most reasonable as it describes the gross appearance, biological behaviour and growing characteristics of the tumour. It helps radiologic interpretation and also has prognostic implications for patients.[13]

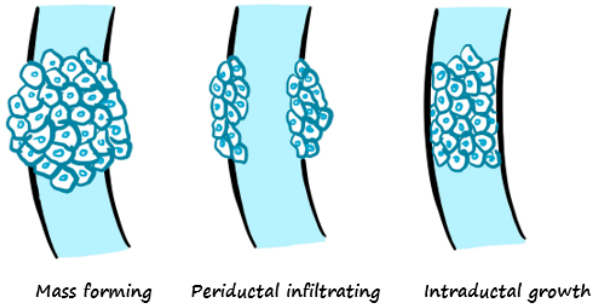

Figure 3: Morphological subtypes of cholangiocarcinoma.

Surgical resection is the potential curative option as the prognosis of CCA is unfavourable. Thus, early diagnosis (in both primary and recurrent diseases) and accurate staging with the evaluation of vascular infiltration, lymph node involvement and distant metastasis are crucial to determine the resectability of the tumour and there comes the main role of imaging. There are various imaging modalities like ultrasonography, computed tomography, MRI and MRCP, PET. Among these CT is the most commonly performed modality (up to 90% of suspected CCA), as it helps in assessing the full extension and determining potential surgical resectability of the tumour. Additionally, pathological details, such as vascular infiltration, presence of lymph nodal and distant metastasis can also be estimated.[2] In this article, we emphasize various imaging patterns and preoperative resectability of cholangiocarcinoma on CT in patients presenting to our tertiary care hospital.

Aims and objectives

- To evaluate various imaging appearances and patterns of cholangiocarcinoma on MDCT
- To determine the resectability of the tumour based on CT findings.

Subjects and Methods

The study design is descriptive. A search of the case records using the keyword cholangiocarcinoma from the hospital

information system was done from January 2017 to December 2020. A retrospective evaluation was done for 62 cases with a diagnosis of cholangiocarcinoma, which was radiologically and histologically proven. Twelve patients were excluded because available records were not optimal. Detailed imaging evaluation of the remaining 50 patients that forms the study group was done. Informed consent was not obtained as the study was retrospective.

The scan was performed on GE OPTIMA 128 SERIAL SLICE CT scanner in all patients. All the patients were scanned using a standard CECT protocol [Table 1]. All images were retrieved from the picture archiving and communication system and viewed on a workstation.

Following criteria was used to diagnose cholangiocarcinoma: intrahepatic or perihilar or distal [either periductal infiltrating or mass forming or intraductal growing mass] enhancing tumour and presence of disproportionately dilated intrahepatic bile ducts with or without vascular infiltration, atrophy-hypertrophy complex, liver parenchymal invasion, lymph nodal and distant metastasis. The Vascular infiltration was considered if there is stenosis or occlusion or deformity of the vessel due to the adjacent tumour mass and/or more than 180 degrees of its circumference involved. The liver parenchymal invasion was considered when there is a direct invasion of the liver parenchyma by tumour mass in hilar and extrahepatic distal cholangiocarcinoma. Lobar atrophy was considered when crowding of intrahepatic ducts was present. Imaging patterns and resectability of the tumour were analysed based on the above findings. In the absence of previous biliary tract surgery, a focal stenotic lesion of the bile duct combined with the appropriate clinical presentation is sufficient for a presumptive diagnosis of cholangiocarcinoma, which is correct in most instances.[14]

Table 1: MDCT protocol used for scanning patients

Parameter	Comment
Area scanned	Plain scan - Domes of the diaphragm to the ischial tuberosity Arterial phase - Domes of the diaphragm to the iliac crest Venous phase - Domes of the diaphragm to the ischial tuberosity Delayed phase - Domes of the diaphragm to the iliac crest
Scan direction	Craniocaudal
Peak voltage (kVp)	120
Tube current (mA)	230
Section thickness (mm)	Arterial: 5, venous: 5, delayed: 5
Pitch	1.2
Rotation time (s)	1
Contrast material injection Volume (ml)	80 ml+20 ml saline
Rate (ml/s)	2-3 ml/sec
Scan delay (s)	30 s for arterial phase followed by venous phase at 70 s and delayed phase at 6-10 min from the start of injection
Three-dimensional technique	Multiplanar reconstruction

Results

We studied 50 patients ranging between 45 to 87 years of age, with the majority of them presenting between 65 to 80 years of age. The sex and age distributions are shown in tables 2 and 3 respectively. All 50 patients had total bilirubin levels done. It was raised in 46 patients (92%). Alkaline phosphatase was done in 50 cases and was elevated in 96% (48 patients) patients. Dilated intrahepatic biliary radicals were seen in 92% (46 patients).

In our study, out of 50 patients, based on anatomical location (table 4), pCCA was the common type accounting for 60% (30 patients) followed by dCCA in 26% (13 patients) and iCCA in 14% (7 patients).

Out of 30 patients showing perihilar cholangiocarcinoma based on morphology [Table 5], Periductal-infiltrating tumour was the commonest form with 70% (21 patients) followed by mass forming 23.35% (7 patients) and intraductal growing

Table 2: Sex wise distribution

Sex	No of patients	Percentage
Male	36	72%
Female	14	28%

Table 3: Age wise distribution

Age (in years)	No of patients	Percentage
< 50	4	8%
50 - 60	14	28%
60 – 70	22	44%
>70	10	20%

type 6.6% (2 patients). According to bismuth corlette (Table 6) classification: type I was seen in one case, type II in 4 cases, type IIIa in 8 cases, IIIb in 10 cases and type IV in 7 cases. Primary confluence was involved in 29 patients (96.66%) and secondary confluence was involved in 22 (73.3%) patients. Adjacent liver parenchymal involvement was present in 6 (20.00%) patients of pCCA

Table 4: Anatomical subtypes of CCA

Location	No. of patients (n=50)	Percentage
Intrahepatic	7	14%
Perihilar	30	60%
Distal	13	26%

Table 5: Morphological subtype in perihilar cholangiocarcinoma

Morphology	No. of patients(n=30)	Percentage
Mass forming	7	23.3%
Periductal infiltrating	21	70%
Intraductal growing	2	6.6%

Out of 13 patients showing dCCA,76.9% (10 patients) showed periductal infiltrating type with or without stricture and 23.1% (3 patients) showed intraductal growing type.

All seven patients of iCCA showed mass forming type and all patients except one showed tumour enhancement in portal venous and delayed phases with capsular retraction.

Out of 50 patients, lobar atrophy was seen in 29 patients (58%) and not seen in 21 patients (42%). Left lobar atrophy in 20 patients (68.9%) and right lobar atrophy in 9 patients (31.1 %). Lobar atrophy was common with perihilar cholangiocarcinoma.

Portal vein involvement was seen in 17 (34%) out of 50 patients. Out of 17 patients, 15 were in perihilar and two were intrahepatic cholangiocarcinoma. Portal vein involvement was present in 9 patients (60.0%), 5 patients (33.3%), and 1 patient (6.6%) in periductal-infiltrating, mass-forming, and intraductal-growing types of perihilar cholangiocarcinoma respectively.

Involvement of either the main hepatic artery or its branches were found in 9 (18 %) cases. Inferior vena cava was involved in one (2.00%) case and hepatic veins involvement was found in two (4.00%) cases. On histopathology, even lymph nodes less than 10mm size have shown metastatic deposits. Hence, size criteria were not used in diagnosing nodal involvement. Any visible lymph nodes on imaging in the pericystic, pericholedochal, hilar, periportal, periduodenal, peripancreatic, superior mesenteric, and celiac locations were documented. Distant metastasis was present in six (12.00%) patients which were seen to liver and lungs. Three out of 50 patients (6%) also showed cholangitic abscess which may be due to ascending infections that subsided with appropriate antibiotic treatment.

Following revised criteria of unresectability by I.Endo et al and Zhang H et al,[15,16] In our study with 50 patients, 21 cases were taught to be resectable based on the findings of CT. out of these 21 cases, 12 cases underwent curative resection and the remaining 9 cases were found to have unresectable tumours giving a positive predictive value of 57.14%. In our institute, none of the patients has undergone any surgery in the remaining 29 patients in whom tumours were detected as unresectable.

Table 6: Bismuth-corlette classification in perihilar cholangiocarcinoma

Bismuth-corlette classification	No. of patients (n=30)	Percentage
Type I	1	3.3%
Type II	4	13.3%
Type IIIa	8	26.67%
Type IIIb	10	33.3%
Type IV	7	23.33%

Discussion

Cholangiocarcinoma is a slow-growing adenocarcinoma that arises from the bile duct epithelium. It is relatively more common in men, occurring frequently between the 6^{th} and 7^{th} decades.[17] In our study patient's ages ranged between 45 to 87 years. The mean age for males was 62.1±11.7 years and for females 64.6±9.8 years. The majority of the patients were in the seventh decade. Our study demographic data were similar to the study conducted by Mahajan MS et al.[18] which was also conducted in the same geographic area. The male to female ratio in our study was 2.57:1. A study by Poomphakwaen K et al.[19] also showed a sex ratio of 2:1.

Cholangiocarcinoma is usually asymptomatic in the early stages. Diagnosis at advanced stages of the disease reduces therapeutic options resulting in a poor prognosis.[7] Hence, imaging plays a crucial role in accurate preoperative evaluation, to determine the tumour resectability and also to select the appropriate surgical procedure.[20] CT is the most commonly performed imaging modality in up to 90% of suspected Cholangiocarcinoma. Multiphase CT scanning protocols are recommended in the primary staging of Cholangiocarcinoma. In the pre-contrast phase, biliary stones (one of the risk factors for CCA) can be identified.[21] In the arterial phase, the exact

vascular anatomy of the liver and its relation with the surrounding structures and tumours can be evaluated precisely, which helps in detailed surgical planning. In the portal venous phase, CCA mainly appears as a central low attenuating mass with peripheral incomplete rim enhancement. It increases the precision in the estimation of the tumour size and also helps in the detection of satellite nodules.[12] In delayed-phase scans (5–10 min after injection of the contrast), delayed tumour enhancement can be appreciated, which represents the amount of fibrous stroma in the tumour. Delayed enhancement may not be seen in the case of tumour necrosis and/or mucin containing cells.[22] Volumetric scanning technique of CT helps in estimating the liver volume and potential liver remnants in preoperative assessment which helps in avoiding postoperative small-for-size syndrome. Alternative procedures like ALPPS (associating liver partition and portal vein ligation for staged hepatectomy) can be considered based on this information.[23–25] One of the main limitations of CT is that it may underestimate metastatic lymph nodal or peritoneal involvement. PET/CT appears to be the best technique in detecting lymph node and distant metastasis but it has no clear role in evaluating the local resectability of the tumor.[16]

Our study showed 14%,60% and 26% of iCCA, pCCA and dCCA respectively based on anatomical subtypes. A study by Ghouri YA et al showed 6–8% of iCCA, 50–67% of pCCA, and 27–42% dCCA.[26]

In our study, all seven cases of peripheral intrahepatic cholangiocarcinoma were of mass forming type. We didn't encounter any periductal infiltrating or intraductal growing type of intrahepatic cholangiocarcinoma. Out of seven, six cases showed portal venous and delayed enhancement and only one case showed early arterial enhancement. All patients showed capsular retraction. Segmental/ lobar Intrahepatic biliary radical dilatation is seen in three out of seven cases. Portal vein involvement was seen in two cases.

Periductal infiltrating iCCA is characterized by a growth pattern along the bile duct without mass formation. The involved bile ducts show diffuse periductal thickening with progressive enhancement on multiphase CT and the involved segment can be either dilated or narrowed in calibre. Often, intrahepatic biliary radical dilatation can be seen proximal to the lesion.[12]

Intraductal growth of iCCA is primarily characterized by an irregular duct calibre. Various imaging patterns are as follows: Diffuse/marked duct ectasia with or without visible papillary mass or Intraductal polypoidal lesion in focally dilated duct or intraductal cast like lesion in a mildly dilated duct or focal stricture like lesion with proximal dilatation. On multiphase CT it appears as a hypoattenuation with irregular margins on pre-contrast imaging, which shows progressive enhancement in subsequent post-contrast images.[12]

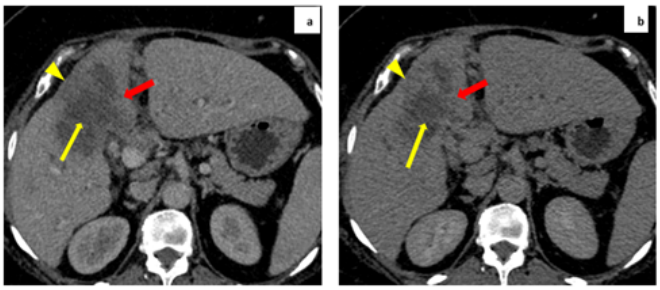

Figure 4: Intrahepatic mass forming cholangiocarcinoma: Axial sections of CT images in portal venous phase (a) and delayed phase (b) showing peripheral enhancement (red arrow) with central non enhancing area (yellow arrow) in segment V of right lobe of liver with adjacent capsular retraction (yellow arrow head).

In the staging of pCCA and dCCA, the exact localization of the tumour with its longitudinal and lateral extensions are of primary importance as the surgical resection method and the patient's prognosis both depend on these factors.[27] Prognosis is poor for lesions affecting the confluence and better for lesions close to the ampulla.

In our study pCCA is the commonest form of cholangiocarcinoma accounting for 60% (30 out of 50 patients). In pCCA, Periductal-infiltrating tumour was the most frequent morphological type followed by mass-forming and intraductal-growing tumours. Mahajan MS et al. and Longlin Y et al.[18,28] also found that the periductal-infiltrating tumour was the most common and the intraductal-growing tumour was the least common morphological type. According to bismuth classification type IIIb was the commonest form in our series.

Out of 13 patients showing dCCA,76.9% (10 patients) showed periductal infiltrating type with or without stricture and 23.1% (3 patients) showed intraductal growing type in our series.

Invasion of adjacent liver parenchyma is important in determining tumour resectability.[29] Our study in 30 patients of perihilar cholangiocarcinoma revealed adjacent liver parenchyma involvement in 6 patients (20%). A study on perihilar cholangiocarcinoma by Mahajan MS et Al.[18] showed liver parenchyma invasion in 50% of patients.

Segmental or lobar atrophy in CCA is a result of portal venous or biliary obstruction or both and its identification while imaging is important as it has implications for management.[14] No liver resection should be performed that leaves an atrophic remnant.[29] Our series showed atrophy in 29(58%) cases. A study by Feydy A et al.[30] showed lobar atrophy in six out of eleven (54.54%) patients on helical CT. In our study, left lobe atrophy was more frequent, seen in 68.9% and right lobar atrophy (either anterior or posterior segment or both) in 31.1%.

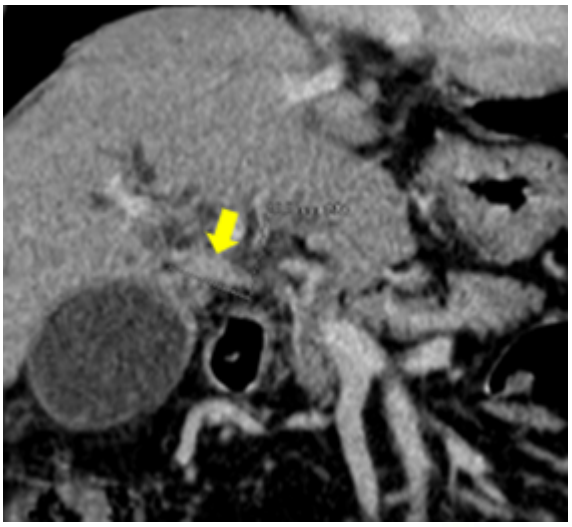

Figure 5: Type 1 Bismuth classification. Coronal section portal venous phase CT showing periductal infiltrating type of perihilar cholangiocarcinoma in common hepatic duct (yellow arrow) without involvement of the primary confluence causing intrahepatic biliary radical dilatation.

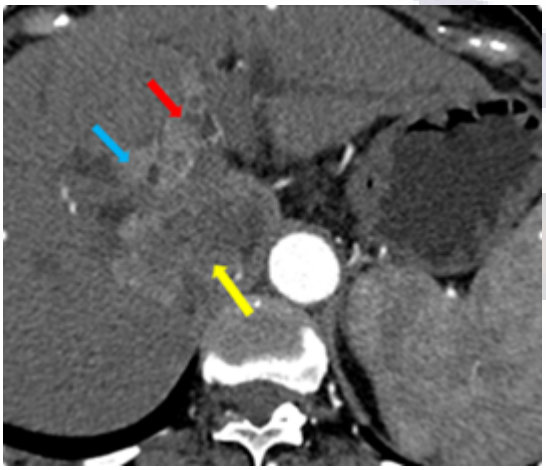

Figure 6: Type IV bismuth classification: Axial CT arterial phase image showing heterogeneously enhancing intraductal growing type of tumour extending beyond primary confluence into right (blue arrow) and left (red arrow) hepatic ducts. Extension into the adjacent liver parenchyma also seen (yellow arrow).

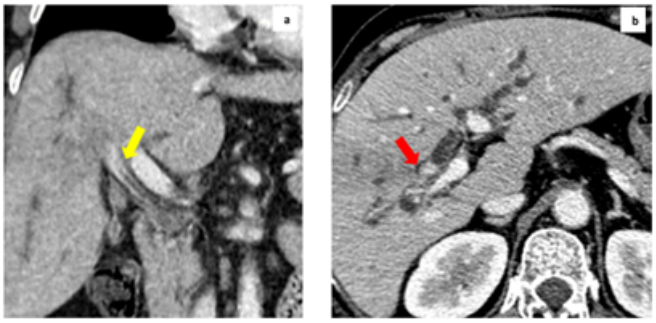

Figure 7: Type IIIa bismuth classification. Coronal section (a) portal venous phase CT showing enhancing periductal infiltrating type of cholangiocarcinoma in the common hepatic duct extending up to the primary confluence (yellow arrow). Axial section (b) portal venous phase CT of the same patient shows extension of tumour beyond the primary confluence into right hepatic duct (red arrow).

Figure 8: Distal cholangiocarcinoma: Coronal portal venous phase CT image showing enhancing wall thickening (yellow arrow) of the common bile duct beyond the insertion of cystic duct causing moderate bilobar IHBRD.

Both right and left lobar atrophy was seen in none of the patients. In our study, involvement of the main hepatic artery or its branches was seen in 9 (18 %) cases. Inferior vena cava was involved in one (2.00%) case and hepatic veins were involved in two (4.00%) cases. Distant metastasis was present in six (12.00%) patients. Three out of 50 patients (6%) also showed cholangitic abscesses.

Following are the Unresectability criteria for cholangiocarcinoma.[15,16]

1. Type IV bismuth classification and tumour extending beyond 2 cm from the hilum
2. Vascular Invasion (either main portal vein or proper hepatic artery) and involved segment greater than 2 cm.

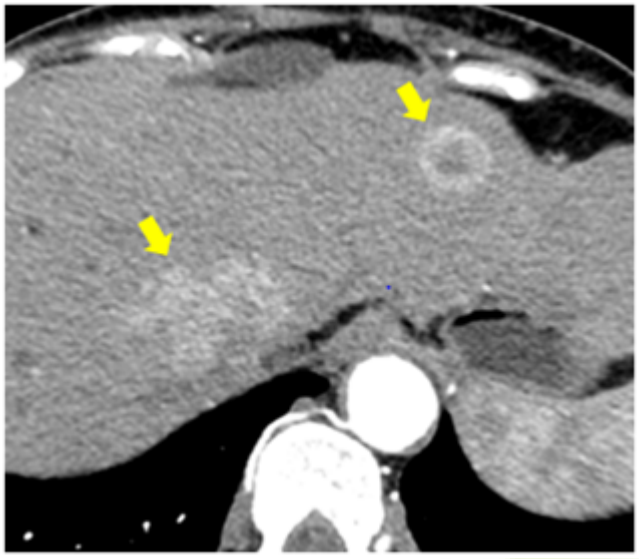

Figure 9: Liver metastasis: Axial sections of CT images showing arterial enhancing masses in segment II and VIII of liver in case of hilar cholangiocarcinoma shown in the figure 6.

3. Lobar atrophy on one side with vascular invasion on contralateral side.
4. Lobar atrophy on one side with an extension of the tumour to secondary biliary confluence on the contralateral side.
5. Tumour invasion of secondary biliary confluence in one lobe and vascular invasion in the contralateral lobe.
6. Metastasis to lymph nodes in celiac, portocaval, or paraaortic locations.
7. Distant metastasis.

Following the above criteria, 21 out of 50 patients were taught to be resectable based on the findings of CT. However, only 12 out of 21 cases underwent curative resection and the remaining 9 cases were found to be unresectable tumours. positive predictive value of CT in detecting tumour resectability in our study was 57.14%. 29 patients in whom tumours were detected as unresectable did not undergo any surgery in our study

In a study by Lee HY et al,[31] positive and negative predictive values for tumour resectability based on CT and cholangiographic findings were found as 71.4% and 84.6% respectively. Sources of inaccuracies were underestimation of bile duct involvement, underestimation of diffuse tumour infiltration extending to the hepatoduodenal ligament, and inaccurate assessment of vascular involvement.

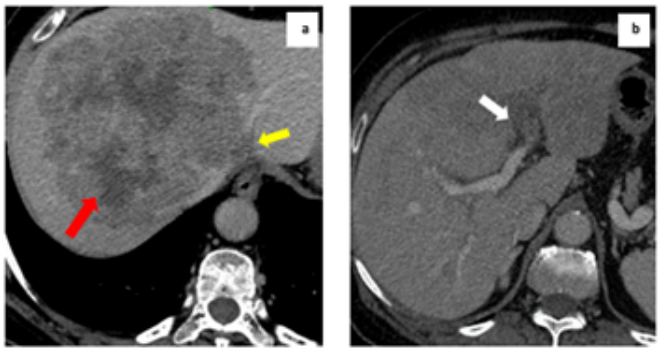

Figure 10: Axial CT portal venous phase image (a) showing a large intrahepatic cholangiocarcinoma (red arrow) with involvement of left hepatic vein near the confluence into IVC (yellow arrow). Also note attenuated calibre of the middle and right hepatic veins. Axial CT portal venous phase image (b) in the same patient shows involvement of the left portal vein and it's branches (white arrow).

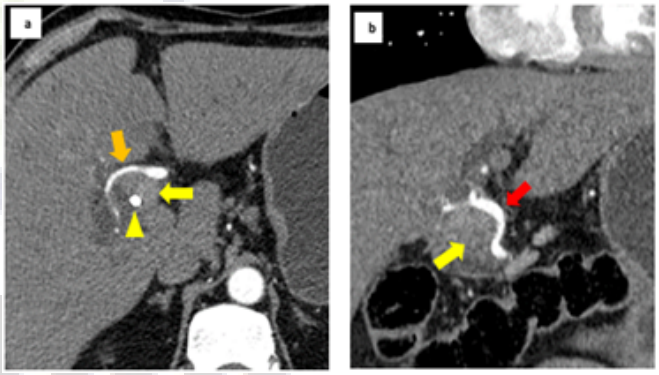

Figure 11: Axial (a) and coronal (b) sections of CT arterial phase images showing distal intraductal growing type of cholangiocarcinoma (yellow arrow) in a patient having long standing CBD stent (yellow arrow head). There is involvement of common hepatic (red arrow) and right hepatic (orange arrow) arteries by the tumour.

Conclusion

Cholangiocarcinoma is a slow-growing malignant tumour arising from the bile duct epithelium. Most of the cases have poor diagnosis due to late presentation leading to delay in diagnosis and unresectability. Imaging plays a crucial role in evaluating typical characteristics and extent of the tumour and determining the resectability of the tumour preoperatively and CT is the most frequently used modality. In our study, we described various imaging appearances and preoperative

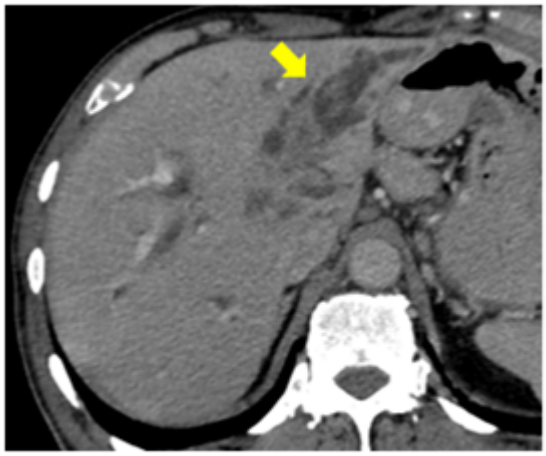

Figure 12: Left lobar atrophy in case of bismuth type II hilar cholangiocarcinoma. Note the crowding of dilated intrahepatic biliary radicals dilatation (yellow arrow).

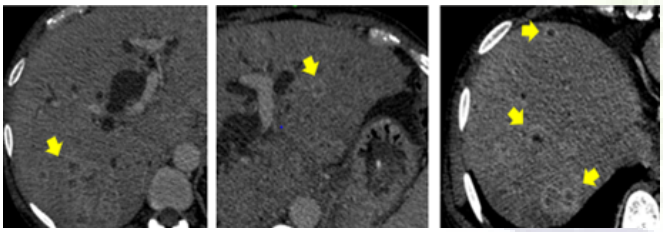

Figure 13: Cholangitic abscess. Axial sections of CT portal venous phase images showing multiple small peripherally enhancing hypodense lesions (yellow arrows) in both lobes of liver in case of a distal cholangiocarcinoma.

resectability of cholangiocarcinoma in a sample of 50 patients presenting to our tertiary care institute.

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