

## *INTRODUCTION*

**L**iving donor liver transplantation (LDLT) is a new modality that has been developed to overcome the shortage of available cadaveric livers for transplantation. This modality now covers a wide range from newborn to advanced age. After basic research, *Thomas Starzl* did the first cadaveric liver transplantation on a human being in 1963. The first success was in 1967 in Denver, Colorado. Owing to the dramatic increase in patient survival brought about by the immunosuppressant cyclosporine as well as the improvement of quality of life, liver transplantation was established as a treatment modality that spread in the 1980s (*Tanaka, 2003*).

Orthotopic replacement of the diseased liver by a whole liver obtained from a heart-beating cadaver is the standard technique for liver transplantation. A main obstacle is the shortage of liver donors compared to the long waiting list of recipients. In some countries in which brain death is not yet accepted as a legal criterion for organ retrieval the liver grafts are simply not available. For infants the shortage of pediatric donors was particularly critical (*Ismail A, 1990*).

The liver has the specific characteristic of regeneration according to internal demand after partial resection. The first clinical living donor liver transplantation was performed by *Raia* and colleagues in **1988** in Sao Paulo, Brazil and the first successful LDLT was reported in Brisbane, Australia, in July 1989. In parallel, in Japan, the first LDLT was done in Shimane Medical College in November 1989, followed shortly thereafter by the series of LDLT of **Kyoto** University and Shinshu University. In LDLT, major advantages would include the good viability of a partial liver donated by a healthy individual; the careful selection of the timing

of the transplantation; and the potential good tissue matching (**Tanaka, 2003**).

Liver transplantation has become an effective therapy for patients with acute or chronic end-stage liver disease. Initially, transplantation was considered the last therapeutic option for patients who were in a very serious clinical condition at the time of surgery, and therefore premature mortality was very high. Currently though, survival rates of over 90-95% and 70% at one year and five years post-transplantation (**Moreno & Berenguer, 2006**).

The liver is an organ that actively interacts with all body systems, so that the patient who receives a liver graft faces a huge set of physiological changes. During and in the immediate postoperative period, the liver is subjected to a wide variety of potentially damaging factors, including hypotension, hypoxia, ischaemia and hepatotoxic drugs, surgical-related aspects (intra- or postoperative hemorrhage, vascular or biliary complications) or immune responses (rejection) might lead to a very different outcome. The main complications in the immediate postoperative period are related to the function of the graft (dysfunction and rejection), the surgical technique, infections (bacterial, fungal, and viral), and systemic problems (pulmonary, renal, or neurological). In the long term, the complications are typically a consequence of the prolonged immunosuppressive therapy, and include diabetes mellitus, systemic arterial hypertension, de novo neoplasia, and organ toxicities, particularly nephrotoxicity (**Moreno and Berenguer, 2006**).

Advances in surgical techniques have contributed to the improved results of living related liver transplantation, which, however, has a high risk of vascular complications because of complex reconstruction of the

hepatic artery and portal vein. Thus, a significant percentage of liver grafts is still lost from vascular complications after living related liver transplantation. Early and accurate diagnosis of vascular complications is crucial for increasing the survival rate of the graft in living related liver transplantation because most stenoses or thromboses are treatable with interventional procedures. If untreated, many vascular complications may progress to severe hepatic failure or overwhelming biliary sepsis, resulting in graft failure (*Kim et al., 2003*).

Arterial complications occurring in the post-transplantation period include: thrombosis or hemodynamically significant hepatic artery stenosis; diffuse aneurysms; and arteriovenous fistulas (*Pawlak et al., 2000*).

Arterial complications, particularly the thrombosis of the hepatic artery are the most frequent ones. Hepatic artery thrombosis is a complication that develops more frequently in the pediatric population. In many centers, vascular anastomoses are accomplished by a vascular surgeon with microsurgical techniques, which remarkably improves the quality of vascular reconstruction. Symptoms are highly variable and depend on the timing of development and diagnosis. When the thrombosis occurs at an early stage, it typically leads to ischemia/necrosis of the graft; in contrast, when it occurs at a later time point, it generally leads to biliary complications (intrahepatic biliomas and biliary stenosis (*Vivarelli et al., 2004*).

Venous complications include: thrombosis; stenosis of the inferior vena cava; occlusion or stenosis of one or more hepatic veins; and

thrombosis or stenosis of the trunk of the portal vein (*Pawlak et al., 2000*).

Portal vein thrombosis is an infrequent complication. It is related to pre-transplantation portal thrombosis, splenectomy, and prior portal hypertension surgery. In the acute form, the clinical picture is dominated by symptoms/signs of hepatic failure; in contrast, portal hypertension is the typical presentation in the late form (*Moreno and Berenguer, 2006*).

In the past, technical difficulties and the potential risk of vessel reconstruction, as well as the higher rate of postoperative complications made Portal vein thrombosis a contraindication of liver transplantation. However, improvement of operative management and advancement of postoperative care have meant that Portal vein thrombosis is no longer a contraindication of liver transplantation (*Egawa et al., 2006*).

Hepatic vein stenosis has emerged as one of the important vascular complications of living donor liver transplantation LDLT. In a case of orthotopic liver transplantation from a cadaveric donor, the anastomosis is performed between the venae cavae without touching the hepatic veins. In LDLT, however, each hepatic vein of the transplanted liver is connected directly to the recipient's inferior vena cava IVC after total hepatectomy has been performed. This surgical technique can induce mechanical or functional stenosis of the hepatic veins, which can cause venous outflow obstruction and even graft loss of the transplanted liver (*Young et al., 2003*).

The success of liver transplantation depends on the early diagnosis and appropriate treatment of complications. Vascular complications are a frequent cause of transplant failure; the most severe of these

complications are those involving the hepatic artery. Diagnostic imaging plays a major role in the prompt diagnosis and treatment of this condition (*Gaetano et al., 2000*).

Ultrasonography (US) is a very useful imaging modality in the early postoperative period after liver transplantation, and it is sometimes the only available modality. Spectral and color Doppler US can provide useful information for monitoring vascular complications. The use of Doppler US in evaluating vascular compromise, particularly of the hepatic artery and portal vein, has been well established, as it offers diagnostic criteria on Doppler spectral examinations (*Young et al., 2003*).

Although an integrated surgical and radiologic approach is required for the management of anastomotic complications in liver transplants, percutaneous intervention has been strongly advocated and has been more recently accepted as the initial treatment for many transplant-related anastomotic abnormalities (*Young et al., 2002*).

## AIM OF THE WORK

The objective of this research is to retrospectively assess vascular complications after living-donor liver transplantation (LDLT) and to make an early diagnosis with different ways of treatment of vascular complications, with clinical follow-up.

## History of Liver Transplantation

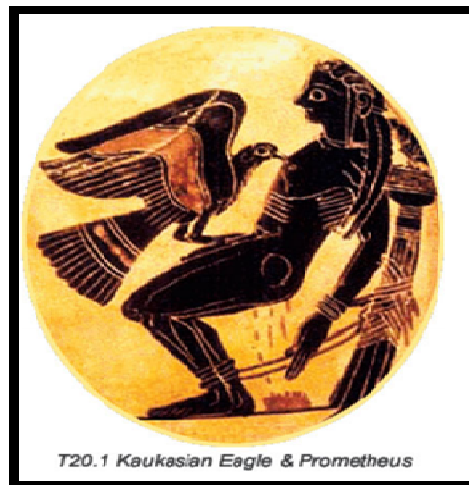
**H**istorically, in ancient civilizations, man had already imagined changes in the morphology, structure and function of the human body. Egyptian and Greco-Roman mythology provides us with countless examples of the metamorphoses sung by Homer and Ovid, symbolic incarnations of the “comédie humaine” with its strength, weaknesses, vices and virtues. The liver has been the noble organ, the organ of life from time immemorial - liver in English, Leber in German, derived from the verb to live. Shakespeare a faithful interpreter of ancient traditions places the liver in first position in his famous list:

*“Liver, brain and heart these sovereign thrones” (Twelfth Night, Act 1, Scene 1) (Calne, 1994).*

The dream of curing illness and injury by transplanting tissues or entire organs is probably as old as the history of healing itself. The earliest evidence of an orthotopic autograft (organ is placed in its normal anatomic position) has been preserved from the Bronze Age. A circular disk of bone was removed from the calvarium to relieve intracranial pressure and later replaced as an autograft. Written accounts from Egypt, China and India dating back many centuries described experimentations in grafting. In 1668 Van Meeneren documented the first successful bone graft. The modern age of organ transplantation began in the twentieth century with Alexis Carrel, based on his pioneering work devoted to vascular replacement (*Sharma and Unruh, 2004*).

The regenerative power of the liver was first described by the Greeks more than 2500 year ago. Greek mythology gives perhaps the most infamous reminder of the liver’s regenerative powers with the

mythological account of Prometheus, who stole fire from Zeus and gave it to humankind. As a punishment, he was chained to one of the Caucasian Mountains, where every day a voracious bird feasted upon his liver, causing excruciating pain (Figure 1). Only at night, while the bird slept, did his liver regenerate, so that the process could begin again the next day. Regeneration is a common feature in invertebrates (e.g., worms) but is very limited in the majority of vertebrates. The mechanisms of liver regeneration remain poorly defined, but the process is central to the success of surgical resections and live donor transplantation (*Galambos, 1979*).



**Figure (1):** The regenerative power of the liver. As punishment for stealing fire from Zeus, Prometheus was bound to a rock where each day a bird ate out his liver, which would then regenerate each night while the bird slept.

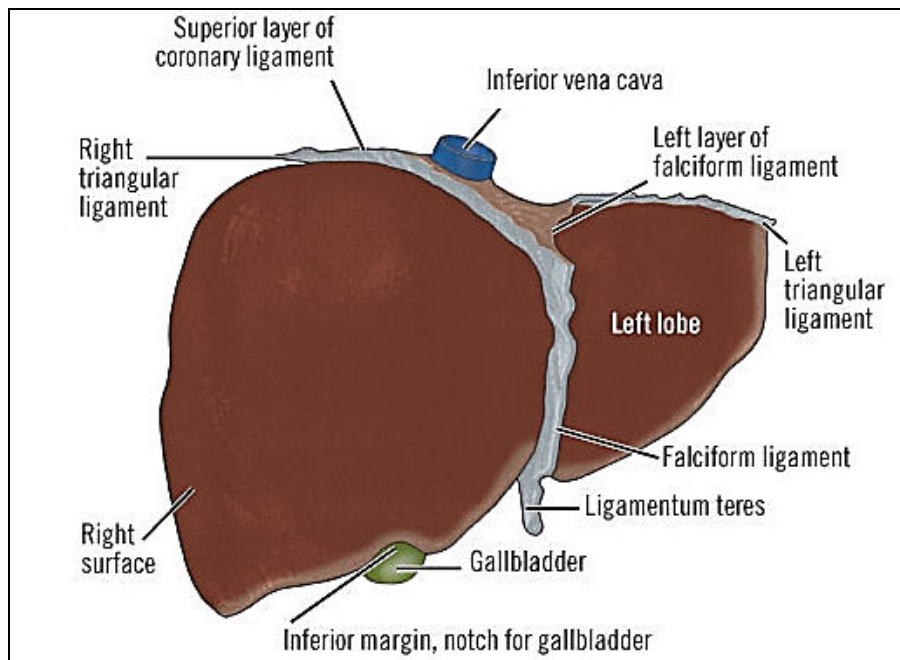


# Surgical Anatomy of the Liver

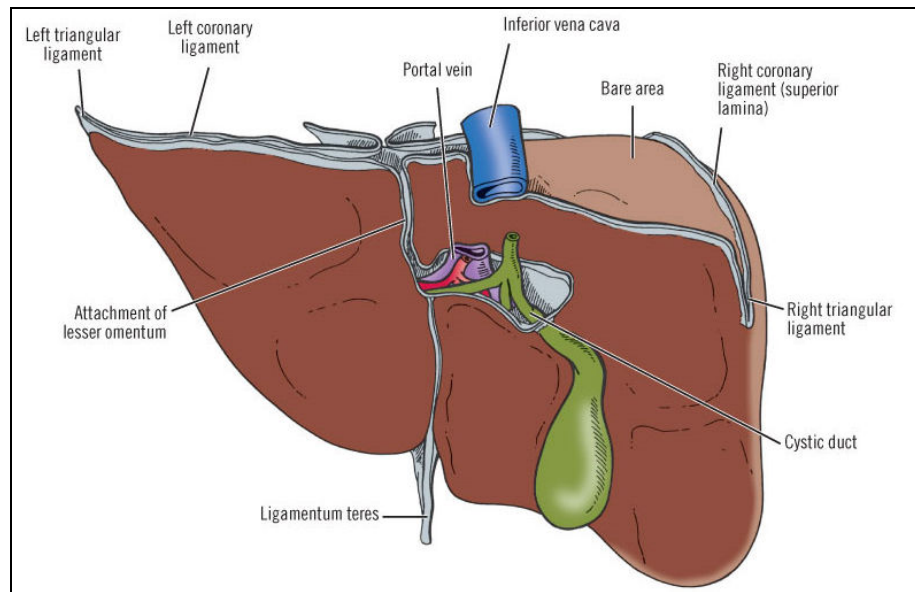
## Topographic Anatomy

Topographic anatomy, initially described in early *Babylon* (3000-2000 BC), divides the liver according to external landmarks. This anatomic system dominated through the late 19<sup>th</sup> century but is only of historical interest today. The principal landmarks defining topographic anatomy include the falciform ligament, umbilical fissure, gallbladder fossa, and transverse hilar fissure.

These landmarks delineate four lobes (Figure 2, 3,4): left (medial to falciform), right (lateral to falciform), quadrate, and caudate (spigelian) (*McClusky et al., 1997*).

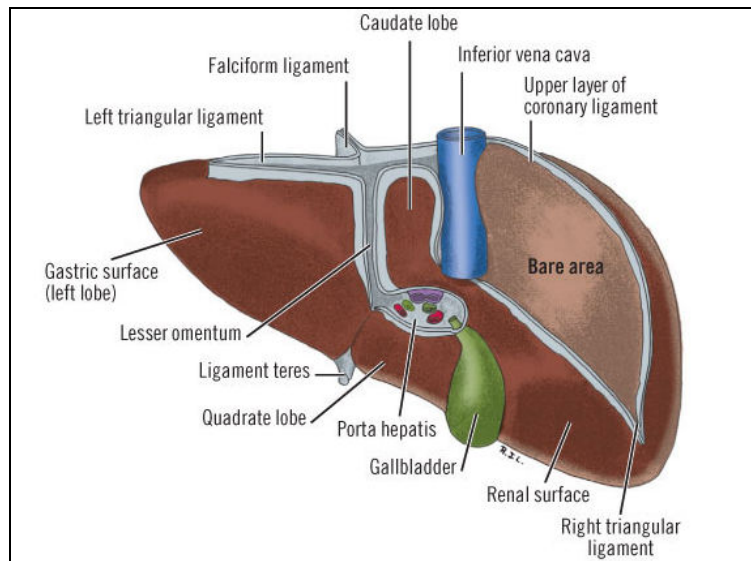


**Figure (2):** Diaphragmatic aspect of the liver illustrating features of the anterior and superior surfaces. The liver measured 21 cm transversely, 20.3 cm vertically, and 14.6 cm in thickness (*Skandalakis et al., 1987*).



**Figure (3):** Diagram of the posterior aspect of the liver to show the arrangement of the peritoneal attachments (*Skandalakis et al., 1987*).

The human liver is the largest solid organ of the body, weighing about 150 gm at birth. The weight of the liver of the adult male ranges from 1.4 kg to 1.8 kg, and the adult female from 1.2 kg to 1.4 kg. Because of the role of the liver in blood formation during fetal life, the organ at birth contributes 4% to 5% to body weight. In the newborn infant, the liver bulges both the left and right hypochondrium. The effect of the weight of the liver on the location of the infant's center of gravity may be an important factor in the development of the ability to attain upright posture and locomotion (*Williams, 1995*).

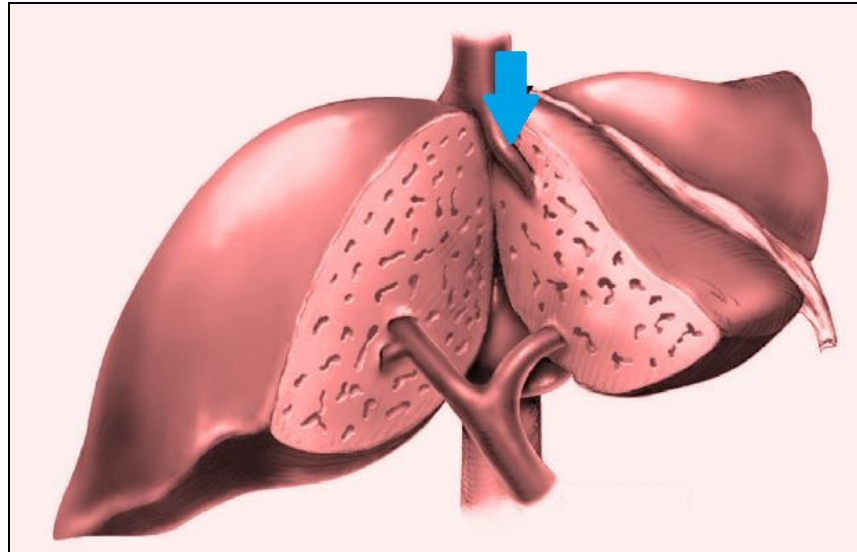


**Figure (4):** Posterior view of the liver. The under surface of the organ, sloping down to the anterior border, is visible from this aspect. The peritoneal attachments are shown. The cut edges around the porta hepatis and in the lower part of the lesser omentum are attached to the lesser curvature of the stomach; all other peritoneal edges seen here are attached to the diaphragm (*Last, 1972*).

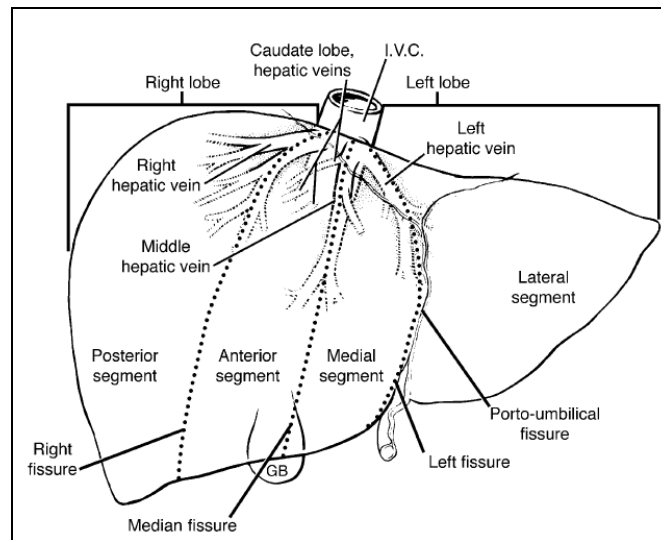
## **Lobar Anatomy**

The concept of *separate* hepatic arterial and portal venous systems reconstituting through the hepatic veins resurfaced in 1888, when **Hugo Rex** studied hepatic corrosion casts from mammals. **Rex** concluded that the right and left branches of the portal vein functioned as unique vascular systems, dividing the liver into separate halves (**Rex, 1888**). **James Cantlie**, in 1898, extended these findings to humans, proposing a functional division of the liver into two lobes (**Cantlie's term**) of relatively equal size based on the branching of the portal vein and hepatic ducts (**Cantlie, 1897**). The proposed plane of demarcation was a connective tissue layer, indistinguishable from surface topography, that bisects the gallbladder fossa and inferior vena cava, incorrectly termed **Cantlie's line** (Figure 5, 6). Cantlie's description shifted the entire quadrate lobe (topographic term), as well as a large component of the

caudate lobe (topographic term), into the anatomic boundaries of Cantlie's left lobe. This classification system, founded on intrahepatic functional anatomy, resulted in a surgical revolution through the performance of successful anatomic resections (*Bismuth, 1982*).



**Figure (5):** Liver hepatotomy along the line of Cantlie. This plane corresponds with the middle hepatic vein and is approximated by a plane going through the gallbladder fossa to the left border of the IVC. (*Liau and Blumgart, 2004*).

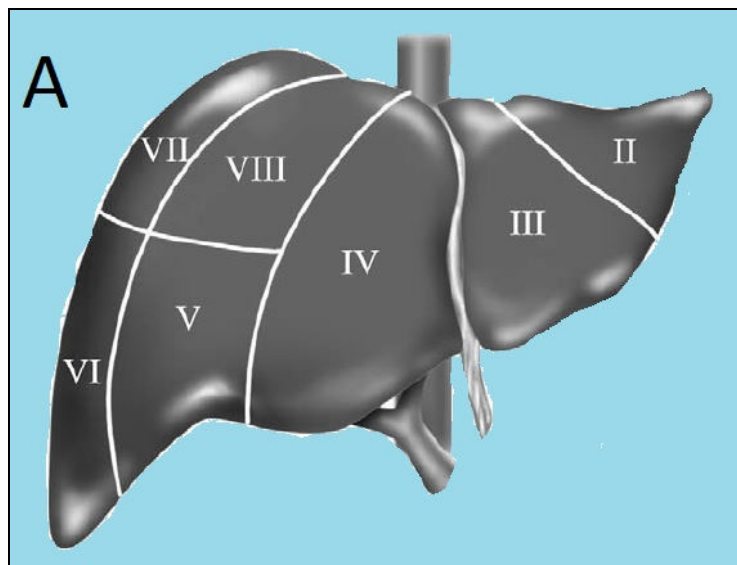


**Figure (6):** The four fissures. GB, gallbladder; IVC inferior vena cava (*Colburn et al., 1987; Strasberg, 1997*).

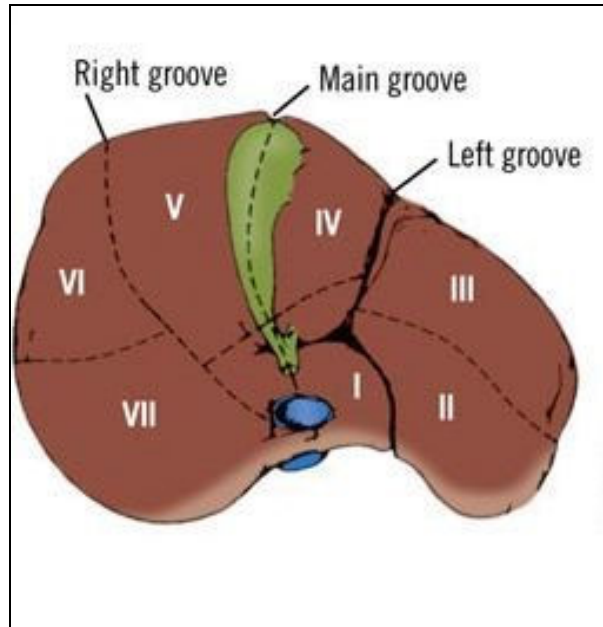
Europeans continue to describe hepatic lobes based on topographic anatomy, whereas North American surgeons adopted “lobectomy” as the hemi liver defined by Cantlie. One must be certain as to the reference system in use (topographic anatomy or Cantlie’s anatomic classification) when applying the term *lobe* or *lobectomy* (**Bismuth, 1982**).

### **Segmental Anatomy**

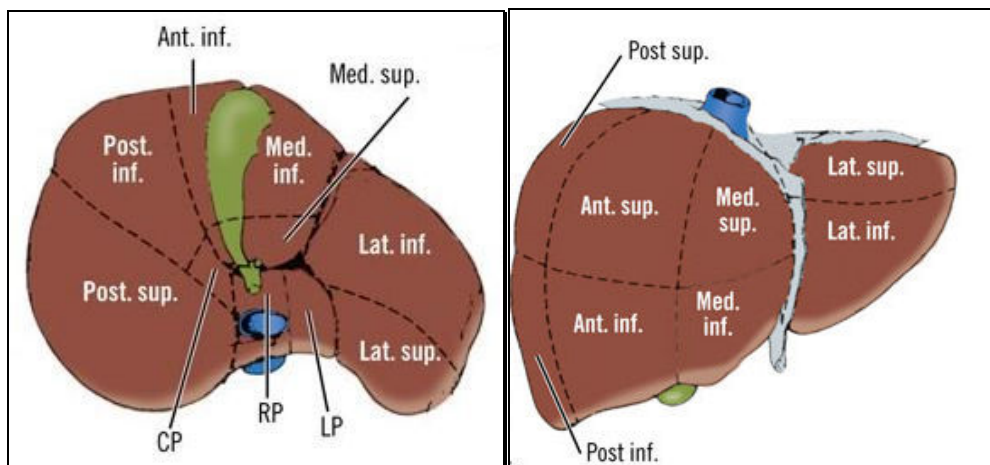
The most sophisticated classification of intrahepatic anatomy is by Couinaud, who in 1954 founded his anatomic description on the portal venous system. Portal vein distribution within the liver was subdivided into eight “segments.” Individual segments each receive a “portal pedicle” consisting of a portal venous branch, hepatic arterial branch, and a bile duct radicle with segmental drainage through a dedicated hepatic venous branch. The eight functional units embrace the hepatic veins that provide outflow to the inferior vena cava (Fig.7,8,9) (**Bismuth, 1982**).



**Figure (7):** Liver segmental anatomy. (A) The eight segments of the liver as defined by Couinaud. Segment I lies between the IVC and segment IV (not shown) (**Liau and Blumgart, 2004**).



**Figure (8):** Terminology of Couinaud (1954).



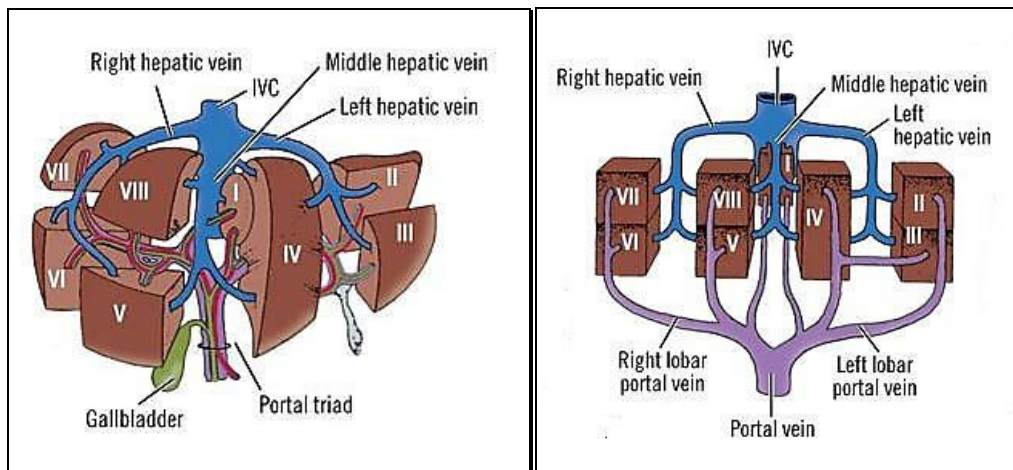
**Figure (2):** E and F. Terminology of Healey and Schroy (1953). (CP, caudate process; RP and LP, right and left portions of the caudate lobe). **G.** Highly diagrammatic presentation of the segmental functional anatomy of the liver emphasizing portal distribution and hepatic veins. **H.** Exploded segmental view of the liver emphasizing the intrahepatic anatomy and hepatic veins (*Skandalakis et al., 2004*).

The hepatic veins travel in connective tissue planes, termed *fissures* or *scissurae*, dividing the liver into four sectors (Figure 10,11). The left portal fissure contains the left hepatic vein; the main portal fissure



corresponds to Cantlie's line and contains the middle hepatic vein, and the lateral-most (right) portal fissure contains the right hepatic vein. Three of the four sectors contain smaller fissures that subdivide each into two segments to form a total of seven segments. Of the accessory lobes, only the caudate (segment I) is a functionally autonomous segment. Segment I is supplied by both the left and right branches of the portal vein and hepaticartery and empties directly into the vena cava (*Couinaud, 1954*).

Rather than perform atypical resections based on the size or location of a lesion, hepatic resections could be performed along functional planes that would minimize intraoperative blood loss and postoperative necrosis of devitalized tissue. This classification revolutionized hepatic surgery by providing a foundation for the development of highly selective anatomic resections as well as innovations in transplantation using surgically created partial-liver grafts (*Bismuth, 1982*).



**Figure (10):** G. Highly diagrammatic presentation of the segmental functional anatomy of the liver emphasizing portal distribution and hepatic veins. H. Exploded segmental view of the liver emphasizing the intrahepatic anatomy and hepatic veins (*Skandalakis et al., 2004*).