

Recent Trends in the Management of Hilar Cholangiocarcinoma

Essay

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General Surgery*

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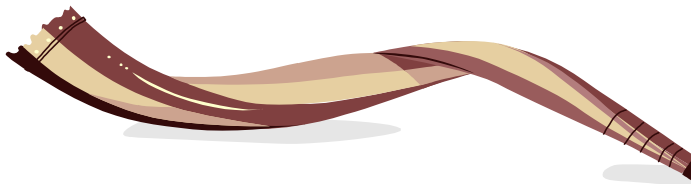
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Introduction

In 1890, Fardel first described a primary malignancy of the extrahepatic biliary tract (**Fardel, 1927**). A report in 1907 described three patients with small adenocarcinomas involving the confluence of the left and right hepatic ducts (**Altmeier, 1907**). Such primary cholangiocarcinomas arising at the bifurcation of the extrahepatic biliary tree are known commonly as Klatskin's tumors, following his report in 1960 of a larger series of patients with these lesions (**Klatskin, 1960**).

A cholangiocarcinoma is a rare form of cancer, accounting for less than 2% of all human malignancies (**Parker, 1997**) and account for approximately 3% of all gastrointestinal cancers (**Khan, 2009**). The estimated incidence of cholangio-carcinoma is 1-3 cases per 100,000 per year (**Shaib, 2009**).

Although the entire biliary tree is at risk, the proximal or hilar cholangiocarcinomas (Klatskin tumours) are most common and account for 40-60 per cent of cases and arise at the biliary bifurcation (**Launois, 2000**).

Hilar cholangiocarcinoma remains among the most challenging and the most difficult management problems faced by surgeons and is one of the most formidable solid organ malignancies to treat and has poor long-term outcome as close proximity of lesions to important structures, such as the hepatic

artery and portal vein, means that a large proportion of patients present with complex disease and it is often unresectable owing to regional extension into the liver, surrounding lymphatics, and, most notably, hilar vascular structures.

Thus hilar cholangiocarcinomas have a poorer prognosis than do carcinomas arising in the middle or distal thirds of the extrahepatic bile duct, which is related directly to the presentation of hilar tumors at a more locally advanced stage with bilobar liver involvement by tumor and resultant lower rates of curative resection (**Kayahara, 1999**).

Regarding diagnosis it is difficult to detect hepatic hilar cholangiocarcinoma early, because there are no significant symptoms in the early stage. This tumor may be misdiagnosed as hepatitis, cholelithiasis or liver cancer.

Generally, the appearance of early symptoms to jaundice took 3-6 months, when jaundice occurred; most patients were in the terminal stage.

Bile cancer cells, tissue biopsy, and examinations of serum CEA, CA19-9, K-ras, MMP-2 and TIMP-2 can improve the quality of diagnosis (**Chen, 2007**). But the lower positive rate is the demerit of such examinations.

Today, combined magnetic resonance imaging-magnetic resonance cholangiopancreatography remains popular for

assessing the extent of the tumour inside and outside the biliary tree. Recently, multidetector computed tomographic angiography and cholangiography with three-dimensional reconstruction have been described, with encouraging results (**Chen, 2007**).

The only effective treatment for hilar cholangiocarcinoma is major surgery (**Hasegawa, 2007**). Surgeons have pushed the technical envelope to achieve negative margins.

Complete tumor resection with a negative histologic margin can be considered potentially curative for patients with HCCA. To achieve this, hepatic resection is often required (**Chamberlain, 2000**). This resectional surgery with negative margins offers hope of long-term survival (**Khan, 2007**). However, the morbidity and mortality raised by hepatectomies should be considered (**Yao-Jen, 2004**) and the anatomical location of the tumour and longitudinal extension within the bile duct make curative resection difficult (**Khan, 2007**).

Occasionally, Klatskin tumours arise within the setting of primary sclerosing cholangitis. Here the tumour may be multifocal, with resectional surgery being followed by high rates of early intrahepatic recurrence, approaching 90 per cent at 1 year in some series (**Khan, 2007**). And so in PSC patients with early cholangiocarcinoma, liver transplantation is the preferred definitive therapy (**Malhi, 2007**).

Liver transplantation, especially living donor liver transplantation, is a new and exciting alternative to resection for hilar cholangiocarcinoma. Integration of neoadjuvant chemoradiation has the potential to further improve the curative potential of liver transplantation. The strategy of combining neoadjuvant chemoradiation and liver transplantation brings new hope for the treatment of this difficult disease (*Durgatosh, ୨୦୦୩*).

Regarding tumour palliation photodynamic therapy, radiation and chemotherapy are all available as palliative options (*Malhi, ୨୦୦୩*). Symptom resolution and improvement in quality of life have been the goals of established palliative therapy.

External beam radiation therapy and chemotherapy have been administered as adjuvants to surgical resection.

In unresectable tumors stents are used to maintain adequate biliary drainage and relieve symptoms, but it should be noted that following palliative stenting, patients can die from recurrent sepsis, biliary obstruction, and stent occlusion as well as disease progression (*Khan, ୨୦୦୩*).

Aim of the Work

The aim of this study is to demonstrate different tools in the diagnosis of hilar cholangiocarcinoma and recent trends in its treatment.

Surgical Anatomy

Anatomy of Gall Bladder and Biliary Tree:

Anatomy of Gall Bladder:

It lies against the under surface of the right hepatic lobe. Its bulbous blind end (the fundus), projects a little beyond the sharp anterior margin of the liver and touches the parietal peritoneum of the anterior abdominal wall at the tip of the ninth costal cartilage where the Trans-pyloric plane crosses the right costal margin at the lateral border of the rectus abdominus muscle.

The body of the gall bladder, narrower than the fundus, passes backwards and upwards from this point towards the right end of the porta hepatis, here it narrows into a neck, from which the cystic duct lies against the porta hepatis to join the common hepatic duct between the two layers of peritoneum that form the free edge of the lesser (gastrohepatic) omentum (*Blumgart, 2001*).

The cystic duct lies immediately in front of the right main branch of the hepatic artery the artery can be caught easily in a clamp placed on the cystic duct.

The gall bladder is located on the visceral surface of the liver at the plane dividing the right lobe from the medial segment of the left lobe. It is 7 to 10 cm long with a capacity of 30 to 50 mL. The gall bladder lies in a shallow fossa of the liver separated from it and surrounded by connective tissue of the Glisson capsule. On the opposite side, the peritoneum of the gall bladder is continuous with that of the liver. After removal of the gall bladder, bile sometimes leaks from small bile ducts in the gall bladder bed. There has been disagreement as to whether these ducts enter the gall bladder (hepato-cystic ducts) but Miches 1955 was unable to find such ducts in his 500 carefully dissected specimens.

He found branches from the right hepatic duct in the gall bladder bed, but they did not communicate with gall bladder. They may cause post-operative bile leakage if they are injured (**Ronald, 1955**).

The fundus of the gall bladder lies on the commencement of the transverse colon just to the left of the hepatic flexure while the body that lies behind it is in contact with the first part of the duodenum. The under surface of the liver is sloping, so the neck of the gall bladder lies at a higher level than the fundus. It lies against the upper part of the free edge of the lesser omentum (**Last, 1955**).

Anatomy of the biliary tree:

The anatomy of the biliary tract can be considered as extra and intrahepatic parts.

I- Intrahepatic bile duct anatomy:

The liver is divided into two major portions and a dorsal lobe. The right liver and the left liver are respectively drained by the right and left hepatic ducts, whereas, the dorsal lobe (Caudate lobe) is drained by one or several ducts joining both the right and left hepatic ducts, they unite near the right end of the portahepatis to form the common hepatic duct (*Blumgart, २००१*).

A) The left hepatic duct:

It drains the three segments (II, III, and IV) which constitute the left liver. The duct draining segment III is located slightly behind the left horn of the umbilical recesses, running backwards to join the duct of segment II at a point where the left branch of the portal vein turns forward and caudally at the recesses of Rex. The left hepatic duct traverses beneath the left liver at the base of segment IV, just above and behind the left branch of the portal vein and joins the right hepatic duct to constitute the hepatic ductal confluence. In its transverse portion it receives one to three small branches from segment IV (*Ronald, २००४*).

B) The right hepatic duct:

It drains segments V, VI, VII and VIII and arises from the junction of two main sectoral ductal tributaries: the posterior or lateral duct and the anterior or medial duct each a satellite of its corresponding vein.

The right posterior sectoral duct has an almost horizontal course and is constituted by the confluence of the ducts of segments VI and VII. The duct then runs to join the right anterior sectoral duct as it descends in a vertical manner. The right anterior sectoral duct is formed by the confluence of the ducts draining segment V and segment VIII. Its main trunk is located to the left of the right anterior sectoral branch of the portal vein, which pursues an ascending course. The junction of these two main right biliary channels usually takes place above the right branch of the portal vein (**Blumgart, 2001**).

The dorsal (Caudate) lobe (segment I):

It has its own biliary drainage. It comprises two portions; a caudate lobe proper located at the posterior aspect of the liver and a caudate process passing behind the portal structures to join the right liver. The caudate lobe proper is divided into right and left portions in 44%, three separate ducts drain, these three parts of the lobe while in 26% there is a common duct between the right portion of the caudate lobe proper and the caudate

process. The site of drainage of these ducts is variable. In 18% of cases, drainage of the caudate lobe is into both the right and left hepatic ducts, in 10% by the left duct only and in 9% into the right duct only (*Blumgart, 2001*).

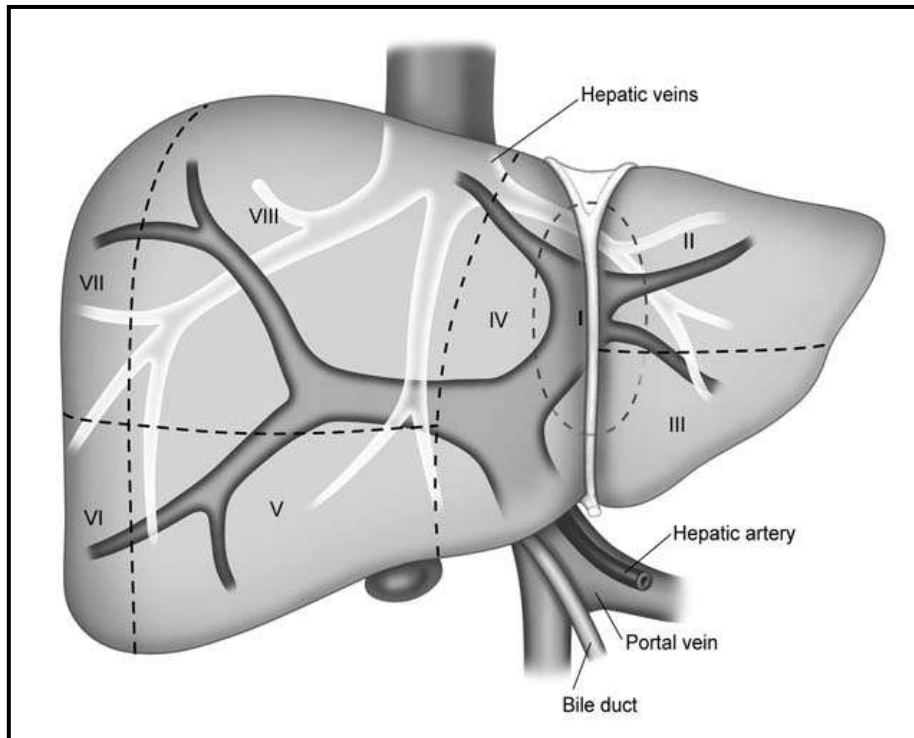


Figure (1): Diagram showing the segmental anatomy of the liver (*Hahn, 2001*).

II - Extrahepatic biliary anatomy:

It includes the extrahepatic segments of the right and left hepatic ducts joining to form the biliary confluence and the main biliary channel which is draining in the duodenum as well