

End Organs Failure in Liver Cirrhotic Patients in Intensive Care Unit

An Essay

*Submitted for partial fulfillment of Master degree in
General Intensive Care*

By

Nesreen Samir Mohammed Alfeky

M.B., B.Ch. (Cairo University)

Under supervision of

Prof. Dr. Sherif Wadie Nashed

*Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine- Ain Shams University*

Prof. Dr. Hazem Mohamed Abdelrahman

Fawzy

*Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine- Ain Shams University*

Dr. Dina Salah Eldin Mahmoud

*Lecturer of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine- Ain Shams University*

**Faculty of Medicine
Ain Shams University
2016**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ وَقَدْ رَبِّ زِدْنِي عِلْمًا ﴾

سورة طه الآية رقم ١١٤



Acknowledgement

First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Prof. Dr. Sherif Wadie Nashed**, Professor of Anesthesia, Intensive Care and Pain Management, faculty of medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work, and tremendous effort he has done in the meticulous revision of the whole work, It is a great honor to work under his guidance and supervision.

I would like also to express my sincere appreciation and gratitude to **Prof. Dr. Hazem Mohamed Abdelrahman Fawzy**, Professor of Anesthesia, Intensive Care and Pain Management, faculty of medicine, Ain Shams University, for his continuous directions and support throughout the whole work,

Really I can hardly find the words to express my gratitude to **Dr. Dina Salah Eldin Mahmoud**, Lecturer of Anesthesia, Intensive Care and Pain Management Care, Faculty of Medicine, Ain Shams University for his continuous directions and meticulous revision throughout the whole work, I really appreciate their patience and support.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.



Nesreen Samir Mohammed Alfeky

Contents

List of Abbreviations	i
List of Tables	iv
List of Figures	v
Introduction and Aim of the Assay	1
Chapter 1:	
Anatomy and physiology of liver.....	3
Chapter 2 :	
Pathophysiology of Cirrhosis and organs failure.....	14
Chapter 3	
Intensive care management of end organs failure in liver cirrhotic patients.....	46
Summary.	89
References.	91
Arabic Summary	--

List of Abbreviations

ACLF	:	Acute-on-chronic liver failure
ACTH	:	Adrenocorticotrophic Hormone
AIDS	:	Acquired immune deficiency syndrome
Ang II	:	Angiotensin II
AKI	:	Acute kidney injury
ALF	:	Acute liver failure
APACHE II	:	Acute Physiology and Chronic Health Evaluation II
ARDS	:	Adult respiratory distress syndrome
AST	:	Aspartate aminotransferase.
ATP	:	Adenosine triphosphate
BNP	:	B-type natriuretic peptide
cAMP	:	Cyclic adenosine monophosphate.
CBV	:	Central blood volume
CCM	:	Cirrhotic cardiomyopathy
CEE	:	Contrast-enhanced echocardiography
cGMP	:	Cyclic guanosine monophosphate
CI	:	Cardiac index
CO	:	Cardiac output
COPD	:	Chronic obstructive pulmonary disease
COX-1	:	Cyclooxygenase-1
CRH	:	Corticotropin-releasing hormone
CRRT	:	Continuous renal replacement therapy
CT	:	Computed tomography.
CTP	:	Child-Turcotte-Pugh
CVP	:	Central venous pressure
DDLT	:	Deceased donor liver transplantation
EBL	:	Endoscopic esophageal variceal band ligation
EBL	:	Endoscopic esophageal variceal band ligation
EDHF	:	Endothelium-derived hyperpolarizing factor
EET	:	Epoxyeicosatrienoic acid

List of Abbreviations (Cont.)

ESLD	:	Decompensated end-stage liver disease
ET-1	:	Endothelin-1
GABA	:	Gamma-Aminobutyric acid
GFR	:	Glomerular filtration rate
HBV	:	Hepatitis B virus
HCC	:	Hepatocellular carcinoma
HCC	:	Hepatocellular carcinoma .
HCV	:	Hepatitis C virus
HE	:	Hepatic encephalopathy
HIV	:	Human immune-deficiency virus
HLA DR	:	Human Leukocyte Antigen - antigen D Related
HPS	:	Hepatopulmonary syndrome
HR	:	Heart rate
HRS	:	Hepatorenal syndrome
HSC	:	Hepatic stellate cells
HSCs	:	Hepatic stellate cells
HVC	:	Hepatitis C virus
HVPG	:	Hepatic venous pressure gradient
HVPG	:	Hepatic venous pressure gradient
ICP	:	Intracranial pressure
ICU	:	Intensive care unit
IHD	:	Intermittent hemodialysis
IL	:	Interleukin
iNOS	:	Inducible NO synthase
INR	:	International normalized ratio
IVC	:	Inferior vena cava
LC	:	Liver cirrhosis
LDLT	:	Living-donor liver transplantation
LOLA	:	L-ornithine-L-aspartate
LSECs	:	Liver sinusoidal endothelial cells

List of Abbreviations (Cont.)

LT	: Liver transplantation
LVEF	: Left ventricular ejection fraction
MAP	: Mean arterial pressure
MARS	: Molecular Adsorbent Recirculating System
MELD	: Model for end-stage liver disease
MOF	: Multiple organ failure
NIV	: Noninvasive ventilation
Nnos	: Neuronal NO synthase
NO	: Nitric oxide
OLT	: Orthotopic liver transplantation
PBC	: Primary biliary cirrhosis
PEEP	: Positive end-expiratory pressure
PET	: Positron emission tomography
PGIs	: Prostacyclin
PGs	: Prostaglandins.
PIGF	: Placental growth factor
PoPH	: Portopulmonary hypertension
PSC	: Primary sclerosing cholangitis
PV	: Portal vein
RAAS	: The renin-angiotensin-aldosterone system
RCA	: Regional citrate anticoagulation
RRT	: Renal replacement therapy
SBP	: Spontaneous bacterial peritonitis .
SNS	: Sympathetic nervous system
SOD	: Superoxide dismutase
SVR	: Systemic vascular resistance
SVR	: Systemic vascular resistance
TIPS	: Transjugular intrahepatic portosystemic shunt
TNF	: Tumor necrosis factor
TXA2	: Thromboxane A2
VEGF	: Vascular endothelial growth factor.

List of tables

<i>Table</i>	<i>Title</i>	<i>Page</i>
1	New diagnostic criteria for the hepatorenal syndrome from the International Ascites Club (2013)	31
2	Diagnostic criteria for the hepatopulmonary syndrome and portopulmonary hypertension	36
3 a	The West Haven criteria for hepatic encephalopathy	42
3b	The West Haven criteria for hepatic encephalopathy	63
4	Differential diagnosis of hepatic encephalopathy	65
5	Common precipitants of hepatic encephalopathy	65
6	Child-Pugh scoring	77
7	Child-Pugh score interpretation	77
8	Modifying MELD scores	81
9	Prognostic models of cirrhosis	82
10	Contraindications to Liver Transplantation	87
11	Model for End-Stage Liver Disease Score	87

List of Figures

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
1	Position of the liver	4
2	Ligaments of the liver	5
3	Lobes of the liver	6
4	Biliary system	7
5	Blood supply of the liver	8
6	Portal hypertension leads to the development of the hyperdynamic circulatory syndrome, characterized by decreased mean arterial pressure (MAP), decreased systemic vascular resistance (SVR) and increased cardiac index (CI)	23
7	Activated hepatic stellate cells (HSCs) in liver cirrhosis increase intrahepatic vascular resistance	26
8	Pathophysiological mechanisms in the development of ascites and the hepatorenal syndrome	23
9	Pathophysiological proposal for the background of a cardiorenal syndrome in cirrhosis	33
10	Gas exchange in the normal lung (left) and mechanism of hepatopulmonary syndrome (right)	37

Introduction

Progressive Liver cirrhosis (LC) is a late stage of Fibrosis characterized by distortion of the architecture and Formation of regenerative nodules and different degrees of Liver function impairment; these patients are prone to a variety of complications reducing life expectancy markedly (*Figueiredo et al., 2012*).

Decompensated end-stage liver disease (ESLD), acute on top chronic liver failure, and acute liver failure (ALF) are critical situations, which lead to hepatic encephalopathy and multiple organ failure (MOF). These critical situations may require admission and end-organ support in an intensive care unit (ICU) (*Martini et al., 2012*).

Decompensated cirrhosis has a poor prognosis with a 6-year survival of only 21%.The liver's position at the apex of multiple synthetic, detoxifying, metabolic, immunological and hormonal processes predisposes to a number of complications. The most important of these are immunoparesis, renal failure and neurological dysfunction. Further liver injury often ensues in the context of an exaggerated systemic inflammatory response, due to alterations in visceral perfusion, impaired microvascular integrity and dysregulated hepatic cellular mediators (*Antoniades et al., 2006*).

The goals of treatment of cirrhotic patients are to prevent further deterioration in liver function, reverse precipitating factors, and support failing organs. Liver transplantation is required in selected patients to improve survival and quality of life (*Aspesi et al., 2002*).

Aim of the Essay

The aim of essay is to discuss Liver Cirrhosis (LC) from the point of view of the pathophysiological alterations present in LC patients, including cardiovascular, renal, coagulopathic, sepsis, pulmonary and encephalopathic which make their admission to an intensive care unit (ICU) more probable and how to deal with these problems.

Anatomy and Physiology of Liver

The liver is the body's second largest organ; only the skin is larger and heavier. The liver performs many essential functions related to digestion, metabolism, immunity, and the storage of nutrients within the body. These functions make the liver a vital organ without which the tissues of the body would quickly die from lack of energy and nutrients. The liver has an incredible capacity for regeneration of dead or damaged tissues; it is capable of growing as quickly as a cancerous tumor to restore its normal size and function (Size can double in as little as three to four weeks through a process that is very similar to the embryonic stage of liver development (*Martini et al., 2012*)).

Anatomy of the Liver

Gross Anatomy

The liver is a roughly triangular organ that extends across the entire abdominal cavity just inferior to the diaphragm. Most of the liver's mass is located on the right side of the body where it descends inferiorly toward the right [kidney](#). The liver is made of very soft, pinkish-brown tissues encapsulated by a connective tissue capsule. This capsule is further covered and reinforced by the peritoneum of the abdominal cavity, which protects the liver and holds it in place within the abdomen (*Martini et al., 2012*). Fig.(1)

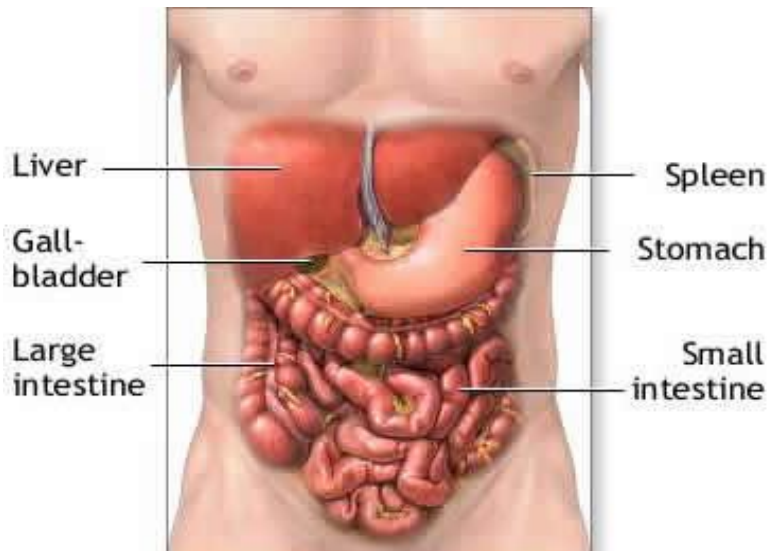


Fig.(1): Position of the liver (*Martini et al., 2012*).

The peritoneum connects the liver in 4 locations: the coronary ligament, the left and right triangular ligaments, and the falciform ligament. These connections are not true ligaments in the anatomical sense; rather, they are condensed regions of peritoneal membrane that support the liver.

- The wide *coronary ligament* connects the central superior portion of the liver to the diaphragm.
- Located on the lateral borders of the left and right lobes, respectively, the left and right triangular ligaments connect the superior ends of the liver to the diaphragm.
- The falciform ligament runs inferiorly from the diaphragm across the anterior edge of the liver to its inferior border. At the inferior end of the liver, the falciform ligament forms the round ligament (*ligamentum teres*) of the liver and connects the liver to the umbilicus. The round ligament is a remnant of the

umbilical vein that carries blood into the body during fetal development (*Timmons et al., 2012*).

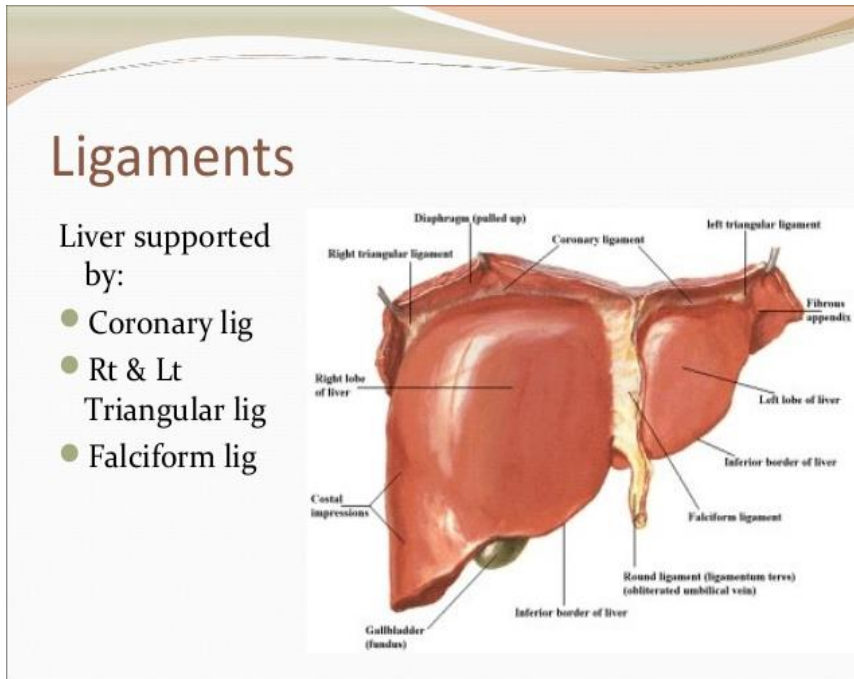


Fig.(2): Ligaments of the liver (*Timmons et al., 2012*).

The liver consists of 4 distinct lobes-the left, right, caudate, and quadrate lobes.

- The left and right lobes are the largest lobes and are separated by the falciform ligament. The **right lobe** is about 5 to 6 times larger than the tapered left lobe.
- The small **caudate lobe** extends from the posterior side of the right lobe and wraps around the inferior vena cava.
- The small **quadrate lobe** is inferior to the caudate lobe and extends from the posterior side of the right lobe and wraps around the gallbladder.

(*Tallitsch et al., 2012*).

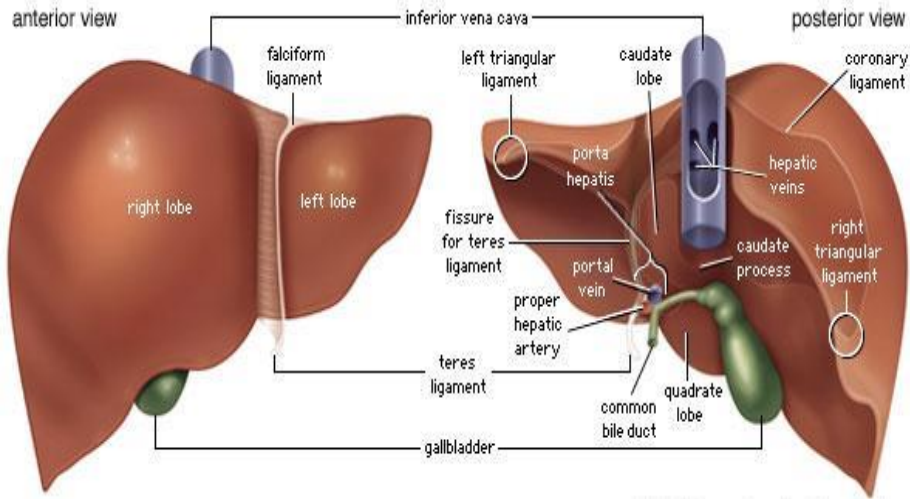


Fig.(3): Lobes of the liver (*Tallitsch et al., 2012*).

Bile Ducts

The tubes that carry bile through the liver and gallbladder are known as bile ducts and form a branched structure known as the biliary tree. Bile produced by liver cells drains into microscopic canals known as bile canaliculi. The countless bile canaliculi join together into many larger bile ducts found throughout the liver. These bile ducts next join to form the larger left and right **hepatic ducts**, which carry bile from the left and right lobes of the liver. Those two hepatic ducts join to form the common hepatic duct that drains all bile away from the liver. The common hepatic duct finally joins with the cystic duct from the gallbladder to form the **common bile duct**, carrying bile to the duodenum of the small intestine. Most of the bile produced by the liver is pushed back up the cystic duct by peristalsis to arrive in the gallbladder for storage, until it is needed for digestion (*Tallitsch et al., 2012*).