Recent Trends in Diagnosis and Management of Cholangiocarcinoma

An Essay
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الوسائل الحديثه في تشخيص و علاج سرطان القنوات المراريه

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Summary

Perihilar cholangiocarcinoma includes extrahepatic and intrahepatic cholangiocarcinomas that involve the hepatic confluence of the bile duct. Although this intractable disease used to be difficult to resect as a result of complex anatomy of the hepatic hilum, diagnostic and surgical strategy has changed drastically over the past two decades. Hepatobiliary resection based on precise preoperative diagnosis of tumor extent has become a standard procedure to obtain curative resection. Despite the advance of preoperative diagnostic techniques, perihilar cholangio-carcinoma is typically diagnosed in an advanced stage at initial presentation. As only surgical resection can offer the superior survival probability, combined portal vein and liver resection and/or hepatopancreatoduodenectomy are aggressively performed at leading centers.

Most patients appear with obstructive jaundice. Even in patients without jaundice, serum alkaline phosphatase and/or g-glutamyltranspeptidase are usually elevated. Those symptoms result from bile congestion due to biliary stricture of the hepatic confluence involved by advanced cholangiocarcinoma. Ultrasonography is performed in those patients and reveals dilated intrahepatic bile ducts, the normal or atrophic gallbladder and sometimes a tumor

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List of abbreviations

- **5FU** : 5-flurouracil
- **AJCC** : American Joint Commission on Cancer
- **ALP** : Alkaline Phosphatase
- **C.sinensis** : Clonorchis Sinensis
- **CA19-9** : Cancer Antigen 19-9
- **CC** : Cholangiocarcinoma
- **CEA** : Carcinoembryionic antigen
- **CHD** : Common Hepatic Duct
- **COX-2** : Cyclo oxyenase -2
- **CT** : Computed Tomography
- **EBRT** : External beam radiotherapy
- **ECC** : Extrahepatic cholangiocarcinoma
- **ERCP** : Endoscopic Retrograde Cholangopancreatography
- **EUS** : Endoscopic Ultrasound
- **FDG** : F-fludrodeoxyglucose
- **FNA** : Fine needle aspiratipon
- **GGT** : Gmma Glutamyltransferase
- **HBsAg** : Hepatitis B surface antigen
- **HBV** :Hepatitis B virus
- **HCC** : Hepatocellular carcinoma
- **HCV** : Hepatitis C virus
- **HHIIUS** : High intensity intraductal ultrasound

- **ICC** **:** Intrahepatic Cholangiocarcinoma
- **ILBT** **:** Intraluminal brachtherapy
- **IUDS** **:** Intraductal ultrasound
- **IVC** **:** Inferior Vena Cava
- **LDLT** **:** Living donor liver transplantation
- **LT** **:** Liver Transplantation
- **MDCT** **:** Multi directional computed tomography
- **MRCP** **:** Magnetic resonance cholangiopancreatographygraphy
- **MRI** **:** Magnetic Resonance Imaging
- **MSKCC** **:** Memorial Sloan-Kettering Cancer Center
- **MUC5AC** **:** The human mucin5,subtype A,C
- **O.viverrini** **:** Opisthorchis viverrini
- **OCT** **:** Optical coherence tomography
- **PBD** **:** Preoperative biliary drainage
- **PDT** **:** Photodynamic therapy
- **PET** **:** Positron Emission Tomography
- **PSC** **:** Primary Sclerosing Cholangitis
- **PTC** **:** Percutaneous transhepatic cholangiography
- **PVE** **:** Portal vein embolisation
- **RCT** **:** Radiochemotherapy
- **SEMS** **:** Self expandable metal stent
- **US** **:** Ultrasound
- **WHO** **:** World Health Organisation

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Introduction

Cholangiocarcinoma is an uncommon adeno-carcinoma which arises from the epithelial cells of bile ducts, anywhere along intrahepatic and extrahepatic biliary tree ***(Parkin et al., 2002)***.

The median age of patients at diagnosis of cholangiocarcinoma is from 60–70 Years. Sex incidence is almost equal. Strong associations have been found between cholangiocarcinoma and gallstones, sclerosing cholangitis, ulcerative colitis, cystic abnormalities of the bile duct. Although gallstones have been reported in one-third of patients with bile duct cancers. A cause-and-effect relation has not been established ***(Vollmer et al., 2002)***.

Over the past few decades, remarkable advances in imaging technology have been made that allow more accurate diagnosis of biliary tract diseases and better planning of surgical procedures and other interventions aimed at managing these conditions ***(Taylor et al., 2006)***.

Ultrasound or computed tomography scans usually detect dilated intrahepatic bile ducts. Transhepatic cholangiography or endoscopic retrograde cholangio-pancreatography clearly detect the lesion and both are

indicated in most cases. Transhepatic cholangiography is of greater value, recently MRI cholangiopancreatography (MRCP) takes the upper hand as the most informative non invasive modality for diagnosis of bile duct tumors ***(Phatak and Kochman, 2004)***.

Operative techniques have been improved as a result of a better understanding of biliary and hepatic anatomy and physiology. Moreover, the continuing evolution of minimally invasive surgery has promoted the gradual adoption of laparoscopic approaches to these complex operations ***(Bartlett et al., 2006)***.

Surgical intervention is recommended for those patients who are otherwise healthy, whose disease appears to be localized, or in whom duodenal or gastric outlet obstruction is present, palliative surgery is directed towards relieving jaundice by creating a biliary-enteric anastomosis, and if a gastric or duodenal outlet obstruction is present or a likely possibility, a gastrojejunostomy should be created at the same time. Although palliative surgery is effective in achieving its goal of circumventing the obstruction, no survival advantage has been described when compared with non-operative techniques *(**Furmanczyk et al., 2005)***.

Surgical resection including major hepatic resection remains the mainstay of treatment of hilar cholangiocarcinoma. Additional evidence is needed to fully define the role of orthotopic liver transplantation ***(Ito et al., 2009)***.

Complete regional lymphadenectomy is essential for curative resection of hilar cholangiocarcinoma. Three recent series demonestrate that in patients undergoing radical lymphadenectomy, regional lymph node involvement does not significantly reduce 5-year survival. ***(Kitagawa et al., 2001)***.

The role of radiotherapy and chemotherapy in the treatment of cholangiocarcinoma is limited. Both modalities, either applied separately or in combination, have shown some promise, but have failed to show any survival benefit ***(Harder et al., 2002)***.

Palliative photodynamic therapy (PDT) and subsequent stenting resulted in longer survival than stenting alone and has a similar survival time compared with incomplete R1 and R2 resection. However, these improvements in palliative treatment by PDT will not change the concept of an aggressive resectional approach ***(Witzigmann et al., 2006)***.

Aim of Work

This work aims to review the recent trends in the diagnosis & management (operative and non-operative) of cholangiocarcinoma.