Recent trends in diagnosis and management of cholangiocarcinoma

A protocol of an essay

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Cholangiocarcinoma is originated by a malignant transformation of cholangiocytes, the epithelial cells lining the biliary ducts, they are anatomically classified as intrahepatic or extrahepatic.

Cholangiocarcinoma is suspected based on signs of biliary obstruction, abnormal liver function tests, elevated tumor markers (carbohydrate antigen 19-9 and carcinoembryonic antigen), and ultrasonography showing a bile stricture or a mass, especially in intrahepatic cholangiocarcinoma. Magnetic resonance imaging (MRI) or computed tomography (CT) is performed for the diagnosis and staging of cholangiocarcinomas. However, differentiation of an intraductal cholangiocarcinoma from a hypovascular metastasis is limited at imaging. Therefore, reasonable exclusion of an extrahepatic primary tumor should be performed. Differentiating between benign and malignant bile duct stricture is also difficult, except when metastases are observed.

The sensitivity of fluorodeoxyglucose positron emission tomography is limited in small, infiltrative, and mucinous cholangiocarcinomas. When the diagnosis of a biliary stenosis remains indeterminate at MRI or CT, endoscopic imaging (endoscopic or intraductal ultrasound, cholangioscopy, or optical coherence tomography) and tissue sampling should be carried out. Tissue sampling has a high specificity for diagnosing malignant biliary strictures, but sensitivity is low. More studies are needed to compare the accuracy of the various imaging methods, especially the new intraductal methods, and the imaging features of malignancy should be standardized.

Radical resection with a microscopically negative margin (R0) is the only way to cure cholangiocarcinoma and is associated with marked survival advantages compared to margin-positive resections. Complete resection of the tumor is the

Aim of the work

The aim of the work is to highlight the recent trends in diagnosis and treatment of cholangiocarcinoma .

Contents

Anatomical overview of the hepatobiliary system.

According to the Couinaud classification, the liver consists of eight distinct hepatic segments, which have their own portal venous supply and hepatic venous drainage system. The anatomically distinct segment I, or caudate lobe, lies between the fissure for the ligamentum venosum and the vena cava inferior. The rest of the liver is divided by the middle hepatic vein into a right and left liver lobes. The right liver lobe consists of segments V-VIII. The superior segments (VII and VIII) are separated from the inferior segments (V and VI) by the horizontal portion of the right portal vein, whereas the anterior segments (V and VIII) are divided from the posterior segments (VI and VII) by a coronal oblique plane containing the right hepatic vein. The left liver lobe contains segments II-IV and is divided into lateral segments (II and III) and a medial segment (IV or quadrate lobe) by the umbilical fissure and falciform ligament. The left hepatic vein forms the coronal separation of the lateral segment: segment II is posterior and superior to the vein, whereas segment III is anterior and inferior to it [1].

The individual biliary drainage system is parallel to the portal venous supply [2] (Fig. 1).

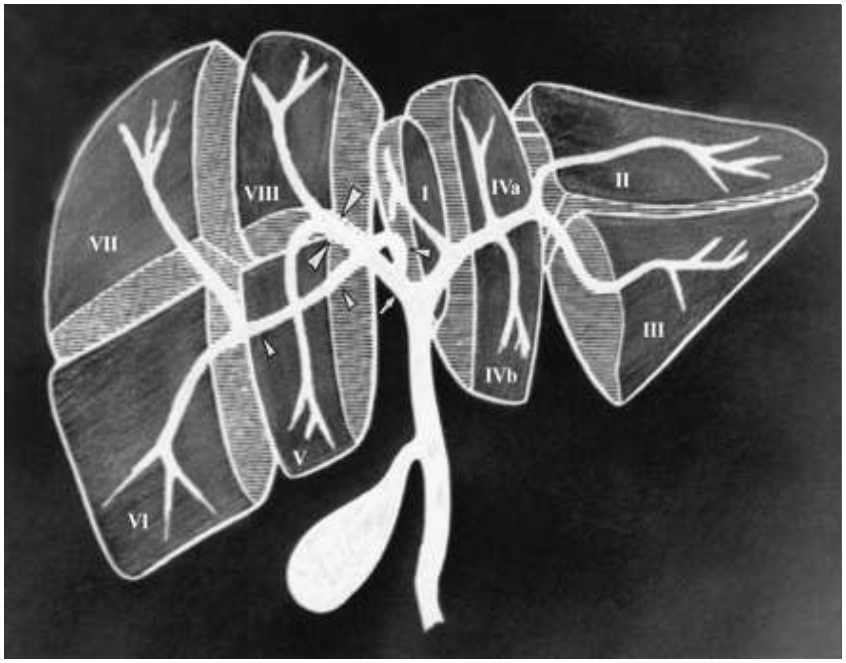

Fig. 1

Normal biliary anatomy. Drawing shows normal hepatic biliary segmental anatomy, as described by Couinaud, and normal fusion of cystic duct with common hepatic duct. Note normal confluence of right posterior duct (*small arrowheads*) and right anterior duct (*large arrowheads*) to form right hepatic duct (*arrow*) [1].

Intrahepatic bile duct anatomy (Figure 2)

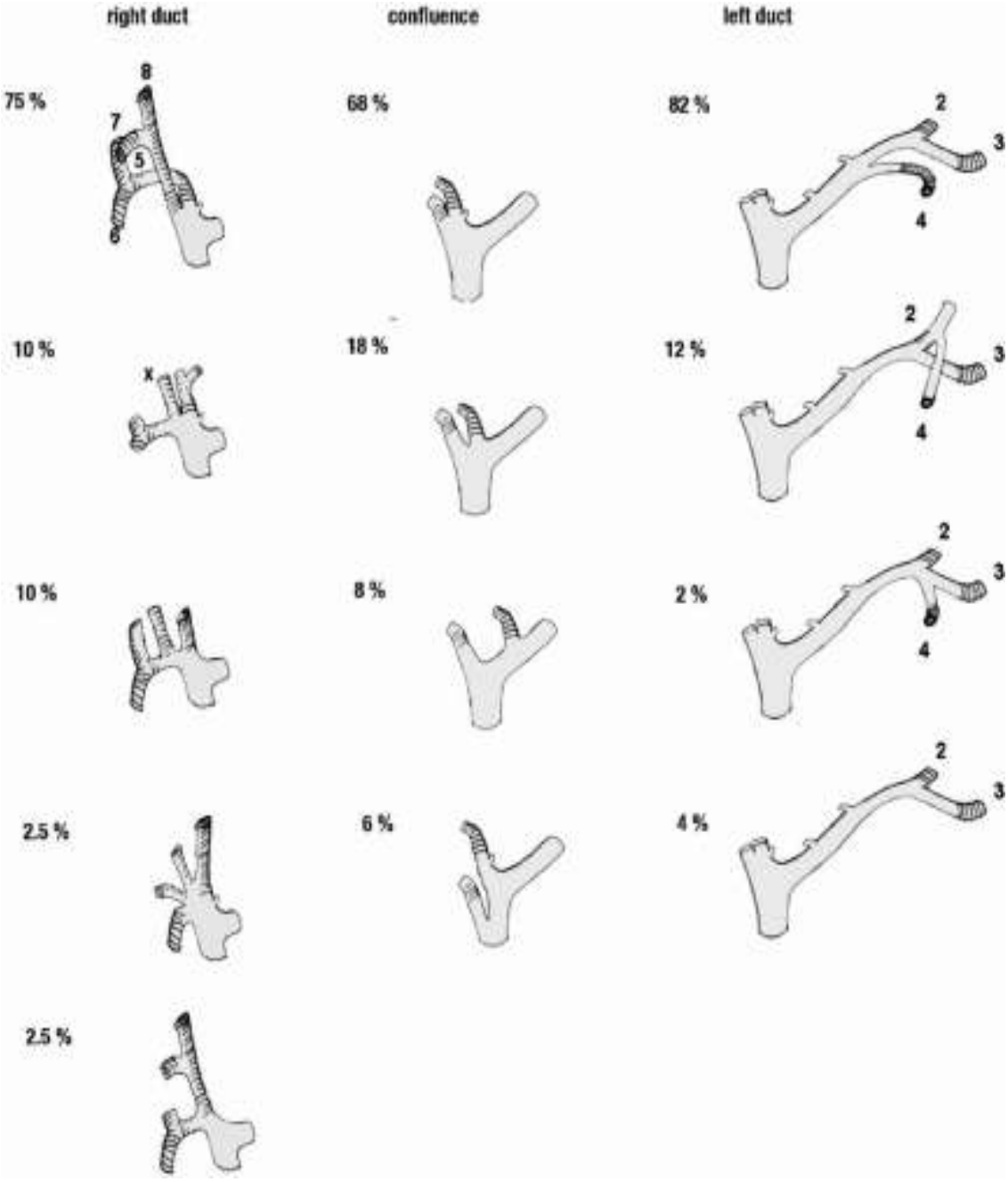

Figure. 2

Intrahepatic duct and biliary confluence anatomy [2].

The left hepatic duct drains segments 2, 3, and 4 of the left hemiliver. The "normal" confluence comprises a duct formed from ducts of segments 2 and 3 and one or more ducts from segment 4. The segment 3 duct follows the left horn of the Rex recessus and joins the segment 2 duct above the segment 2 portal branch (at the level of the curve of the hilar part in the posterior-anterior portion of the portal branch). This duct is 2.5 cm long, from 2 to 5 cm, depending on the size of the posterior margin of the quadrate lobe. Being extrahepatic in this portion, it runs transversely in the hilum, from left to right. Running first above and behind the left portal branch, it crosses the superior edge and joins the right hepatic duct to form the biliary confluence. For the left hepatic duct, this normal anatomy is reported in 82%. In 4% of patients, a right sectoral duct can join the left hepatic duct (3% posterior and 1% anterior) [2].

The right hepatic duct drains all segments of the right hemiliver (segments 5, 6, 7, and 8). The ducts of segments 6 and 7 form the posterior right hepatic duct, and those of segments 5 and 8 form the anterior right hepatic duct. The anterior hepatic duct lies vertical, located to the left of the anterior branch of the portal vein. The direction of the posterior duct is more horizontal, running superior (being epiportal in the Hjortsjö crook) to the anterior portal branch and joins the anterior duct. In approximately 20% of instances, the right duct runs inferiorly (being hypoportal) to the anterior portal branch. A complete anterior duct was present in 35% and a complete posterior duct in 61%. The "normal" confluence of these two ducts forms the right hepatic duct, above the right portal branch, in an extra-hepatic position [3].

The right hepatic duct can be absent, the anterior and posterior ducts joining directly to the left hepatic duct, forming a triple confluence (12%). The right hepatic duct may join the main hepatic duct below the normal confluence in 25% of cases (9% the anterior and 16% the posterior). This anatomical variation is

known as “convergence étagée” or selved confluence. The normal right duct is short and vertical and 1 cm in length [3].

Biliary confluence (Figure 2)

The main biliary confluence is formed outside the liver parenchyma, before becoming distal to the common hepatic duct. It runs along and anterior to the origin of the right branch of the portal vein. The duct is displaced superiorly and medially to the left of the main portal vein. This classic junction occurs in 61% of instances. During a right hepatectomy, the anatomical situation of the main biliary confluence explains the risk of ligating the confluence or the left duct. The Bismuth–Corlette classification is valid only for a “normal” confluence. In the event of biliary abnormality, it is necessary to take into account not only the type of confluence, but also its height in relation to the portal vein[3].

At the level of the hilum, Glisson's capsule is both thicker and denser, forming the connective tissue of the hilar plate. The biliary ducts are enclosed within this tissue. Adhesions between this capsule and arterial and portal branches are less important. It is therefore easy to dissect the portal branches at the hilum, but more difficult for the arterial branches and almost impossible to separate the bile duct of the hilar plate (Figure 3). In the case of hilar cholangiocarcinoma, the proximity of the portal triad explains the frequent tumor invasion of portal branches. A lobar atrophy may result from the vascular invasion and/or from a biliary obstruction. Owing to the absence of vascular interposition at the anterior part of the hilar plate, it is also possible to separate the hilar plate and hepatic parenchyma of segment 4[3].

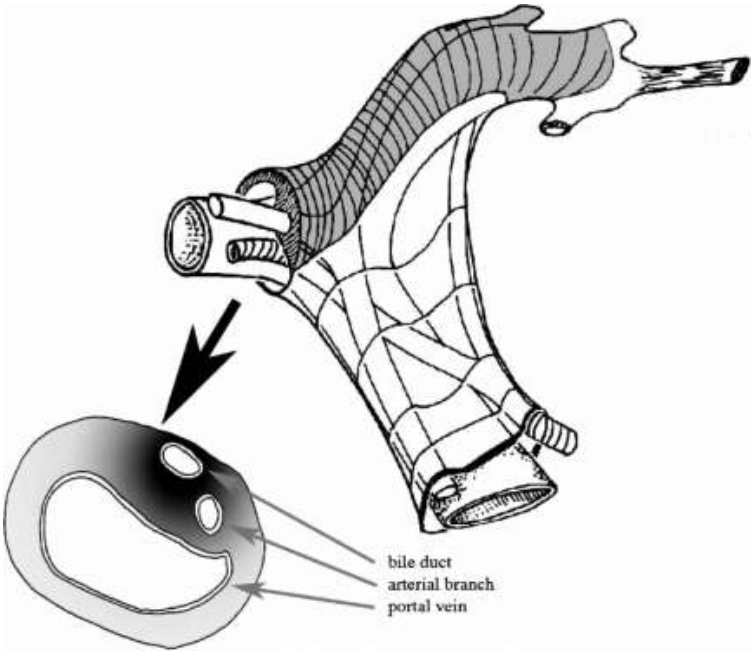

Fig. 3

The hilar plate [2].

Segment 1/segment 4

The number of portal branches of segment 1 varies from 1 to 6 (average 3). Segment 1 has its own biliary drainage. The left hepatic duct receives one (or more) duct of segment 4 and one or two ducts of segment 1. The right duct receives one duct of segment 1. Biliary drainage of segment 1 goes to both hepatic ducts (80%). However, in 15% its goes only to the left hepatic duct and in 5% to the right, always close to the biliary confluence at a variable location [2].

The segment 1 ducts are posterior, running above the portal branch and joining the corresponding bile duct on its posterior margin. In the event of hilar bile duct cancer, which may spread along the bile duct, especially into the dorsal ducts, caudate lobectomy and segmentectomy 4 are routinely necessary for resecting the corresponding bile duct and for complete extirpation of the tumor [2].

Main bile duct

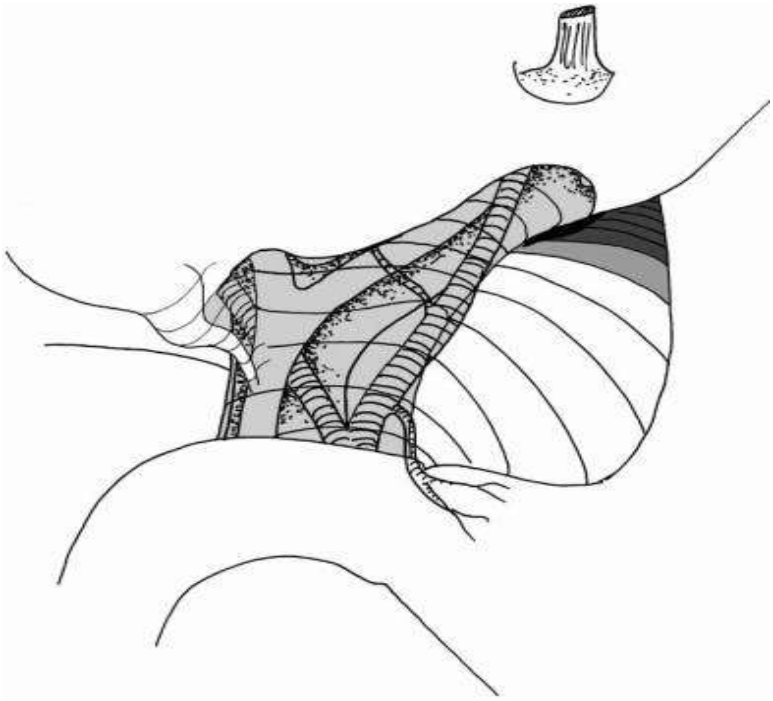

Fig. 4

Anterior aspect of the biliary anatomy in the hepatic pedicle [2].

The common hepatic duct receives the cystic duct and then forms distally to the choledochus. This distinction is arbitrary, because the cystic duct joins at a variable site, which must be carefully considered during gallbladder operation. It is better to call it the main bile duct, in general below the biliary confluence [2].

The main bile duct courses downwards and anterior to the portal vein, joining its left margin in the middle part of the hepatic pedicle. The hepatic artery, which runs upwards, is usually located to the left. The right branch of the hepatic artery crosses the common hepatic duct posteriorly and the portal vein anteriorly, although it can exit anterior to the superior part of the hepatic pedicle. The common hepatic duct constitutes the left border of the triangle of Calot with the inferior surface of the right lobe as the upper border and the cystic duct below [2].

Accessory biliary apparatus

Composed of the gallbladder and cystic duct, joins the common hepatic duct to form the common bile duct that drains bile into the duodenum [4] .

Gallbladder and cystic duct:

The gallbladder is a reservoir of bile in the shape of a piriform sac partly contained in a fossa on the inferior surface of the right hepatic lobe. It extends from the right extremity of the porta hepatis to the inferior border of the liver. It is 7 to 10 cm long and 3 to 4 cm broad at its widest part, and can hold from 30 to 50 ml. The gallbladder is divided into a fundus, body, infundibulum and neck. The fundus extends about 1 cm beyond the free edge of the liver. The body is the largest segment. The infundibulum is the transitional area between the body and the neck. Hartmann's pouch is a bulge on the inferior surface of the infundibulum [4].
Gallstones may become impacted here and can cause obstruction of the cystic duct. The neck is the tapered segment of the infundibulum that is narrow and joins the cystic duct. The cystic duct is 3 to 4 cm long and passes posteriorly inferior and to the left from the neck of the gallbladder to join the common hepatic duct to form

the common bile duct (CBD).The mucosa of the cystic duct is arranged with spiral folds known as the valves of Heister. A number of anomalies occur in the gallbladder. Furthermore, the cystic duct inserts into the bile duct at a variety of sites [4].

The duct of Luschka

The duct of Luschka is a small bile duct, running in the bed of the gallbladder, outside the wall. It is present in 50% of individuals. This duct is surgically significant because it may be injured during cholecystectomy and may result in bile fistula unless ligated. Recent reports demonstrated a 1.5 to 2.0% incidence of bile leak from the duct of Luschka after laparoscopic cholecystectomy. Ligation has no consequences as it is an end duct that drains an isolated segment [5].

Sphincter of Oddi

The common bile duct enters the duodenum approximately 8 cm from the pylorus in the second part of the duodenum. The site entry is marked by a papilla (major papilla). Its position can be variable; in approximately 13% of individuals it can be located at the junction of the second and third part of the duodenum, or even more distally [14]. A transverse fold of mucosa usually covers the papilla. The papilla is identified as a small nipple or pea-like structure in the lumen of the duodenum [5].
The main pancreatic duct of Wirsung joins the common bile duct and forms a common channel in approximately 85% of individuals. In 15%, they open either separately or as a V junction with the duodenal mucosa. In 4% of individuals, the body and tail of the pancreas drain via the duct of Santorini (pancreas divisum) to