



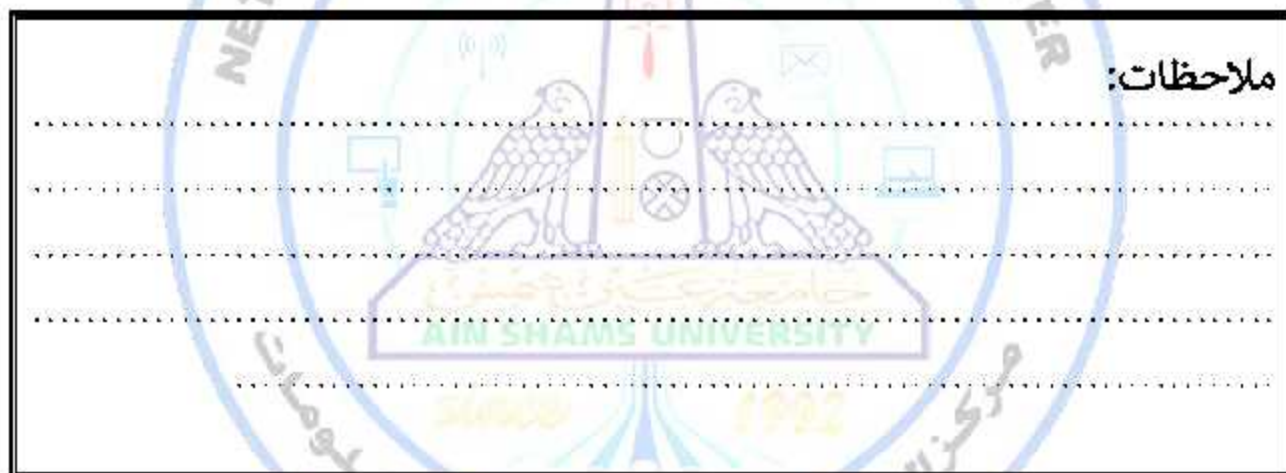
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تم رفع هذه الرسالة بواسطة / سنوي محمود عقل

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات:





The Outcome of Living-donor Versus Deceased-donor Liver Transplantation for Hepatocellular Carcinoma

A Systematic Review and Meta-analysis

*Submitted for partial fulfillment of master's degree in
General Surgery*

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List of Abbreviations

Abb.	Full term
<i>AASLD</i>	<i>American association of study of liver disease</i>
<i>AFP</i>	<i>Alfa fetoprotein</i>
<i>BCLC</i>	<i>Barcelona Clinic Liver Cancer</i>
<i>DDLT</i>	<i>Deceased donor liver transplant</i>
<i>DFS</i>	<i>Disease free survival</i>
<i>HBV</i>	<i>Hepatitis B virus</i>
<i>HCC</i>	<i>Hepatocellular carcinoma</i>
<i>HCV</i>	<i>Hepatitis C virus</i>
<i>HDV</i>	<i>Hepatitis D virus</i>
<i>ITT-OS</i>	<i>Intention to treat overall survival</i>
<i>IVC</i>	<i>Inferior vena cava</i>
<i>LDLT</i>	<i>Living donor liver transplant</i>
<i>LT</i>	<i>Liver transplant</i>
<i>MC</i>	<i>Milan criteria</i>
<i>N/A</i>	<i>Not applicable or not available</i>
<i>OS</i>	<i>Overall survival</i>
<i>PEI</i>	<i>Percutaneous ethanol injection</i>
<i>RFA</i>	<i>Radiofrequency ablation</i>
<i>TAC</i>	<i>Trans arterial chemoembolization</i>
<i>VI</i>	<i>Vascular invasion</i>

INTRODUCTION

Liver cancer remains a global health problem and its incidence is rising worldwide ^{1,2}. It is estimated that, by 2025, >1 million people will be diagnosed with liver cancer annually ³. Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and accounts for ~90% of cases. ⁴

Therapeutic treatment options are available for patients with local disease and include ablation, resection, and liver transplantation (LT) ⁵. Liver transplantation (LT) is a recognized treatment choice for patients with cirrhosis of the liver and hepatocellular carcinoma (HCC) ⁶.

The greatest obstacle in liver transplant is the shortage of donors that has contributed to a remarkable increase of the waiting lists. Therefore, there is an increase in the time from the decision of transplantation to the liver transplant itself. During this period, the HCC may progress and drop out from the waiting list. ^{7,8,9}

Several strategies have been evaluated to reduce this risk: increasing the pool of donors by including live donors, treatment of HCC upon enlistment, and priority policies by identifying patients with lower rates of HCC recurrence and higher rates of survival to fairly allocate liver grafts. However, the long-term outcomes of living donor liver transplant (LDLT) versus deceased donor liver transplant (DDLT) for hepatocellular carcinoma

(HCC) are still controversial. Several studies demonstrate that LDLT was associated with better overall survival (OS) as well as disease free survival (DFS) when compared to DDLT ^{10,11}. While other studies illustrated that HCC patients undergoing LDLT would result in worse OS and DFS ^{12,13}. Moreover, some studies showed equal overall survival between the two modalities ^{10,14}. In addition to that, there are many predictors of recurrence other than type of the graft such as level of AFP, vascular invasion and tumor grade that could be used to fairly allocate graft to those with lower incidence of recurrence. ^{15,16,17}

AIM OF THE WORK

Our aim was to assess 4 primary outcomes of LDLT and DDLT for HCC patients in this meta-analysis, including patient long-term overall survival from the time of transplant (1-, 2-, 3-, 4-,5-, 6- and 10-year OS), patient long-term overall survival from the time of listing to transplantation (1-, 2-, 3-, 4-,5-, 6- and 10-year ITT-OS), disease free survival (1-, 2-, 3-, 4-,5-, 6- and 10-year DFS) and recurrence rate. In addition to that, we wanted to detect the effect of age of recipient, sex of recipient, level of alfa fetoprotein and tumor biology (presence of vascular invasion and tumor grade) on the survival and recurrence of HCC after transplantation.

Chapter 1

LIVER

Anatomy

The liver is the largest solid organ in the body, weighing approximately 1500 g. It resides in the right upper abdominal cavity beneath the diaphragm and is protected by the rib cage. It is surrounded by a fibrous sheath known as Glisson's capsule.¹⁸

Segmental Anatomy

The liver is grossly separated into the right and left lobes by the plane from the gallbladder fossa to the inferior vena cava (IVC), known as Cantlie's line. The right lobe typically accounts for 60% to 70% of the liver mass, with the left lobe (and caudate lobe) making up the remainder. The caudate lobe lies to the left and anterior of the IVC.¹⁸

The caudate lobe is defined as segment I, and the remaining segments are numbered in a clockwise fashion up to segment VIII. The features are extremely consistent between individuals. (Figure 1)

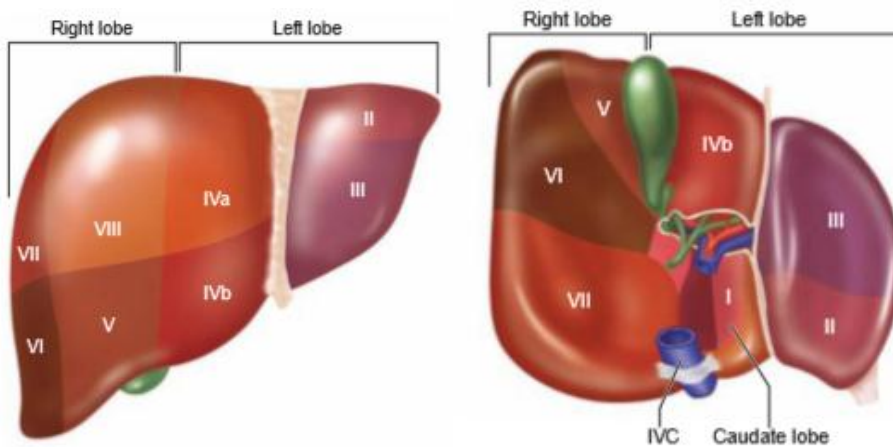


Figure 1: Segmental anatomy of the liver

Ligaments

The liver is held in place by several ligaments.

The round ligament is the remnant of the obliterated umbilical vein and enters the left liver hilum at the front edge of the falciform ligament.

The falciform ligament separates the left lateral and left medial segments and anchors the liver to the anterior abdominal wall.

Ligamentum venosum (Arantius' ligament) which is the obliterated ductus venosus and is covered by the plate of Arantius. It is located deep in the plane between the caudate lobe and the left lateral segment.

The left and right triangular ligaments secure the two sides of the liver to the diaphragm. Extending from the triangular ligaments anteriorly on the liver are the coronary ligaments. The right coronary ligament also extends from the right undersurface of the liver to the peritoneum overlying the right kidney, thereby anchoring the liver to the right retroperitoneum.

Centrally and just to the left of the gallbladder fossa, the liver attaches via the hepatoduodenal and the gastrohepatic ligaments. The hepatoduodenal ligament is known as the porta hepatis and contains the common bile duct, the hepatic artery, and the portal vein. From the right side and deep (dorsal) to the porta hepatis is the foramen of Winslow, also known as the epiploic foramen.¹⁸(Figure 2)

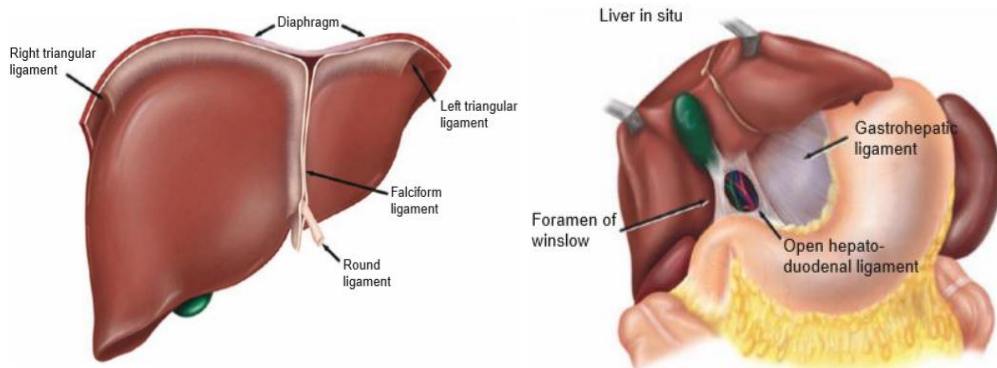


Figure 2: Ligaments of the liver

Blood supply

The liver has a dual blood supply consisting of the hepatic artery and the portal vein. The hepatic artery delivers approximately 25% of the blood supply, and the portal vein approximately 75%.

Hepatic artery

The hepatic artery arises from the celiac axis (trunk), which gives off the left gastric, splenic, and common hepatic arteries. The common hepatic artery then divides into the gastroduodenal artery and the hepatic artery proper. The right gastric artery typically originates off of the hepatic artery proper. The hepatic artery proper divides into the right and left hepatic arteries. (Figure 3)

Portal vein

The portal vein is formed by the confluence of the splenic vein and the superior mesenteric vein. The inferior mesenteric vein usually drains into the splenic vein upstream from the confluence. The main portal vein traverses the porta hepatis before dividing into the left and right portal vein branches. (Figure 4)¹⁸

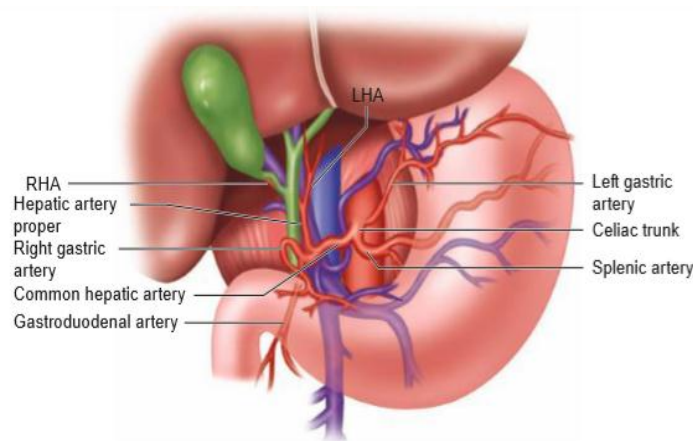


Figure 3: Branches of celiac trunk Figure

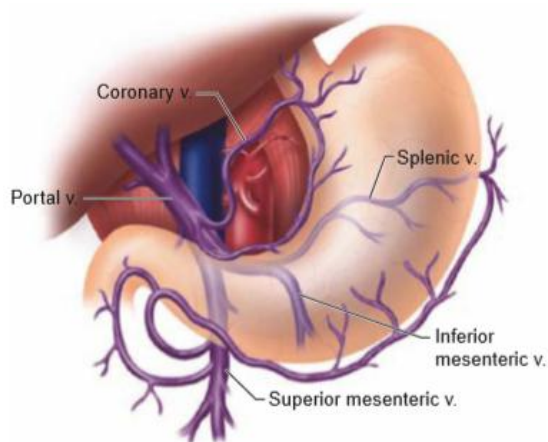


Figure 4: Tributaries of portal vein