

Efficacy of loco-regional treatment for Hepatocellular Carcinoma Prior to Living Donor Liver Transplantation

Thesis

**Submitted for Partial Fulfillment of Master Degree in
Tropical Medicine**

BY

Hesham Abd El-Aty Fadl
M.BB.ch.

Under Supervision of

Prof. Mohammed Kamal Shaker

Professor of Tropical Medicine
Faculty of Medicine
Ain Shams University

Prof. Mohammed El Ghareeb Abd El Moaty

Assistant Professor of Radiodiagnosis
Faculty of Medicine
Ain Shams University

Dr. Iman Mohammad Fawzy Montasser

Lecturer of Tropical Medicine
Faculty of Medicine
Ain Shams University

2015

List of Contents

Title	Page No.
▪ Contents	II
▪ List of tables.....	IV
▪ List of figures.....	VII
▪ List of abbreviations.....	VIII
▪ Review of literature.....	1
▪ Chapter 1 : Hepatocellular Carcinoma	1
❖ Introduction.....	1
❖ Epidemiology	1
❖ Etiology.....	3
❖ Clinical picture	10
❖ Diagnosis of HCC	13
❖ Pathology of HCC	16
❖ Staging	19
❖ Screening and surveillance	24
❖ Prevention	29
❖ Management	30
▪ Chapter 2 : Liver Transplantation	41
❖ Introduction and historical perspective.....	41
❖ Indications.....	42

❖ Priority for HCC patients on waiting list...	47
❖ Contraindication	56
❖ Living donor liver transplantation (LDLT).....	57
❖ Immunosuppressant drugs.....	59
❖ Complications	61
❖ Retransplantation	71
■ Patients and method.....	72
■ Results.....	77
■ Discussion.....	105
■ Summary	114
■ Conclusion & Recommendations.....	118
■ References.....	119
■ Arabic summary.....	1

List of tables

Table No.	Title	Page No.
Tables of review		
1	Okuda classification of hepatocellular carcinoma	19
2	Child-Pugh Score	20
3	Barcelona Clinic Liver Cancer	21
4	The Cancer of the Liver Italian Program	22
5	TNM classification of hepatocellular carcinomas	23
6	Recommendations for HCC surveillance: categories of adult patients in whom surveillance is recommended.	25
7	Timing of liver transplantation in chronic liver disease	44
8	Down-Staging Protocol for Patients with HCC Initially Exceeding UNOS T2 Criteria for Liver Transplantation	53
9	Additional Guidelines in UCSF Down-Staging Protocol	54
10	Specific types of biliary complications	64
Tables of results		
1	Socio-demographic characteristics of the studied patients	78
2	Medical characteristics of the studied patients	79
3	Initial hepatopathy of the studied patients at time of transplantation	80

4	Description of laboratory data before transplantation	81
5	Description of results of abdominal US at time of first Diagnosis	82
6	Size, site, number of focal lesions and Milan criteria according to results of triphasic spiral abdominal C.T before intervention	83
7	Detailed description of results of triphasic spiral CT before intervention regarding the size and number of focal lesions among different patient group	84
8	Detailed description of results of Triphasic spiral abdominal CT before intervention regarding site of focal lesions among different patient group	85
9	Different modalities of locoregional therapy done for the studied patient	86
10	Patients distribution according to triphasic spiral abdominal CT findings Before and after (LRT)	87
11	Changes in Milan criteria after locoregional therapy	89
12	Comparison between alpha fetoprotein level before and after locoregional therapy	90
13	Descriptive analysis of results of last triphasic spiral abdominal CT after locoregional therapy	91
14	Discreptive analysis of size and site of focal lesions in different patients groups after LRT	92

15	Effect of LRT on HCC in different patients groups according to last spiral abdominal CT before transplantation	93
16	Descriptive analysis of histopathological results after transplantation	94
17	Comparison between focal lesions total size before and after locoregional therapy	95
18	Comparison between the results of last CT before transplantation and histopathological examination of explanted liver regarding total size and number of focal lesions	96
19	Comparison between last spiral abdominal CT result and histopathological examination of explanted liver as regards viable tumor tissue	97
20	Comparison between the results of last spiral CT and histopathological results regarding TNM classification	98
21	Characters of patient beyond Milan after intervention	99
22	Comparison between Milan and beyond Milan patients regarding waiting time, Child Pugh and MELD scores	100
23	Comparison between Milan and beyond Milan patients regarding intervention type	101
24	Comparison between Milan and beyond Milan patients regarding the effect LRT in last CT results	102
25	Comparison between Milan and beyond Milan patients regarding the histopathological examination results:	103

List of figures

Figure No.	Title	Page No.
Figures of review		
1	Diagnostic algorithm and recall policy. (EASL , 2012)	28
2	Barcelona-Clinic Liver Cancer (BCLC) staging classification and treatment schedule.	31
Figures of results		
1	Patient within Milan before and after LRT	88
2	Patient beyond Milan before and after LRT	88
3	Change in Milan criteria after LRT	89

List of abbreviations

Abbreviation	Full Name
AASLD	American Association for the Study of Liver Diseases
ACR	Acute cellular rejection
AFP	Alpha-fetoprotein
ALF	Acute liver failure
ASCOT	Ain Shams Center for Organ Transplantation
AST	Aspartate Transaminase
CMV	Cytomegalovirus
CNS	Central nervous system
CT	Computerized tomography
CTP	Child-turcotte-Pugh
DDLT	Deceased Donor Liver Transplantation
DM	Diabetes mellitus
EASL	European Association for the Study of the Liver
EBV	Epstein Barr virus infection
Eslc	Egyptian Society of Liver Cancer
ESLD	end-stage liver disease
ETV	Entecavir

FL	focal lesion
FLs	focal lesions
HA	Hepatic artery
HAS	Hepatic artery stenosis
HAT	Hepatic artery thrombosis
HBc Ab	Hepatitis B virus antibody
HBs Ag	Hepatitis B virus antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HCV Ab	Hepatitis C virus antibody
HDV	Hepatitis d virus
HFL	Hepatic focal lesion
HIV	Human immunodeficiency virus
HTN	Hypertension
HVD	Hepatic vena cava
HVPG	hepatic venous pressure gradient
ICGHN	International Consensus Group of Hepatocellular Neoplasia
INR	international normalized ratio
IVC	inferior vena cava

IVCO	inferior vena cava obstruction
LAM	lamivudine
LD	living donor
LDLT	living donor liver transplant
LRLT	Living Related Liver Transplantation
LRT	locoregional therapy
LT	liver transplantation
HIV	human immunodeficiency virus
HTN	Hypertension
HVD	Hepatic vena cava
HVPG	hepatic venous pressure gradient
ICGHN	International Consensus Group of Hepatocellular Neoplasia
INR	international normalized ratio
IVC	inferior vena cava
IVCO	inferior vena cava obstruction
MELD	The Model for End Stage Liver Disease
mRECIST	Modified Response Evaluation Criteria in Solid Tumors
MRI	Magnetic resonance imaging
n	Number
NAFLD	non-alcoholic fatty liver disease

NASH	non-alcoholic steatohepatitis
OCs	contraceptive
OLT	orthotopic liver transplantation
PBC	Primary Biliary Cirrhosis,
PSC	Primary Sclerosing Cholangitis
PCR	polymerase chain reaction
PELD	Pediatric End Stage Liver Disease
PTA	percutaneous transluminal angioplasty
PTLD	post transplantation lymphoproliferative disease
PV	portal vein
PVS	Portal vein stenosis
PVT	Portal vein thrombosis
RAI	Rejection Activity Index
RCT	randomized controlled trial
RFA	radiofrequency ablation
SBP	Spontaneous bacterial peritonitis
SD	standard deviation
TACE	transarterial chemoembolization
TARE	transarterial radioembolisation
TDF	tenofovir

TIPS	transjugular intra-hepatic porto-systemic shunt
TNM	classification of hepatocellular carcinomas
UCSF	University of California, San Francisco protocol
UNOS	United Network for Organ Sharing
US	ultra sound
WHO	World Health Organization
YMDD	Tyrosine-methionine-aspartate-aspartate MUTATION