Combination of alpha-1-acid glycoprotein and Alpha-fetoprotein as an improved diagnostic tool for hepatocellular carcinoma

Thesis

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Presented by

Moustafa Ahmed Hassan
M.B.B.CH
Faculty of medicine – Ain Shams University

Supervisors

Prof. Dr. Samir AbdElHamid Ghait
Professor of internal medicine
Faculty of Medicine, Ain Shams University

Dr. Ghada Amer Farghaly
Assistant Professor of internal medicine
Faculty of Medicine, Ain Shams University

Dr. George Safwat Riad
Lecturer of internal medicine
Faculty of Medicine, Ain Shams University

Faculty of medicine
Ain Shams University
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رسالة

توطئة للحصول علي درجة الماجيستير في الباطنة العامة

مقدمة من

الطبيب / مصطفى احمد حسن.

المشرفين

الأستاذ الدكتور / سمير عبد الحميد غيط

أستاذ الباطنة العامة

كلية الطب ، جامعة عين شمس

الدكتور / غادة عامر فرغلي

أستاذ مساعد الباطنة العامة

كلية الطب ، جامعة عين شمس

دكتور / جورج صفوت رياض

مدرس الباطنة العامة

كلية الطب ، جامعة عين شمس.

كلية الطب

جامعة عين شمس

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Summary

Hepatocellular carcinoma (HCC) is one of the commonest cancers worldwide. It is a major health problem and its incidence is increasing. The presence of cirrhosis of the liver is the major risk factor and worldwide this is largely due to chronic hepatitis C virus (HCV) and hepatitis B virus (HBV) infection. The diagnostic modalities, especially with respect to hepatic imaging, have improved in recent years. This, along with HCC surveillance in patients with cirrhosis, has led to the detection of HCC at an earlier stage, when curative therapy is likely to be more successful. The major diagnostic techniques for HCC include serum markers, various imaging modalities and histological analysis ***(Gomaa et al., 2009).*** According to recent reports, the incidence of HCC has increased sharply in the last 5–10 years, with an especially high incidence in Egypt (***Anwar et al., 2008).***

The main goal of our study was to evaluate the role of AAG in the diagnosis of HCC in combination with alpha-fetoprotein which is the most widely used tumor marker for diagnosis as well as surveillance of HCC.

The study was performed on 40 patients recruited from the Internal Medicine & Hepatology Department, Ain Shams University Hospitals. Patients were classified into 2 groups; **Group I** consisted of 20 HCC patients , their ages are

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Abbreviations

AAG	Alpha 1 acid Glycoprotein
AASLD	American Association for the study of the liver disease
AFB-FABY	AFB1-formamido pyrimidine adduct
AIDS	Acquired immune deficiency syndrome
AFB1	Aflatoxin B1
AFP	Alpha-fetoprotein
AFPIC	Alpha-fetoprotein immunocomplexes
AFP L3	Lens culinaris agglutinin reactive alpha fetoprotein
AFU	Alpha-L-fucosidase
AJCC	The American Joint Committee of Cancer
AKT	(PKB) protein kinase B
ALT	Alanine transaminase
AUC	Area under curve
AST	Aspartate transaminase
BCLC System	The Barcelona-Clinic- Liver-Cancer system
CP	Child- pugh
CTP	Child –pugh -Turcotte
CECT	Contrast enhanced helical computed tomography
CEUS	Contrast enhanced ultrasound
CLD	Chronic liver disease
CLIP	The Cancer of the Liver Italian Program
CT	Computed tomography
CUPI	Chinese University Prognostic Index
CYP	Cytochrome P
DCP	Des-gamma carboxyprothrombin
DGCP	Des-gamma -carboxyprothrombin
DNA	Deoxyribonucleic acid
EASL	European association for the study of the liver
EDTA	Ethylenediaminetetraacetic acid
EGFR	Epidermal growth factor receptor
ELISA	Enzyme-linked immunosorbent assay
EPI	Expanded program of immunization
ESR	Erytrocyte sedimentation rate
FDA	Food and Drug Administration

F-FDG	F-flurodeoxyglucose
FNAB	Fine needle aspiration biopsy
HA	Hepatic artery
HBIG	Hepatitis B immunoglobulin
HBV	Hepatitis B virus
HBsAG	Hepatitis B surface anrigen
HBeAG	Hepatitis B e anrigen
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HFL	Hepatic focal lesion
HH	Heriditary Haemochromatosis
HE	Hepatic encephalopathy
HIV	Human immune deficiency syndrome
HIFU	High intensity focused ultrasound
HMG CoA reductase	Hydroxy methyl glutaryl coenzyme A reductase
HMRS	Proton Magnetic Resonance Spectroscopy
ICG	Indocyanine Green
ICG R15(%)	Indocyanine Green retention rate at 15 minutes
IGF	Insulin like growth factor
IQR	Interquartile range
IFN	Interferon
IRS-1	Intracellular receptor substrate - 1
ITRAQ	sobaric tags for relative and absolute quantitation
INR	International normalized ratio
JIS Score	The Japan Integrated Staging score
KEAP1	Kelch-like ECH-associated protein **1**
LCSGJ	The Liver Cancer Study Group of Japan
LDH	Lactate dehydrogenase
LT	Liver Transplantation
MAF	Macrophage activating factor
MDCT	Multidetector helical CT
MELD	The Model for End Stage Liver Disease
mJIS	The modified Japan Integrated Staging
mTOR	Mammalian targeted of rapamycin
MPCT	Multiphasic helical CT
MRI	Magnetic resonance imaging

NASH	Nonalcoholic steatohepatitis
NAFLD	Non alcoholic fatty liver disease
NPV	Negative predictive value
NRV	Nuclear receptor factor
OLT	Orthotopic liver transplantation
OS	Overall survival
PAT	Parenteral anti-schistosomal treatment
PBC	Primary biliary cirrhosis
PC	Prothrompin concentration
PI3K	Phosphatidyl inositol-3-kinase
PIVKA-II	Protein induced by vitamin K absence or antagonist II
PAHO	Pan American Health Organization
PET	Positron emission tomography
PPV	Positive predictive value
PS	Performance status score
PSC	Primary sclerosing Cholangitis
Ras	Rat Sarcoma
RCT	Randomized Controlled Trial
ROC	The receiver operating characteristic curve
SD	Standard Deviation
SELDI-TOF	Surface-enhanced laser desorption/ionization-time of flight mass spectrometry
SLiDe	S : stage - Li : liver damage – De : des-γ-carboxy prothrombin
TNM Staging System	Tumor, Node and Metastases Staging System
TPO	Human thrompoietin
UNOS	United Network of Organ Sharing
US	Ultrasonography
VEGF	Vascular endothelial growth factor
VEGFR	Vascular endothelial growth factor receptor
VSV	Vesicular Stomatitis virus
WHO	World Health Organization

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Introduction

Globally, hepatocellular carcinoma (HCC) is one of the leading causes of cancer related deaths, and is the fifth most commonly diagnosed solid tumor. The majority of HCC patients occur in sub-Saharan Africa and parts of South East Asia; however, incidence rates appear to be on the rise in developed nations such as the United States, Japan and Western Europe. The lack of HCC biomarkers prevents early detection resulting in a poor prognosis of the disease ***(Stefaniuk et al., 2010).***

In Egypt the incidence of HCC has doubled in the last ten years, and it is now the second most incident and lethal cancer in men. The heavy burden of HCC parallels high rates of hepatitis C virus (HCV) while hepatitis B virus (HBV) rates have declined after the introduction of the vaccine in 1992 Nevertheless, the age standardized HBV incidence rate in males (20.6/100, 000) is seven times higher than what is found in the Middle East Cancer Consortium, and more than three times the incidence rates ***(Asmis et al., 2010).***

Prognosis and survival of patients with HCC is heavily affected by the disease stage at the time of diagnosis. The availability of reliable markers would greatly improve the chances of detecting early stage HCC. Imaging modalities, such as ultrasonography, are currently limited by their low positive