CHAPTER 2

REVIEW OF RELATED LITERATURE

CHOLANGIOCARCINOMA (CHCA) AND HILAR CHCA

Cholangiocarcinoma (CHCA) is the second most common hepatobiliary cancer after hepatocellular carcinoma (HCCA) in most parts of the world(1, 58). It is accounts for 5% to 30% of all primary hepatobiliary malignant tumors. However, it is the most common primary hepatobiliary tumor found in Northeast Thailand and represents the highest prevalence in the world (2-4). The prevalence is 94.8:100,000 amongst males and 39.4:100,000 amongst female (2-4). CHCA accounted for 89% of all primary hepatic tumors in this region(4).

Hilar CHCA or Klaskin tumors are adenocarcinomas that arise in the biliary epithelium at the confluence of the right and left hepatic ducts within the portahepatis (59). The reported prevalence of hilar CHCA varies in different regions. In Srinagarind hospital, the prevalence of hilar CHCA accounted for 65% to 70% of all CHCA, nearly equal to the prevalence found at Johns Hopkins Hospital, Baltimore, USA(60).

Intrahepatic CHCA or peripheral CHCA is a primary adenocarcinoma of the liver arising from the biliary epithelium of intrahepatic bile ducts.

The remaining CHCA originates from the extrahepatic bile duct at the common duct.

Clinically, therapeutically, and radiologically, the different locations of CHCA have different characteristics. Hilar CHCA carries a dismal prognosis if left

untreated, with a mean survival time of approximately 3 months after initial presentation. Obstructive jaundice, episodes of cholangitis and progressive liver failure have poor survival outcomes and ensure a poor quality of life.

Histologically, CHCA is divided into seven subtypes according to predominant features. These are papillary adenocarcinoma, papillotubular adenocarcinomama, tubular adenocarcinoma, adenosquamous carcinoma, squamous cell carcinoma, mucinous carcinoma, and anaplastic carcinoma(61, 62) The most frequent type of CHCA is tubular adenocarcinoma.

SURGICAL TREATMENT OF HILAR CHCA

Complete surgical resection provides the only cure for CHCA patients. Controversy surrounds issues regarding the extent of resection for hilar CHCA whether the histopathologies of such cancer are similar. Adjunctive therapy, such as the administration of intraarterial chemoembolization, chemotherapy, postoperative radiation (60), external beam radiotherapy (RT), combined with expandable metallic biliary stent (EMS), embolization portal branches (16), preoperative irradiation and chemotherapy (6) and preoperative endoscopic drainage (18) were advised. All aimed at increasing the surgical curability rate in hilar CHCA.

Several reports have been conducted hilar CHCA from many parts of the world from 1998 to 2000. Countries included the USA (6, 8, 14, 60, 63), Japan (9, 16, 21, 64), Italy (7, 15), Germany (12, 13), Spain (17), and Korea (11) amongst others. All reports suggested that satisfactory long-term survival for hilar CHCA can be obtained by aggressive surgery. Better prognosis was observed for patients in the early stages of hilar CHCA.

Hilar CHCA is one of the most difficult tumors to stage and treat. There are different surgical procedures for hilar CHCA, common duct CHCA and intrahepatic CHCA. There is evidence suggesting that more aggressive surgery in hilar CHCA can improve long term survival. Improvement of preoperative imaging and refined operative techniques have allowed a more radical approach to the treatment of hilar CHCA. Imagings can also provide information on whether a tumor is resectable or not (7, 17, 18, 44, 47). They also help in the selection of patients who might be benefit from extensive surgical resection.

IMAGINGS OF THE BILIARY SYSTEM AND THE MRCP

Imaging ductal anatomy and delineating duct obstruction can usually be achieved by using noninvasive techniques such as transabdominal ultrasound (US) and computed tomography (CT). This can also be achieved by invasive direct cholangiography such as endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiopancreatography (PTC), percutaneous transhepatic biliary drainage (PTBD), and intraoperative cholangiography. However, CT is limited to the axial plane, and US has a limited field of view and is operator dependent. The results of imaging are usually inferior to those of invasive procedures (48, 51). The invasive techniques, such as ERCP or PTC, provide a good overview of the whole biliary system. Images can be obtained on different planes, although these procedures do carry a certain degree of risk and failure (37, 38, 65). Serious complications (sepsis, bile leakage, bleeding and death) may occur in both ERCP and PTC, which has an overall incidence of approximately 3%. Sepsis in the most common of these complications.

Figure 1. Computed tomography of hepatobiliary system.

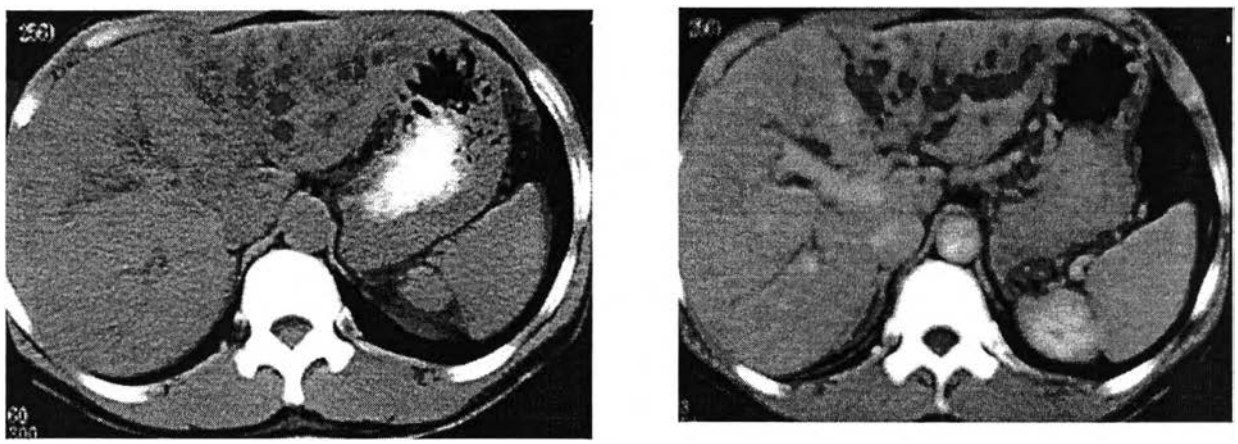


Figure2. Endoscopic retrograde cholangiopancreatography (ERCP) : imaging of biliary tree performed by ERCP

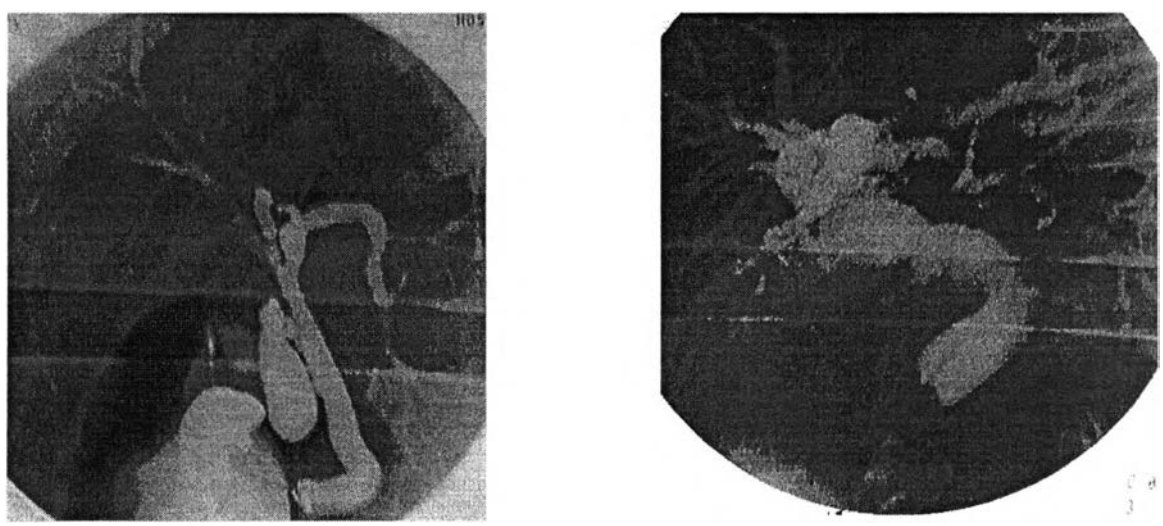
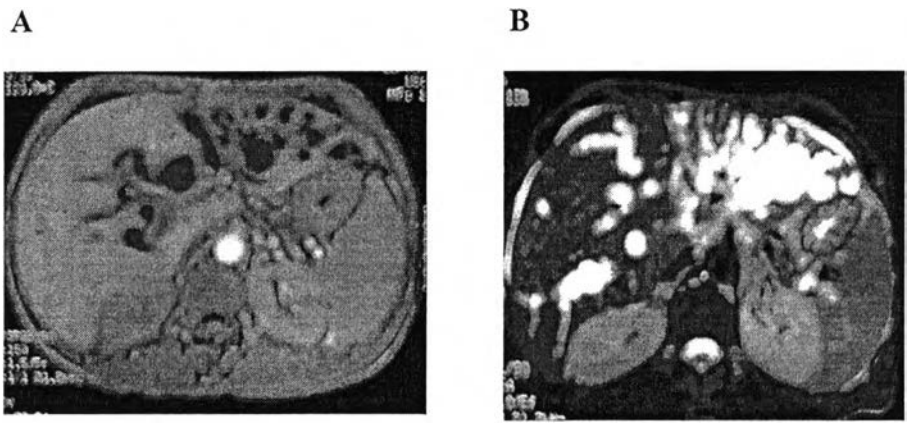


Figure 3. Magnetic resonance imaging (MRI) : MRI of hepatobiliary system in T1 weighted(A) and T2 weighted images(B).



ERCP is regarded as the diagnostic modality of choice for abnormalities of the biliary system, however it carries a certain degree of risk and also a significant failure rate. The morbidity rate in ERCP varies from 1% to 7%, with a 0.2% to 1% variation in mortality rate (37, 38, 65). The failure rate of duct canulation in ERCP varies between 3% and 30%, depending on the operator (37, 38, 47, 54, 65).

In clinical practice, particularly before the MRCP was available, duct dilatation and obstructed sites might be shown by the US or CT. However, direct cholangiography (ERCP or PTC) was normally required to determine the exact site of biliary obstruction prior to surgical treatment. However, CT and US provide tomographic images.

Direct cholangiography (ERCP or PTC) can demonstrate the whole biliary system as projection images on different planes. This is useful in establishing the relationship between the biliary branches and the site of obstruction.

MRI has been used to assess hepatic tumors for several purposes. These are to characterize the tumor (26, 27, 46, 62, 66, 67), to assess parenchymal and

bile duct invasion of the tumor (57, 66, 67) and to ascertain whether tumors are resectable or not.

MRCP, a special MRI technique, has been developed as a noninvasive cholangiographic technique in the assessment of the pancreatobiliary tree in patients whose pancreatic or biliary disease is suspected, especially for evaluating biliary tract obstruction and its cause. MRCP is expected to produce a projection image comparable with direct cholangiogram (ERCP and PTC). It can be obtained noninvasively and could to reveal the precise location of the obstruction. The relation between tumor and biliary trees can be determined without direct cholangiography. Initial reports have focused on the accuracy of MRCP for the detection of biliary duct dilatation (39, 43, 45, 47, 52, 57) and cholelithiasis (54). Many reports using different techniques with different mean parameters to perform biliary images have been described and published (68-70). MRCP requires neither the use of a contrast agent nor a biliary intervention. Some reports conclude that MRCP offered a high diagnostic accuracy in the assessment of the occurrence and location of biliary obstruction (39, 48, 51, 54), and was particularly high for choledocholithiasis and malignant obstruction (39, 51, 54). MRCP may also provide tentative diagnosis of pancreatic carcinoma (42,47). A large number of studies focused on the development of a new technique to perform MRCP were suspected (51, 52, 56, 68-73). However, previous reports about MRCP suggested it offered high diagnostic accuracy in the assessment of the occurrence and location of biliary duct obstruction. Information regarding MRCP and diagnosis and assessment of CHCA have received less attention.

Other new imaging modalities such as endoscopic ultrasonography, (EUS) is helpful in the detection of cholelithiasis and the evaluation of the periampulary region, the periductal structures, and regional lymph nodes in the neoplastic disease. Cholescintigraphy is most useful in the diagnosis of gallbladder and the sphincter of Oddi dysfunction and post-operative leakage. The development of

3 dimension ultrasonography (3D US) and 3 dimension computed tomography (3D CT) may further expand their future role in biliary mapping of complex strictures.

SUMMARY OF THE REVIEW OF RELATED LITERATURE

CHCA AND HILAR CHCA

CHCA is the second most common primary hepatobiliary tumor after hepatocellular carcinoma, but is the most common primary hepatobiliary tumor in Northeast Thailand. The hilar CHCA or Klaskin tumor is an adenocarcinoma that originates in the biliary epithelium at the confluence of the right and left hepatic ducts within the porta-hepatis. This is the most common location for patients with CHCA in Northeast Thailand. Hilar CHCA carries a dismal prognosis if left untreated.

SURGICAL TREATMENT FOR HILAR CHCA

Surgical resection provides the only chance of cure in patients with CHCA, although adjunctive therapies have been reported. Recently in 1998-2000, the majority of reports for surgical treatment of hilar CHCA suggested that aggressive surgical resection of the hilar CHCA could improve patient survival. Preoperative biliary imaging provides essential information regarding decisions concerning patient selection for operation and operative planning.

IMAGING OF THE BILIARY SYSTEM AND MRCP

Imagings of the biliary system can be achieved by using noninvasive techniques (US, CT) or invasive techniques (ERCA, PTC). Results of noninvasive imagings are usually inferior to invasive imagings. ERCP is regarded as the diagnostic modality of choice for abnormalities of the biliary tree, but this

procedure not only carries a certain degree of risk, it is also prone to failure. MRCP, a special MRI technique, has been developed as a none invasive cholangiographic technique requiring neither contrast medium injection nor any other form of biliary intervention. Studies regarding several aspects of MRCP have been conducted, however the use of MRCP in the diagnosis and assessment of hilar CHCA has received less attention.