Role of Golgi protein 73(GP73) as a marker for Hepatocellular carcinoma(HCC)

Thesis

Submitted for partial fulfillment of Medical Doctorate in Internal Medicine

By

Ahmed Abbas Ahmed Radwan
MSC of Internal Medicine
Ain Shams University

Under Supervision of

Professor/ Dr. Mohamed Marie Makhlouf
Prof. of Internal Medicine
Faculty of Medicine – Ain Shams University

Professor/ Dr. Mohamed Abd El Mabood
Prof. of Internal Medicine
Faculty of Medicine – Ain Shams University

Professor/ Dr. Ehab Hassan Nashaat
Prof. of Internal Medicine
Faculty of Medicine – Ain Shams University

Dr. Shereen Abou Bakr Saleh
Assistant Prof. of Internal Medicine
Faculty of Medicine Ain Shams University

Dr. Sarah Abdel Kader Ali El Nakeep
Lecturer of Internal Medicine
Faculty of Medicine Ain Shams University

Faculty of Medicine
Ain Shams University
2016

سورة البقرة الآية ٣٢

Table of Contents

List of Abbreviations

AASLD	American Association for the Study of Liver Diseases
Ab	Antibody
AFB1	Aflatoxin B1
AFP	alpha-fetoprotein
AFP L3	Lens culinaris agglutinin A reactive AFP
Ag	Antigen
AIH	Autoimmune hepatitis
AJCC	American Joint Committee on Cancer
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AMACR	Alpha-methylacyl-CoA racemase
ARID2	AT Rich Interactive Domain 2
AST	Aspartate aminotransferase
BCLC	Barcelona Clinic Liver Cancer
BCP	basal core promoter
CHB	Chronic hepatitis b
CLD	Chronic liver disease
CLIP	Cancer of the Liver Italian Program
CLU	Clusterin
DCP	Desgamma-carboxy prothrombin
EASL	European Association for the Study of the Liver
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
ER	endoplasmic reticulum
FES	Feline sarcoma oncogene
GGTII	Gamma-glutamyl transferase isoenzyme II
GP73	Golgi protein 73
HBV	hepatitis B virus

HCC	Hepatocellular carcinoma
HCV	hepatitis C virus
HDV	hepatitis D virus
HH	hereditary hemochromatosis
IARC	International Agency for Research on Cancer
LT	Liver transplantation
MC	Milan criteria
MELD	Model of end-stage liver disease
MRI	Magnetic resonance imaging
NAFLD	Non-alcoholic fatty liver disease
NASH	non-alcoholic steatohepatitis
PC	proprotein convertase
PDGFR	platelet-derived growth factor receptor
PEI	Percutaneous ethanol injection
PELD	Pediatric end-stage liver disease
PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
PST	Performance status test
PTHrP	parathyroid hormone–related protein
RFA	Radiofrequency ablation
ROC	Receiver operator characterizing curve
sGP73	serum Golgi protein 73
TACE	Transcatheter arterial chemoembolization
TAE	Transcatheter arterial embolization
TGF	Tumor Growth Factor
TM	transmembrane domain
TNF-α	Tumor necrosis factor alpha
VEGFR	vascular endothelial growth factor receptor
WHO	World Health Organization
WNT	Wingless-type MMTV integration site family member

List of tables

List of figures

Acknowledgment

First of all thanks to ALLAH who gave us the knowledge and activity to complete this work, without his help nothing could be reached.

I wish heartily to express my deep appreciation and profound gratitude to my Prof. Dr. Mohamed Marie Makhlouf, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for his kind close supervision and encouragement. He has his fingerprints in every single piece in this thesis; his valuable instructions and sincere advice have been the main factors to complete this work, I offer him many thanks and I owe him a lot.

Greatest thanks to Prof. Dr. Mohamed Abd El Mabood, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for his generous and advice guidance and helpful suggestions throughout this work.

I would like to express my deepest gratitude and cordial appreciation to Prof. Dr. Ehab Hassan Nashaat, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for his meticulous supervision, continuous assistance and endless help.

No words can adequately assure my deepest thanks to Dr. Shereen Abou Bakr Salah, Assistant Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for her kind patience, intensive unlimited support and endless assistance throughout this work, I am extremely indebted to her.

I am also delighted to express my gratitude and appreciation to Dr. Sarah Abdel Kader Ali El Nakeep, Lecturer of Internal Medicine, Faculty of Medicine, Ain Shams University, for her supervision and guidance during all stages of this work.

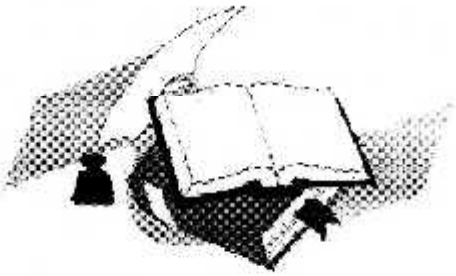
Also, I would like to express my deepest thanks to all my dear professors and my colleagues that without their help, this work could not have been completed.

In few grateful words I would like to express my deepest gratefulness and greatest thanks to my father for his unconditional support, both financially and emotionally throughout my degree. In particular, the patience and understanding shown by him. I would like to thank my mother, her support; encouragement, quiet patience and unwavering love were undeniably the bedrock upon which the past years of my life have been built. I can't deny that without the unyielding devotion and love of my sister and my brother I can't continue my life.

Last, but not least, thanks to all the patients who participated in this work. I hope that with this and other studies we can alleviate their sufferings.

Ahmed Abbas

Introduction



Introduction

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and represents the third leading cause of cancer-related mortality worldwide. HCC is particularly prevalent in Asia and Africa.***(Thun MJ et al., 2010).***

Unfortunately, patient survival with HCC has only been marginally improved over the last 20 years. Between 1981 and 1998, the 5-year survival rate only rose from 2% to 5%. The poor survival rate is mainly related to late diagnosis of HCC, when effective therapies are lacking. Surveillance of patients at highest risk for developing HCC (i.e., patients with cirrhosis) is an important strategy that can potentially decrease the HCC related mortality rate. Although HCC meets the criteria of a tumor that would benefit from a surveillance program, the poor sensitivity and specificity of currently available tools has prevented widespread implementation of HCC surveillance. ***(Sangiovanni A et al., 2004).***

The majority of HCC cases are detected at advanced stages of the disease, which precludes the use of curative

surgical therapy. The prognosis of HCC is generally poor and the mortality rate is similar to the incidence rate. Consequently, detection of early-stage HCC remains an effective approach to substantially improve the overall outcome of individuals with HCC. ***(Fattovich G et al., 2004).***

The diagnosis of HCC is usually determined via tumor biomarkers in serum and by instrumental tests, including hepatic ultrasonography, computed tomography, magnetic resonance imaging and biopsy. Although a number of studies have investigated positive cancer biomarkers for HCC, none have been identified as the optimal choice. At present, a-fetoprotein (AFP) detection has been widely adopted for the diagnosis of HCC despite its low sensitivity ***(Zoli M et al., 1996).***

The use of serological markers in patients at the highest risk for developing HCC can thus decrease the cancer-related mortality and reduce medical costs. Alpha-fetoprotein (AFP) has been the only standard serum marker for the detection of HCC for the last 40 years, even though its sensitivity of 39-65% is not very satisfactory.