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Review

A dichotomous imaging classification for cholangiocarcinomas based on new histologic concepts

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ABSTRACT

We noted the limitations of applying conventional macroscopic patterns to classify the imaging features of cholangiocarcinoma (CCA). Therefore, we hereby propose a dichotomous imaging classification of "parenchymal" and "ductal" types, based on recent developments in the histopathologic concepts of CCA. This new imaging classification of CCA is simple and easy to apply, and can be useful to describe underlying carcinogenesis and correlate clinicopathologic characteristics with imaging patterns of CCA.

1. Introduction

Cholangiocarcinoma (CCA) presents varying appearances on imaging according to the location, morphologic growth pattern, and cell type [1]. Imaging features of CCA have commonly been grouped into three patterns of gross morphologic manifestations: mass-forming (MF), periductal infiltrating (PI), and intraductal growing (IG) [2,3]. This classification is useful to illustrate typical imaging patterns but may not accurately reflect pathogenesis or the new concept of histologic classifications. According to the current histological classifications, CCA can be divided into small duct and large duct types [2,4]; the former is regarded as originating from small ductules or the canals of Hering and the latter from mature cholangiocytes or the peribiliary glands of the large bile duct (Fig. 1) [5]. Here, we propose an imaging classification of CCA in accordance with the new histologic concepts by dividing tumors into either the 'parenchymal' or 'ductal' type. The parenchymal type represents mass-forming tumors with no gross involvement or dilation of the bile duct, and the ductal type represent any tumors (e.g., MF, MF + PI, or PI) with the imaging features of peritumoral duct dilation or periductal tumor spread.

2. Varying imaging features of cholangiocarcinoma

Cholangiocarcinomas (CCA) present a wide variety of imaging features [1]. The varying appearances of CCA on imaging may be partly attributed to various cells of origin of the tumors such as mature cholangiocytes, the peribiliary gland, hepatic progenitor cells, or mature hepatocytes [6]. Another reason may be that they arise from different anatomical environments in the form of either intrahepatic (iCCA), perihilar (pCCA), or distal (dCCA) CCA [3]. In addition, CCA may present different macroscopic growth patterns manifesting different imaging features.

The imaging features of CCA have commonly been grouped into three morphologic growth patterns: mass-forming (MF), periductal infiltrating (PI), and intraductal growing (IG) (Fig. 2) [7]. Typically, an MF-CCA manifests as a non-encapsulated mass showing irregular rim-like enhancement at the early dynamic phase and gradual central enhancement with peripheral washout in later-phase images [1]. A PI-CCA presents as irregular wall thickening and upstream dilation of the obstructed bile duct. However, IG-CCA may also exhibit varying appearances due to the degree and extent of ductal dilation (diffuse, cystic, or minimal dilation), the degree of mucin excretion, and the size (poorly or highly visible) and extent (focal or diffuse papillomatosis) of the intraductal lesion [1,8–11].

3. Problems in conventional morphologic classifications

The gross morphologic classifications are useful to describe the typical imaging patterns of CCA but have some limitations in explaining atypical or complex tumors and also in relating the macroscopic growth patterns of the tumors with their pathogenesis and clinicopathologic characteristics.

3.1. MF and mixed type

Among the macroscopic growth patterns, the MF type accounts for

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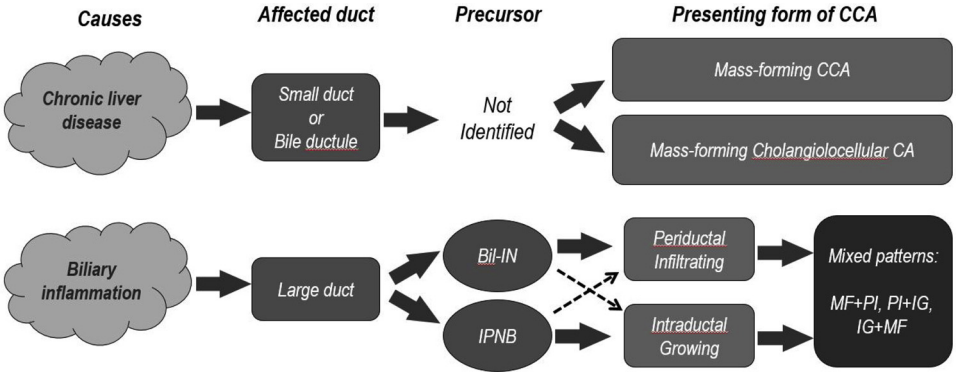

Fig. 1. Carcinogenesis and evolution of cholangiocarcinoma (CCA). Small duct type CCA is associated with chronic liver disease, and arises from progenitor cells then progresses to MF-CCA or cholangiolocellular carcinoma. Large duct type CCA is associated with chronic biliary inflammation, and arises in the form of Bil-IN or IPNB then progresses to periductal infiltrating, intraductal growing, or mixed form of CCA.

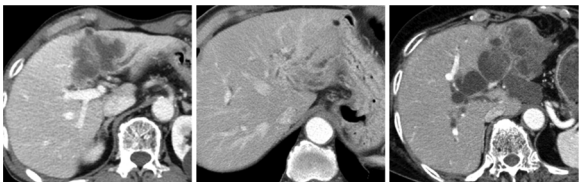

Fig. 2. Macroscopic growth patterns of intrahepatic CCA. A–C. Based on CT imaging, the tumors depicted were regarded as a mass-forming (A), periductal infiltrating (B), and intraductal growing (C) CCA. However, they were reported as a mass-forming and periductal infiltrating (A), periductal infiltrating and mass-forming (B), and intraductal and periductal and mass-forming (C) CCA on pathologic reports.

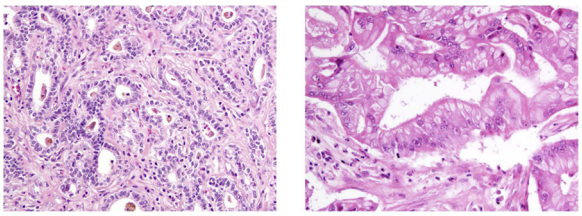

Fig. 3. Small duct type CCAs are composed of cuboidal to low columnar tumor cells with scant eosinophilic or amphophilic cytoplasm forming small monotonous glands. (Fig. 1A, original magnification 200×) In contrast, large duct type CCAs consist of tall columnar tumor cells resembling epithelia of large intrahepatic bile duct arranged in a large glandular pattern. Large duct type CCAs often have a clear cytoplasm suggesting mucin production. (Fig. 1B, original magnification 200×).

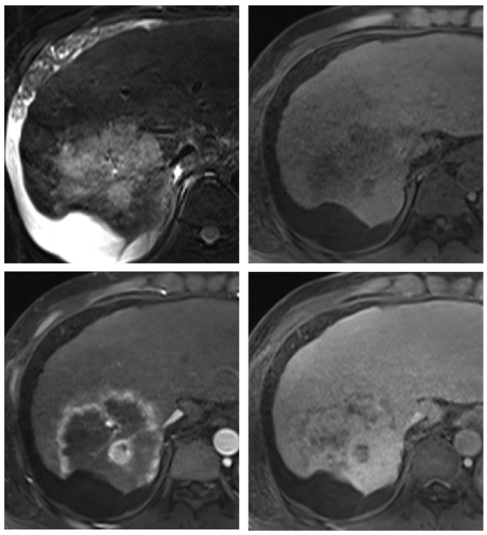

Fig. 4. Parenchymal type CCA in a 40-year-old man with B-viral cirrhosis. A, B. The irregularly marginated mass is hyperintense on the T2-weighted fast spin-echo image (A) and hypointense on the T1-weighted 3D fat-suppressed gradient-echo image (B). C, D. The dynamic arterial (C) and delayed (D) phase images show irregular peripheral enhancement and delayed central enhancement. Note that there is no biliary dilation in either the peritumoral or remote areas of the liver even though the mass is relatively large.

more than 80% of iCCA [12,13], but this figure also includes some mixed type tumors such as MF + PI, which is the second most common type of growth pattern in iCCA [14,15]. Mixed MF + PI type tumors are not only common, but also represent a different pathogenesis and origin from pure MF-CCA because the former (MF + PI type) are mostly large duct type tumors and the latter (MF type) are typically the small duct type according to the new histopathological concept [30]. Although the MF + PI pattern was initially introduced as a distinctive type [16], other mixed patterns, such as MF + IG or PI + IG, can also exist [15]. However, on imaging, the less dominant component of the mixed pattern may not be well depicted, leading to a discrepancy between the imaging and pathological classifications (Fig. 2). For example, a tumor that was considered a PI or MF tumor may be reported as an MF + PI-iCCA after pathologic examination [17,18]. Therefore, MF-CCA and MF + PI-CCA have been commonly grouped together to explain the imaging features for analysis of the clinical characteristics in radiologic literature [18–20].

3.2. PI type

A pure PI-type tumor is not only rare in iCCA but also typically presents as a smaller lesion at the time of diagnosis compared to other gross type tumors and tends to have better survival than MF- or MF + PI-iCCA with a lower incidence of intrahepatic and nodal metastases [14,18,21]. These characteristics of PI-iCCA – lower incidence, small size at presentation, and better outcome after surgery – suggest that the PI type is an earlier or intermediate stage of CCA in the progression to more advanced forms, such as MF + PI type CCA, presenting with a larger size and worse post-surgical outcome [14]. Therefore, the two macroscopic patterns may represent different stages of one type of tumor.

3.3. IG type

In addition, IG-CCA is commonly either described together or sometimes confused with intraductal papillary neoplasms of the bile duct (IPNB) [7,11,22,23]. Intraductal tumors may be IPNB or its invasive forms [24] or may also represent early stage tumors or intraductal tubular or tubulopapillary carcinomas of different origins [25–29]. When an intraductal growing tumor extends outside of the bile duct, it may manifest as a mixed pattern of IG + MF or IG + PI CCA [30]. However, a colloid carcinoma, which is thought to arise from IPNB [31], may manifest as only a mass-forming tumor without a grossly visible intraductal component.

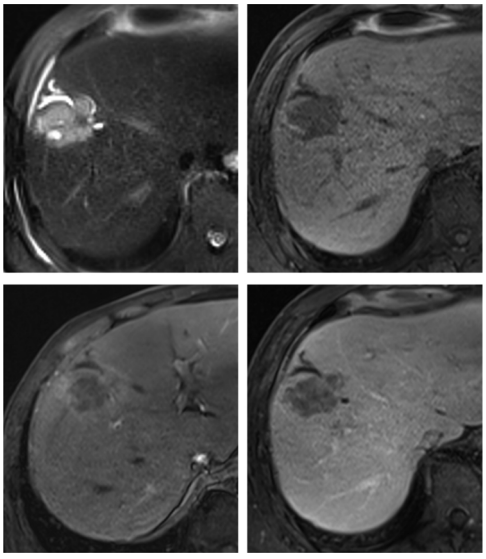

Fig. 5. Ductal type CCA in a 67-year-old man with no known risk factors. A, B. The lobulated mass is hyperintense on the T2-weighted fast spin-echo image (A) and hypointense on the T1-weighted 3D fat-suppressed gradient-echo image (B). C, D. On the dynamic arterial (C) and venous (D) phase images, the mass shows irregular peripheral enhancement and progressive internal enhancement. Although the mass is relatively small and located periphery of the liver, the adjacent bile duct is dilated at the peritumoral area.

3.4. Size and locations

The gross morphologic classifications also seem more closely related with the size of a tumor or the diameter of the involved bile duct rather than the underlying pathogenesis of the tumors. For example, the PI and IG patterns are uncommon in iCCA and are usually seen in pCCA and dCCA [14,15,17], but most CCA arising in the large perihilar bile duct is the MF + PI pattern [2,32]. For dCCA, some authors advocate application of the same morphologic classifications, but in iCCA and dCCA, the MF pattern does not have the same imaging appearance. Additional terms such as nodular, papillary, or sclerosing are therefore also used to classify the morphologic type of dCCA [33–36].

4. Recent histologic classifications

Histologically, CCA has been traditionally classified into classical (well-, moderately, and poorly differentiated) and variant forms of carcinomas such as adenosquamous or squamous carcinomas [37]. However, during the last decade, several new histological classifications have been introduced [4,38–41]. Although those classifications have used different histopathologic criteria, they are similar in reflecting their anatomical origin and pathogenesis [2]. According to one new histological classification, CCA can be divided into the conventional (ductal) type, the ductular type, the intraductal type, and rare variants [4,13]. In the case of iCCA, the ductal type can be further divided into the small bile duct type and the large bile duct type (Fig. 3) [30,38]. While ductular type tumors are only present in iCCA, the intraductal type can be seen in iCCA, pCCA, or dCCA. Additionally, ductular and small bile duct CCA may be grouped together as the small duct type [30].

On microscopic examination, small bile duct type CCA is composed of cuboidal or low columnar cells with scant cytoplasm and enlarged nuclei, and exhibits a tubular or ductular pattern of growth. Contrarily, the large bile duct type is composed of tall columnar cells with eosinophilic cytoplasm, and they are characterized by low cellularity, abundant mucin, and a fibrous stroma [41].

Studies have shown that histologic subtype is a significant prognostic factor of iCCA. Hayashi et al. [42] have used scoring of mucin productivity and immunophenotype to classify iCCA into type 1 and type 2. Their study showed that type 1, which shared the characteristics of large duct, CCA were more frequently associated with poor prognostic factors, such as poor differentiation or perineural invasion, and also showed significantly worse recurrence-free and overall survival after surgical resection. Similar results have been reported by Aishima et al. [38], Liau et al. [41], and Akita et al. [31]. In radiological reports, CCA showing small duct CCA also tended to have better postsurgical outcomes [20,43].

4.1. Histologic classification and pathogenesis

When tumor carcinogenesis is explained according to the new classifications, large duct type tumors are regarded as having developed in association with chronic biliary inflammation (e.g., primary sclerosing cholangitis, intrahepatic stone disease, or chronic biliary infection). They arise from large bile duct epithelia or the peribiliary glands as a form of Bil-IN or IPNB as its precursor lesion then progress to the various morphologic types including PI, IG, IG + MF, or MF + PI CCA [30]. However, small duct type tumors are associated with chronic liver disease and are suspected to arise from progenitor cells near the canals of Hering without a known premalignant lesion then progress to MF-CCA of the small ducts or ductular (cholangiolocellular) type CCA.

According to this new histological classification, small duct type CCA may be assumed to be found in the peripheral liver and large duct type tumors in a more central part of the liver. However, this topographical relationship may be difficult to demonstrate on cross-sectional imaging because of the complex structure of the intrahepatic biliary tree, even though a higher frequency of extensive bile duct encasement has been shown in large duct type tumors [43].

4.2. Imaging and histologic correlation

Several imaging studies have demonstrated a relationship between dynamic enhancement patterns on CT or MRI and the clinicopathologic characteristics of CCA [19,20,44,45]. A study using CT showed that large duct type iCCA tends to show hypovascular enhancement, but the small duct type more frequently exhibits rim enhancement or hypervascular enhancement [20]. More recently, Nam et al. [43] reported that small duct type iCCA more frequently showed arterial

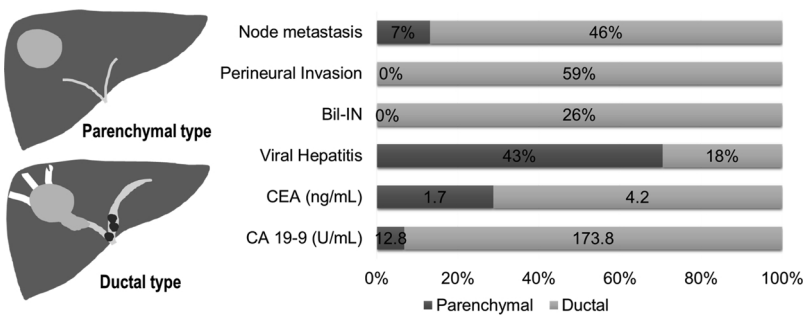

Fig. 6. Schematic drawings and clinicopathologic characteristics of parenchymal and ductal type cholangiocarcinomas (CCA). Parenchymal type CCA is characterized by absence of ductal abnormalities and association with viral hepatitis. Ductal type CCA is characterized by peritumoral dilation, periductal spread, or underlying biliary disease in the background liver, and shows more frequent node metastasis, perineural invasion, and biliary intraepithelial neoplasm (Bil-IN). Serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 are significantly higher in ductal type CCA.

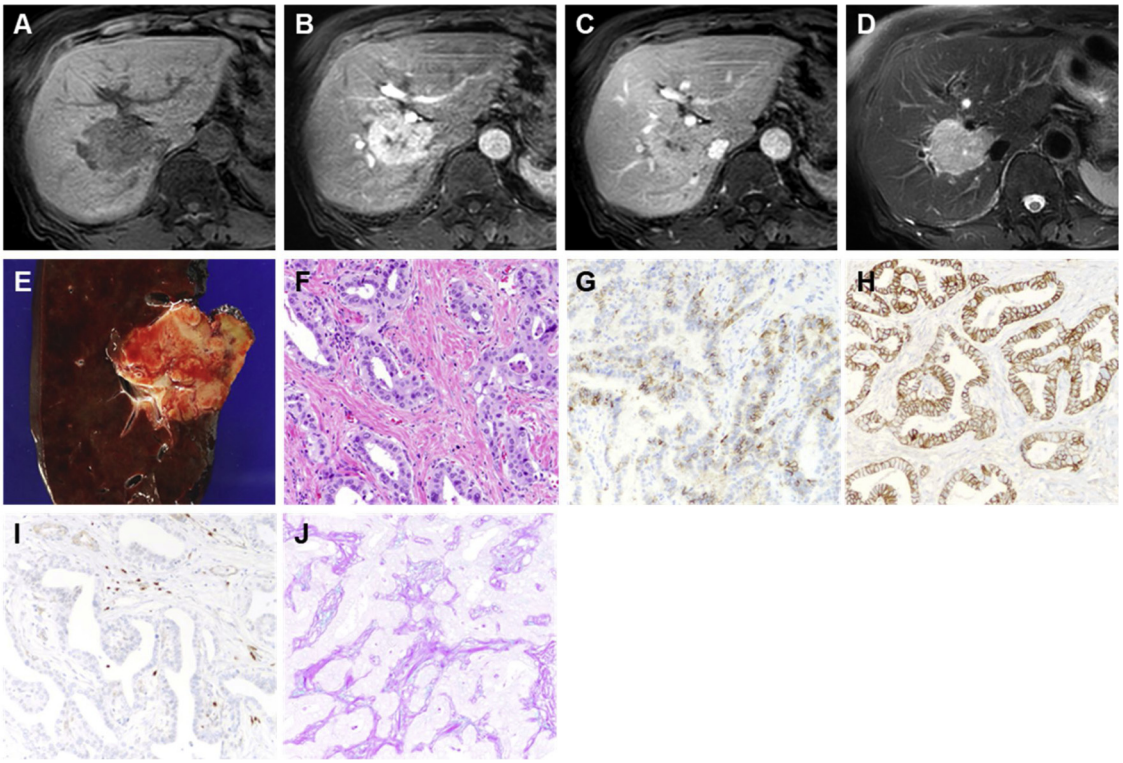

Fig. 7. Parenchymal type CCA in a 79-year-old woman. A 5-cm mass lesion showing hypointensity on T1-weitghted image (A), arterial enhancement (B), no apparent washout on portal phase (C), and hyperintensity on T2-weighted image (D). No biliary dilatation or periductal infiltration was noted on MR images or gross specimen (E). Microscopic exam showed that the tumor was composed of small glands with cuboidal cells (F, hematoxylin-eosin stain), suggesting small duct type CCA. Tumor cells were positive for two small duct type CCA markers (G, CD56; H, N-cadherin), negative for large duct type CCA marker (I, S100 P), and also negative for mucin (J, Alcian Blue stain).

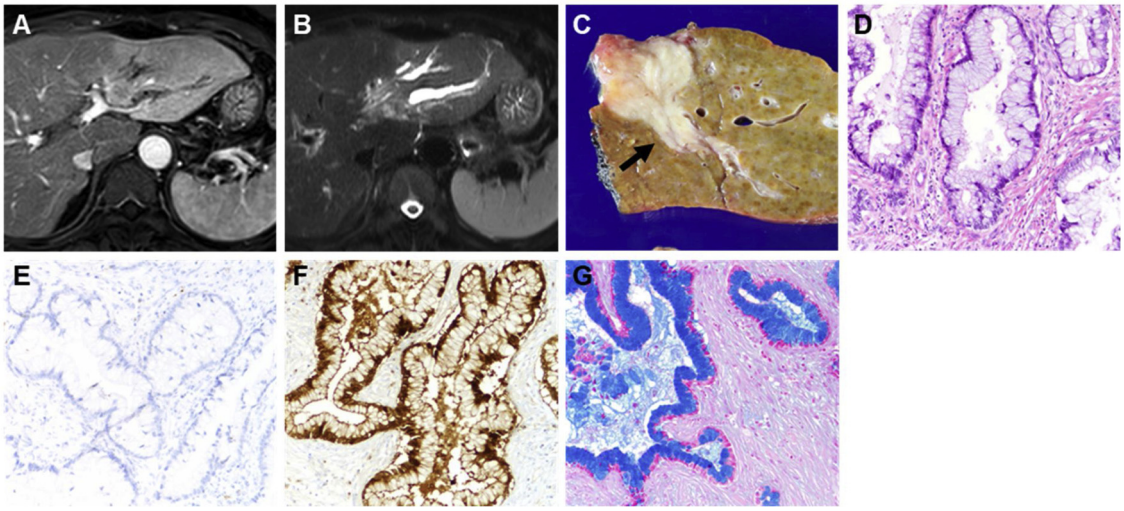

Fig. 8. Ductal type CCA in a 73-year-old woman. A 2.8-cm nodular lesion in left lateral section of liver, causing distal biliary dilatation (A, B). On gross examination, periductal infiltration of tumor was noted (C, arow). Tumor was composed of tall columnar tumor cells arranged in a large glandular pattern (D, hematoxylin-eosin stain). On immunohistochemical stain, tumor cells were negative for small duct type CCA marker (E, CD56), and positive for large duct type CCA marker (F, S100 P). In addition, there were abundant intracellular and extracellular mucin, which are common in large duct type CCA (G, Alcian Blue stain).

hyperenhancement, round or lobulated contours (compared to an irregular shape), a left lobar location (compared to right lobar), and a lack of bile duct encasement and less commonly presented with lymph node enlargement. In a detailed pathologic study correlating with MRI, Komuta et al. [40] showed that mucinous iCCA corresponding to large duct type tumors tend to show homogeneous T2 intensity and concentric filling in dynamic venous phase images, whereas iCCA corresponding to small duct type tumors tend to show mixed T2 intensity and washout patterns [40]. Additionally, cholangiolocellular carcinomas, a ductular type or a subtype of small duct type tumor, tend to show imaging features similar to cholangiocarcinoma in terms of progressive dynamic enhancement, target appearance, and vessel penetration along with some features similar to HCC such as hypervascular enhancement [46–48].

However, there have been considerable discrepancies in the proportion of tumors showing hypervascular patterns reported in previous

literature [19,20,49–52], indicating some interobserver differences in determining whether a tumor shows hypervascular or rim-like enhancement. Moreover, the degree of the correlation between enhancing patterns and histologic types seems not high enough to determine the histologic type using enhancement pattern alone.

5. Proposal of dichotomous imaging classifications

Given that the new histologic classifications indicate that there could be substantial differences in the involved bile ducts at the anatomical level, it is surprising that current studies have not correlated imaging features and the histologic type of CCA in the context of the relationship between the tumor and morphological changes in the affected biliary tree [19,20].

As described above, pure MF type CCA is likely a small duct type tumor associated with chronic liver disease that shows either no or minimal biliary dilation, while mixed type CCA is likely a large duct type tumor that shows ductal dilation or abnormality. Based on this assumption, we have proposed a simple, dichotomous imaging classification by dividing CCA into a “parenchymal” type or a “ductal” type to correlate the macroscopic growth pattern with the underlying clinicopathologic characteristics.

5.1. Imaging and clinicopathologic features of parenchymal and ductal type CCA

In this dichotomous imaging classification, “parenchymal” type represents tumors with no gross involvement or dilation of the bile duct, and “ductal” type represents tumors with imaging features of periductal tumor spread or ductal dilation (Figs. 4 and 5): Periductal tumor spread may be represented by soft tissue thickening along the periportal space. Ductal dilation may present as peritumoral dilation due to tumor invasion, or as diffuse biliary dilation due to underlying chronic biliary disease. According to an our recent study [54], parenchymal type CCA was more frequently associated with viral hepatitis, while ductal type CCA showed higher frequency of node metastasis and higher serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9. Coexistence of biliary intraepithelial neoplasm or perineural invasion was noted only in ductal type CCA (Fig. 6, 7 and 8).

5.2. Relationship with other classifications

According to the proposed imaging classification, ‘parenchymal’ type CCA will mainly correspond to small duct type tumors showing a pure MF pattern, and the ‘ductal’ type will mainly correspond to large duct type tumors showing an MF + PI pattern, but would also include the pure PI or IG patterns as well as other mixed patterns, such as an MF + IG pattern, of large duct origin of all locations (iCCA, pCCA, or dCCA).

However, imaging types may not exactly match histologic types. Therefore, we suggest that the imaging classification should be used separately from histologic classifications because it is possible some small duct type tumors to be present with ductal involvement, especially at the area of off-center to the tumor when a tumor is larger or located near the central liver. Additionally, some large duct type tumor may not present peritumoral duct dilation. Therefore, we avoid using the histological terms of ‘small duct’ or ‘large duct’ to classify the imaging patterns because those histologic types should be determined based on various histopathologic findings. Nonetheless, the proposed imaging classification dividing the CCA into ‘parenchymal’ and ‘ductal’ types may be useful to explain the imaging findings based on current clinicohistologic concepts and in future research addressing the significance of imaging findings in relation to carcinogenesis and clinical outcomes.

We note that our classification is also in line with a new proposal of pathologic classification of CCA proposed by Bragazzi et al. [32], in which CCA was also divided into “primary liver parenchymal” and “primary biliary” CCA. The former type may correspond to our “parenchymal” type tumor, and the latter to our “ductal” type tumors. However, the differences of imaging features or clinicopathologic features between the two types have not yet been explained. Fernandez Moro et al. [53] also demonstrated that iCCA may represent heterogeneous group in terms of immunohistochemical characteristics by showing similar patterns with perihilar or extrahepatic CCA in one group.

In conclusion, we propose a new imaging classification to categorize CCA into ‘parenchymal’ and ‘ductal’ types, which should be determined separately from the histologic type. This dichotomous imaging classification is simple and easy to apply, and it may also be useful to describe underlying carcinogenesis and have relevant relationship with clinicopathologic characteristics of iCCA. Further research is warranted to address the feasibility and clinical utility of this imaging classification.

Conflict of interest

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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References

[1] Y.E. Chung, M.J. Kim, Y.N. Park, J.Y. Choi, J.Y. Pyo, Y.C. Kim, H.J. Cho, K.A. Kim, S.Y. Choi, Varying appearances of cholangiocarcinoma: radiologic-pathologic correlation, Radiographics 29 (3) (2009) 683–700.
[2] J.M. Banales, V. Cardinale, G. Carpino, M. Marzioni, J.B. Andersen, P. Invernizzi, G.E. Lind, T. Folseraas, S.J. Forbes, L. Fouassier, A. Geier, D.F. Calvisi, J.C. Mertens, M. Trauner, A. Benedetti, L. Maroni, J. Vaquero, R.I. Macias, C. Raggi, M.J. Perugorria, E. Gaudio, K.M. Boberg, J.J. Marin, D. Alvaro, Expert consensus document: cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA), Nat. Rev. Gastroenterol. Hepatol. 13 (5) (2016) 261–280.
[3] N. Razumilava, G.J. Gores, Cholangiocarcinoma, Lancet 383 (9935) (2014) 2168–2179.
[4] Y. Nakanuma, Y. Sato, K. Harada, M. Sasaki, J. Xu, H. Ikeda, Pathological classification of intrahepatic cholangiocarcinoma based on a new concept, World J. Hepatol. 2 (12) (2010) 419–427.
[5] V. Cardinale, G. Carpino, L. Reid, E. Gaudio, D. Alvaro, Multiple cells of origin in cholangiocarcinoma underlie biological, epidemiological and clinical heterogeneity, World J. Gastrointest. Oncol. 4 (5) (2012) 94–102.
[6] S. Rizvi, G.J. Gores, Pathogenesis, diagnosis, and management of cholangiocarcinoma, Gastroenterology 145 (6) (2013) 1215–1229.
[7] I. Joo, J.M. Lee, J.H. Yoon, Imaging diagnosis of Intrahepatic and perihilar cholangiocarcinoma: recent advances and challenges, Radiology 288 (1) (2018) 7–13.
[8] J.H. Lim, K.H. Yoon, S.H. Kim, H.Y. Kim, H.K. Lim, S.Y. Song, K.J. Nam, Intraductal papillary mucinous tumor of the bile ducts, Radiographics 24 (1) (2004) 66–67 53-66; discussion.
[9] K.M. Kim, J.K. Lee, J.U. Shin, K.H. Lee, K.T. Lee, J.Y. Sung, K.T. Jang, J.S. Heo, S.H. Choi, D.W. Choi, J.H. Lim, Clinicopathologic features of intraductal papillary neoplasm of the bile duct according to histologic subtype, Am. J. Gastroenterol. 107 (1) (2012) 118–125.
[10] S. Ying, M. Ying, W. Liang, Z. Wang, Q. Wang, F. Chen, W. Xiao, Morphological classification of intraductal papillary neoplasm of the bile duct, Eur. Radiol. 28 (4) (2018) 1568–1578.
[11] H.J. Park, S.Y. Kim, H.J. Kim, S.S. Lee, G.S. Hong, J.H. Byun, S.M. Hong, M.G. Lee, Intraductal papillary neoplasm of the bile duct: clinical, imaging, and pathologic features, AJR Am. J. Roentgenol. 211 (1) (2018) 67–75.
[12] J. Bridgewater, P.R. Galle, S.A. Khan, J.M. Llovet, J.W. Park, T. Patel, T.M. Pawlik, G.J. Gores, Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma, J. Hepatol. 60 (6) (2014) 1268–1289.
[13] Y. Nakanuma, Y. Kakuda, Pathologic classification of cholangiocarcinoma: new concepts, Best Practice Res. 29 (2) (2015) 277–293.

[14] M. Uno, K. Shimada, Y. Yamamoto, S. Nara, M. Esaki, Y. Sakamoto, T. Kosuge, H. Ojima, Periductal infiltrating type of intrahepatic cholangiocarcinoma: a rare macroscopic type without any apparent mass, Surg. Today 42 (12) (2012) 1189–1194.
[15] K. Uchiyama, M. Yamamoto, H. Yamaue, S. Ariizumi, T. Aoki, N. Kokudo, T. Ebata, M. Nagino, M. Ohtsuka, M. Miyazaki, E. Tanaka, S. Kondo, T. Uenishi, S. Kubo, H. Yoshida, M. Unno, S. Imura, M. Shimada, M. Ueno, T. Takada, Impact of nodal involvement on surgical outcomes of intrahepatic cholangiocarcinoma: a multicenter analysis by the Study Group for Hepatic Surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery, J. Hepatobiliary. Sci. 18 (3) (2011) 443–452.
[16] M. Yamamoto, K. Takasaki, T. Yoshikawa, K. Ueno, M. Nakano, Does gross appearance indicate prognosis in intrahepatic cholangiocarcinoma? J. Surg. Oncol. 69 (3) (1998) 162–167.
[17] A. Guglielmi, A. Ruzzenente, T. Campagnaro, S. Pachera, A. Valdegamberi, P. Nicoli, A. Cappellani, G. Malfermoni, C. Iacono, Intrahepatic cholangiocarcinoma: prognostic factors after surgical resection, World J. Surg. 33 (6) (2009) 1247–1254.
[18] S. Yamasaki, Intrahepatic cholangiocarcinoma: macroscopic type and stage classification, J. Hepatobiliary Surg. 10 (4) (2003) 288–291.
[19] S.A. Kim, J.M. Lee, K.B. Lee, S.H. Kim, S.H. Yoon, J.K. Han, B.I. Choi, Intrahepatic mass-forming cholangiocarcinomas: enhancement patterns at multiphasic CT, with special emphasis on arterial enhancement pattern–correlation with clinicopathologic findings, Radiology 260 (1) (2011) 148–157.
[20] N. Fujita, Y. Asayama, A. Nishie, K. Ishigami, Y. Ushijima, Y. Takayama, D. Okamoto, K. Moirta, K. Shirabe, S. Aishima, H. Wang, Y. Oda, H. Honda, Mass-forming intrahepatic cholangiocarcinoma: enhancement patterns in the arterial phase of dynamic hepatic CT - Correlation with clinicopathological findings, Eur. Radiol. 27 (2) (2017) 498–506.
[21] K. Imai, M. Yamamoto, S. Ariizumi, Surgery for periductal infiltrating type intrahepatic cholangiocarcinoma without hilar invasion provides a better outcome than for mass-forming type intrahepatic cholangiocarcinoma without hilar invasion, Hepatogastroenterology 57 (104) (2010) 1333–1336.
[22] N. Seo, D.Y. Kim, J.Y. Choi, Cross-sectional imaging of intrahepatic cholangiocarcinoma: development, growth, spread, and prognosis, AJR Am. J. Roentgenol. 209 (2) (2017) W64–W75.
[23] I.S. Oliveira, A. Kilcoyne, J.M. Everett, M. Mino-Kenudson, M.G. Harisinghani, K. Ganesan, Cholangiocarcinoma: classification, diagnosis, staging, imaging features, and management, Abdom. Radiol. (NY) 42 (6) (2017) 1637–1649.
[24] Y. Nakanuma, K.T. Jang, N. Fukushima, T. Furukawa, S.M. Hong, H. Kim, K.B. Lee, Y. Zen, J.Y. Jang, K. Kubota, A statement by the Japan-Korea expert pathologists for future clinicopathological and molecular analyses toward consensus building of intraductal papillary neoplasm of the bile duct through several opinions at the present stage, J. Hepatobiliary Sci. 25 (3) (2018) 181–187.
[25] D.H. Lee, J.M. Lee, K.W. Kim, H.S. Park, S.H. Kim, J.Y. Lee, J.K. Han, B.I. Choi, MR imaging findings of early bile duct cancer, J. Magn. Reson. Imaging 28 (6) (2008) 1466–1475.
[26] J.H. Lim, K.T. Jang, D. Choi, W.J. Lee, H.K. Lim, Early bile duct carcinoma: comparison of imaging features with pathologic findings, Radiology 238 (2) (2006) 542–548.
[27] C.H. Wu, Y.C. Yeh, Y.C. Tsuei, L.K. Huang, C.I. Lin, C.A. Liu, H.S. Tseng, Y.Y. Chiou, N.C. Chiu, Comparative radiological pathological study of biliary intraductal tubulopapillary neoplasm and biliary intraductal papillary mucinous neoplasm, Abdom. Radiol. (NY) 42 (10) (2017) 2460–2469.
[28] J.E. Kim, J.M. Lee, S.H. Kim, J.H. Baek, S.K. Moon, I.S. Yu, S.H. Kim, J.Y. Lee, J.K. Han, B.I. Choi, Differentiation of intraductal growing-type cholangiocarcinomas from nodular-type cholangiocarcinomas at biliary MR imaging with MR cholangiography, Radiology 257 (2) (2010) 364–372.
[29] T. Tsukahara, Y. Shimoyama, T. Ebata, Y. Yokoyama, T. Igami, G. Sugawara, T. Mizuno, J. Yamaguchi, S. Nakamura, M. Nagino, Cholangiocarcinoma with intraductal tubular growth pattern versus intraductal papillary growth pattern, Mod. Pathol. 29 (3) (2016) 293–301.
[30] S. Aishima, Y. Oda, Pathogenesis and classification of intrahepatic cholangiocarcinoma: different characters of perihilar large duct type versus peripheral small duct type, J. Hepatobiliary Pancreat. Sci. 22 (2) (2015) 94–100.
[31] M. Akita, K. Fujikura, T. Ajiki, T. Fukumoto, K. Otani, T. Azuma, T. Itoh, Y. Ku, Y. Zen, Dichotomy in intrahepatic cholangiocarcinomas based on histologic similarities to hilar cholangiocarcinomas, Mod. Pathol. 30 (7) (2017) 986–997.
[32] M.C. Bragazzi, L. Ridola, S. Safarikia, S.D. Matteo, D. Costantini, L. Nevi, V. Cardinale, New insights into cholangiocarcinoma: multiple stems and related cell lineages of origin, Ann. Gastroenterol. 31 (1) (2018) 42–55.
[33] L.E. Hann, K.V. Greatrex, A.M. Bach, Y. Fong, L.H. Blumgart, Cholangiocarcinoma at the hepatic hilus: sonographic findings, AJR Am. J. Roentgenol. 168 (4) (1997) 985–989.
[34] J.H. Lim, Cholangiocarcinoma: morphologic classification according to growth pattern and imaging findings, AJR Am. J. Roentgenol. 181 (3) (2003) 819–827.
[35] Y. Asayama, A. Nishie, K. Ishigami, Y. Ushijima, Y. Takayama, D. Okamoto, N. Fujita, T. Ohtsuka, T. Yoshizumi, S. Aishima, Y. Oda, H. Honda, Prognostic significance of contrast-enhanced CT attenuation value in extrahepatic cholangiocarcinoma, Eur. Radiol. 27 (6) (2017) 2563–2569.
[36] M. Miyazaki, M. Ohtsuka, S. Miyakawa, M. Nagino, M. Yamamoto, N. Kokudo, K. Sano, I. Endo, M. Unno, K. Chijiiwa, A. Horiguchi, H. Kinoshita, M. Oka, K. Kubota, M. Sugiyama, S. Uemoto, M. Shimada, Y. Suzuki, K. Inui, S. Tazuma, J. Furuse, A. Yanagisawa, Y. Nakanuma, H. Kijima, T. Takada, Classification of biliary tract cancers established by the Japanese Society of Hepato-Biliary-Pancreatic Surgery: 3(rd) English edition, J. Hepatobiliary Pancreat. Sci. 22 (3) (2015) 181–196.
[37] S. Vijgen, B. Terris, L. Rubbia-Brandt, Pathology of intrahepatic cholangiocarcinoma, Hepatobiliary Surg. Nutr. 6 (1) (2017) 22–34.
[38] S. Aishima, Y. Kuroda, Y. Nishihara, T. Iguchi, K. Taguchi, A. Taketomi, Y. Maehara, M. Tsuneyoshi, Proposal of progression model for intrahepatic cholangiocarcinoma: clinicopathologic differences between hilar type and peripheral type, Am. J. Surg. Pathol. 31 (7) (2007) 1059–1067.
[39] C. Sempoux, G. Jibara, S.C. Ward, C. Fan, L. Qin, S. Roayaie, M.I. Fiel, M. Schwartz, S.N. Thung, Intrahepatic cholangiocarcinoma: new insights in pathology, Semin. Liver Dis. 31 (1) (2011) 49–60.
[40] M. Komuta, O. Govaere, V. Vandecaveye, J. Akiba, W. Van Steenbergen, C. Verslype, W. Laleman, J. Pirenne, R. Aerts, H. Yano, F. Nevens, B. Topal, T. Roskams, Histological diversity in cholangiocellular carcinoma reflects the different cholangiocyte phenotypes, Hepatology 55 (6) (2012) 1876–1888.
[41] J.Y. Liau, J.H. Tsai, R.H. Yuan, C.N. Chang, H.J. Lee, Y.M. Jeng, Morphological subclassification of intrahepatic cholangiocarcinoma: etiological, clinicopathological, and molecular features, Mod. Pathol. 27 (8) (2014) 1163–1173.
[42] A. Hayashi, K. Misumi, J. Shibahara, J. Arita, Y. Sakamoto, K. Hasegawa, N. Kokudo, M. Fukayama, Distinct clinicopathologic and genetic features of 2 histologic subtypes of intrahepatic cholangiocarcinoma, Am. J. Surg. Pathol. 40 (8) (2016) 1021–1030.
[43] J.G. Nam, J.M. Lee, I. Joo, S.J. Ahn, J.Y. Park, K.B. Lee, J.K. Han, Intrahepatic mass-forming cholangiocarcinoma: relationship between computed tomography characteristics and histological subtypes, J. Comput. Assist. Tomogr. 42 (3) (2018) 340–349.
[44] H.T. Jeong, M.J. Kim, Y.E. Chung, J.Y. Choi, Y.N. Park, K.W. Kim, Gadoxetate disodium-enhanced MRI of mass-forming intrahepatic cholangiocarcinomas: imaging-histologic correlation, AJR Am. J. Roentgenol. 201 (4) (2013) W603–W611.
[45] Y. Asayama, K. Yoshimitsu, H. Irie, T. Tajima, A. Nishie, M. Hirakawa, T. Nakayama, D. Kakihara, A. Taketomi, S. Aishima, H. Honda, Delayed-phase dynamic CT enhancement as a prognostic factor for mass-forming intrahepatic cholangiocarcinoma, Radiology 238 (1) (2006) 150–155.
[46] H. Haradome, T. Unno, H. Morisaka, Y. Toda, T.C. Kwee, H. Kondo, K. Sano, T. Ichikawa, F. Kondo, M. Sugitani, T. Takayama, Gadoxetic acid disodium-enhanced MR imaging of cholangiolocellular carcinoma of the liver: imaging characteristics and histopathological correlations, Eur. Radiol. 27 (11) (2017) 4461–4471.
[47] U. Motosugi, T. Ichikawa, H. Nakajima, T. Araki, M. Matsuda, T. Suzuki, H. Fujii, T. Nakazawa, H. Yamaguchi, Cholangiolocellular carcinoma of the liver: imaging findings, J. Comput. Assist. Tomogr. 33 (5) (2009) 682–688.
[48] Y. Asayama, T. Tajima, D. Okamoto, A. Nishie, K. Ishigami, Y. Ushijima, D. Kakihara, S. Aishima, A. Taketomi, H. Honda, Imaging of cholangiolocellular carcinoma of the liver, Eur. J. Radiol. 75 (1) (2010) e120-5.
[49] A. Nanashima, T. Abo, G. Murakami, A. Matsumoto, K. Tou, H. Takeshita, M. Kunizaki, S. Hidaka, I. Sakamoto, H. Hayashi, T. Fukuda, T. Kudo, T. Nagayasu, Intrahepatic cholangiocarcinoma: relationship between tumor imaging enhancement by measuring attenuation and clinicopathologic characteristics, Abdom. Imaging 38 (4) (2013) 785–792.
[50] S. Ariizumi, Y. Kotera, Y. Takahashi, S. Katagiri, I.P. Chen, T. Ota, M. Yamamoto, Mass-forming intrahepatic cholangiocarcinoma with marked enhancement on arterial-phase computed tomography reflects favorable surgical outcomes, J. Surg. Oncol. 104 (2) (2011) 130–139.
[51] Y. Yamamoto, M.A. Turkoglu, T. Aramaki, T. Sugiura, Y. Okamura, T. Ito, R. Ashida, S. Uemura, T. Miyata, Y. Kato, Y. Kakuta, Y. Nakanuma, K. Uesaka, Vascularity of Intrahepatic Cholangiocarcinoma on computed tomography is predictive of lymph node metastasis, Ann. Surg. Oncol. 23 (Suppl. 4) (2016) 485–493.
[52] M.A. Turkoglu, Y. Yamamoto, T. Sugiura, Y. Okamura, T. Ito, R. Ashida, S. Uemura, T. Miyata, Y. Kakuda, Y. Nakanuma, K. Uesaka, The favorable prognosis after operative resection of hypervascular intrahepatic cholangiocarcinoma: a clinicopathologic and immunohistochemical study, Surgery 160 (3) (2016) 683–690.
[53] C. Fernandez Moro, A. Fernandez-Woodbridge, M. Alistair D'souza, Q. Zhang, B. Bozoky, S.V. Kandaswamy, P. Catalano, R. Heuchel, S. Shtembari, M. Del Chiaro, O. Danielsson, M. Bjornstedt, J.M. Lohr, B. Isaksson, C. Verbeke, B. Bozoky, Immunohistochemical typing of adenocarcinomas of the pancreatobiliary system improves diagnosis and prognostic stratification, PLoS One 11 (11) (2016) e0166067.
[54] H. Rhee, et al., A proposal of imaging classification of intrahepatic mass[HYPHEN] forming cholangiocarcinoma into ductal and parenchymal types: clinicopathologic significance, Eur. Radiol. (2019), https://doi.org/10.1007/s00330-018-5898-9 Epub Date 2018/12/19.