# *Recent advances in the management of Hepatocelluler carcinoma*

**Essay**
Submitted for partial fulfillment of the
Master Degree in General Surgery

By
**El-Sayed Mohammed El-Awady Hemdan**

Under supervision of

**Prof. Dr. Abd El-Wahab Mohammed Ezzat**
Professor of General Surgery
Ain Shams University

**Prof. Dr. Amr Ahmed Abd El-Aal**
Professor of General Surgery
Ain Shams University

**Dr. Gamal Fawzy Samaan**
Lecturer of General Surgery
Ain Shams University

Faculty of medicine
Ain Shams University
2011

# الطرق الحديثة فى علاج الأورام الخبيثة للكبد

رسالة
توطئة للحصول على درجة الماجستير فى الجراحة العامة

مقدمة من
**الطبيب / السيد محمد العوضى حمدان**
بكالوريوس الطب والجراحة
جامعة الاسكندرية

تحت إشراف
**الأستاذ الدكتور / عبد الوهاب محمد عزت**
أستاذ الجراحة العامة
كلية الطب
جامعة عين شمس

**الأستاذ الدكتور / عمرو أحمد عبد العال**
أستاذ الجراحة العامة
كلية الطب
جامعة عين شمس

**الدكتور / جمال فوزى سمعان**
مدرس الجراحة العامة
كلية الطب
جامعة عين شمس

**كلية الطب**
**جامعة عين شمس**
**٢٠١١**

# Summary and Conclusion

Hepatocellular carcinoma (HCC) is a primary cancer of the liver with an established causal link to cirrhosis mostly due to viral hepatitis and alcohol. It is one of the leading causes of cancer death world wide and exhibits marked regional variation in both etiology and mode of presentation. In developing countries HCC often present at late stage with large symptomatic tumor associated with malaise, anorexia, right upper quadrant pain, abdominal bloating, jaundice and liver failure. Patient in developed countries diagnosed in early stages by routine screening of people at risk groups.

The management of HCC is dependent on the size, number and location of the tumor and severity of the underlying liver disease. The choice of therapy is determined by local resources and expertise and so will vary considerably between institutions. Note with regular screening as few as 20% of patient will be suitable for curative treatments such as surgical resection and liver transplantation and therapy of the remainder will be palliative.

Diagnosed HCC is classified (a) resectable (b) nonresectable. Resectable HCC; this depends on liver function, portal hypertension, location, number and size of the tumor. So treatment may be liver resection or liver transplantation.

# ***INDEX***

# *List Of Abbreviations*

| | | |
|---|---|---|
| ***5-FU*** | **:** | **5-fluorouracil** |
| ***AFP*** | **:** | **Alpha feto-protein** |
| ***AH*** | **:** | **Adenomatous hyperplesia** |
| ***AP*** | **:** | **Alkalin phosphatase** |
| ***BCLC*** | **:** | **Barcelona Clinic Liver Cancer** |
| ***BCS*** | **:** | **Budd Chiari syndrome** |
| ***BDNF*** | **:** | **Brain-derived neurophilic factor** |
| ***CBD*** | **:** | **Common Bile Duct** |
| ***CDKs*** | **:** | **Cyclin-dependant kinases** |
| ***CEA*** | **:** | **Carcino Embryonic Antigen** |
| ***CGH*** | **:** | **Comparative genomic hybridization** |
| ***CLIP*** | **:** | **Cancer of liver Italian program** |
| ***CMV*** | **:** | **Cytomegalovirus** |
| ***CT*** | **:** | **Computed tomography** |
| ***CTA*** | **:** | **CT Arteriography** |
| ***CTAP*** | **:** | **CT Arterial Portography** |
| ***CTHA*** | **:** | **Computed tomography hepatic arteriography** |
| ***CTP*** | **:** | **Computed tomography portography** |
| ***CVP*** | **:** | **Central Venous Pressure** |
| ***DCP*** | **:** | **Des-γ-carboxy prothrombin** |
| ***EBV*** | **:** | **Ebstien-Barr Virus** |
| ***ERCP*** | **:** | **Endoscopic Retrograde Cholangio Pancreaticography** |
| ***FNH*** | **:** | **Focal nodular hyperplasia** |
| ***GSK*** | **:** | **Glycogen synthetase kinase** |
| ***HA*** | **:** | **Hepatic Artery** |
| ***HAI*** | **:** | **Hepatic artery infusion** |
| ***HBV*** | **:** | **Hepatitis B Virus** |
| ***HCC*** | **:** | **Hepatocellular carcinoma** |
| ***HCV*** | **:** | **Hepatitis C-virus** |
| ***HIV*** | **:** | **Human Immunodefeciency Virus** |
| ***ILT*** | **:** | **Interstitial Laser Thermotherapy** |
| ***INF*** | **:** | **Interferon** |

| | | |
|---|---|---|
| ***IVC*** | **:** | **Inferior vena cava** |
| ***LAK*** | **:** | **Lymphokine Activated Killer cells** |
| ***LDLT*** | **:** | **Living donor liver transplantation** |
| ***LHV*** | **:** | **Left hepatic vein** |
| ***LITT*** | **:** | **Laser-induced Interstitial Thermotherapy** |
| ***LPB*** | **:** | **Left portal branch** |
| ***LTA*** | **:** | **Laser Thermal Ablation** |
| ***MDR*** | **:** | **Multi drug resistance** |
| ***MHV*** | **:** | **Middle hepatic vein** |
| ***MRI*** | **:** | **Magnetic Resonance Image** |
| ***NASH*** | **:** | **Non Alcoholic Steatohepatitis** |
| ***PEIT*** | **:** | **Percutaneous Ethanol Injection Therapy** |
| ***PMCT*** | **:** | **Percutaneous Microwave Coagulation Therapy** |
| ***PT*** | **:** | **Prothrombin Time** |
| ***PVE*** | **:** | **Portal vein embolization** |
| ***PVTT*** | **:** | **Portal vein tumor thrombosis** |
| ***RCTs*** | **:** | **Randomized controlled trials** |
| ***RFA*** | **:** | **Radiofrequency ablation** |
| ***RHV*** | **:** | **Right hepatic vein** |
| ***RPB*** | **:** | **Right portal branch** |
| ***RT*** | **:** | **Radiation therapy** |
| ***SMA*** | **:** | **Superior Mesenteric Artery** |
| ***SMV*** | **:** | **Superior Mesenteric Vein** |
| ***TACE*** | **:** | **Transarterial Chemoembolization** |
| ***TGF*** | **:** | **Transforming growth factor** |
| ***TNM*** | **:** | **Tumor-node-metastasis** |
| ***TRAIL*** | **:** | **Tumor necrosis factor related apoptosis-including ligand** |
| ***TSG*** | **:** | **Tumor suppressor gene** |
| ***USG*** | **:** | **Ultrasonography** |
| ***VEGF*** | **:** | **Vascular endothelial growth factor** |

# *List of Figures*

# *List of tables*

# Introduction

Hepaocellular Carcinoma (HCC) accounts for 80% to 90% of primary liver cancer. HCC is a major health problem worldwide, with an estimated incidence ranging between 500 000: 1000 000 new cases annually. It is the fifth most common cancer in the world, and the third most common cause of cancer-related death. (***Lai and Lau.,2005***).

Unfortunately, HCC is often diagnosed only at an advanced stage due to the absence of specific symptoms during the initial course of the disease (***Llovet et al., 2003***).

The diagnosis of HCC is typically made by radiological liver imaging in combination with serum alpha fetoprotein (AFP). **( *Lok ,et al.2010*).**

Therapies for HCC can be divided into four categories: surgical interventions (tumor resection and/or liver transplantation), percutaneous interventions (ethanol injection, radiofrequency thermal ablation), transarterial interventions (embolization, chemo perfusion, or chemoembolization) and drugs including gene and immune therapy. Potentially curative therapies are tumor resection, liver transplantation, and percutaneous interventions that can result in complete responses and improved survival in a large number of patients. In selected

cases, transarterial interventions result in palliation with good response rates and improved survival in some cases. Drugs as well as conventional radiotherapy have no proven efficacy. ***(Alsowmely and Hodgson, 2002)***.

Liver resection is the operation of choice for patients with tumors less than 5 cm in the absence of cirrhosis. These patients can often tolerate resection of up to 50% of the total liver volume. In these patients, an operative mortality rate of less than 2% can be expected in experienced centers. ***(Llovet et al., 2004)***.

Liver transplantation is the best treatment for patients with single lesions and advanced liver diseases, such as decompensate cirrhosis and multicentric small tumors. Percutaneous interventions, in selected patients, result in a 5-year survival rate of 40-50% ***(Blumgart et al.,2006)***

Sorafenib is a small molecule that inhibits tumor-cell proliferation and tumor angiogenesis and increases the rate of apoptosis in a wide range of tumor models. ***(Wilhelm et al.,2004).***

# ANATOMY OF THE LIVER

## GROSS ANATOMY

### MORPHOLOGICAL ANATOMY

The liver is the largest internal organ in the body, accounting for approximately 2% to 3% of the total body weight of an adult. The liver is covered with the capsule of Glisson which envelops the hepatic artery, portal vein, and bile duct at the hilum of the liver **(*Skandalakis et al., 2004).***

**Surface anatomy (of anterior surface):**

***1- Upper border:***

A line concave upwards, which extends from the left $5^{th}$ rib in midclavicular line to the $4^{th}$ right intercostal space in midclavicular line, passing by the xiphisternal joint, then continuous to the right $7^{th}$ rib in midaxillary line.

***2- Right border:***

Vertical line from right $7^{th}$ to $11^{th}$ ribs in midaxillary line then extends for 1/2 inch below costal margin.

***3- Inferior border:***

Oblique line which joins the ends of upper and right borders crossing the left $8^{th}$ then right $9^{th}$ costal margin. ***(Shilla and Dolley, 1997).***

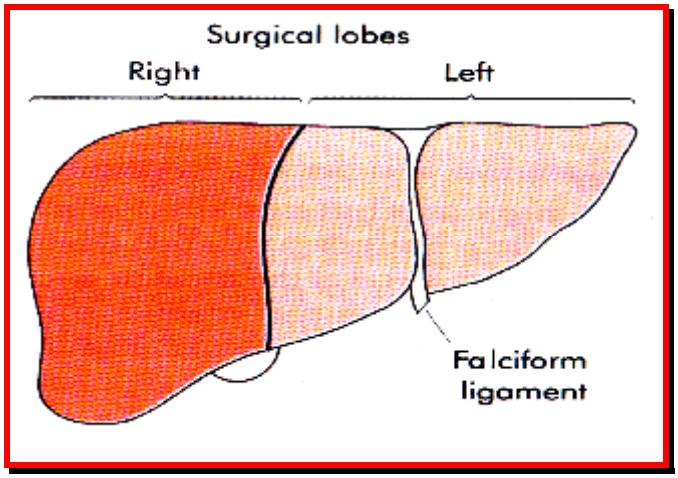


**Fig. ( 1 ) :** Lobar anatomy of liver ***(Skandalakis, 2004).***

## *Surfaces of the liver and their relations:*

The three surfaces of the liver in sagittal section are the posterior surface, the anterosuperior surface, and the inferior surface.

### *Posterior surface :*

The posterior surface is related to the vertical part of the diaphragm and for all practical purposes, is retroperitoneal. Three anatomic entities are related to the posterior surface: the retrohepatic part of the IVC, the right adrenal gland, and the upper pole of the right kidney. The IVC travels through the hepatic parenchyma. The bare area of the liver may also be considered part of the posterior surface.

### *Anterosuperior surface :*

The anterosuperior surface is related to the diaphragmatic dome to be more specific, the anerosuperior surface is located behind the ribs and cartilages, part of the diaphragm, pericardium, the pleurae, and the pulmonary parenchyma. This superior surface is covered by peritoneum except for the attachment of the falciform liament and where more dorsally, the superior reflection of the coronary ligament bounds the bare area of the liver.

### *Inferior surface:*

The inferior surface is the visceral hepatic surface. It is related to several intraperitoneal anatomic entities and spaces. The space under the right lobe is the subhepatic space of morison;while that under the left lobe is the lesser sac. The inferior visceral hepatic surface under the right lobe is related to the gallbladder, right adrenal gland, right kidney, right renal vessels, head of pancreas, proximal part of the pancreatic neck, first and second parts of the duodenum, common bile duct, portal vein, hepatic artery, IVC, and hepatic colonic flexure ***(Skandalakis et al., 2004)***.