Alpha-fetoprotein Level as a Predictor of Hepatocellular Carcinoma Recurrence after Adult Living donor Liver Transplantation within Milan criteria

Thesis

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Abstract

The value of an elevated pretransplantation AFP level has a good predictive value of HCC recurrence after Iiver transplantation.

This study was conducted in Ain Shams Specialized Hospital to evaluate Alpha fetoprotein as a predictor of HCC recurrence after Liver transplantation. It included 75 patients underwent Liver transplantation for HCC, recurrence occurred in 6.7% of patients. pretransplantation Alpha fetoprotein was higher in patients with HCC recurrence after liver transplantation.

Keywords: Anti-thymocyte polyclonal antibodies - Azathioprine - Budd–Chiari syndrome - Body mass index

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Christine Raafat Lofty Sedrak

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List of Abbreviations

Abb.	Full term
AAH	Acute alcoholic hepatitis
AASLD	American Association for the Study of Liver Diseases
AFP	alpha-fetoprotein
AIH	Autoimmune hepatitis
ALG	Anti-lymphocyte polyclonal antibodies
ARID2	AT-Rich Interaction Domain containing protein 2
ATG	Anti-thymocyte polyclonal antibodies
AZA	Azathioprine
BCLC	Barcelona-Clínic Liver Cancer
BCS	Budd–Chiari syndrome
beta-hCG	Beta human chorionic gonadotrophin
BMI	Body mass index
CAD	Coronary artery disease
CMV	Cytomegalovirus
CNIs	Calcineurin inhibitors
CsA	Cyclosporine
CT	Computerized tomography
DCD	Donation after cardiac death
DCP	Des-gamma-carboxy prothrombin
DEB	Drug-Eluting Beads
DNA	Deoxyribonucleic acid
EASL	European association for the study of the liver
ECOG	Eastern Cooperative Oncology Group
ELTR	European Liver Transplant Registry
ERCP	Endoscopic retrograde cholangiopancreatogram
ESRD	End-stage renal disease

List of Abbreviations (Cont...)

Abb.	Full term
EST	Endodermal sinus tumor
EVR	Everolimus
FDA	Food and Drug Administration
GFR	Glomerular filtration rate
HAV	Hepatitis A virus
HBeAg	Hepatitis B virus e antigen
HBIG	Hepatitis B immunoglobulin
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HH	Hereditary haemochromatosis
HHV-8	Human herpes virus 8
HIV	Human immunodeficiency virus
HMG-CoA	3-hydroxy-3-methyl-glutaryl coenzyme A
HPS	Hepatopulmonary syndrome
HSV-1	Herpes simplex virus 1
HSV-2	Herpes simplex virus 2
HVPG	Hepatic venous pressure gradient ()
IBD	Inflammatory bowel disease
ICU	Intensive care unit
IFN	Interferon
IMPDH	Inosine monophosphate dehydrogenase
IQR	Interquartile range
IVC	In ferior vena cava
LDLT	Living donor liver transplantation
LT	Liver transplantation
MDRD6 formula	Modification of Diet in Renal Disease 6

List of Abbreviations (Cont...)

Abb.	Full term
MELD	Model for End-Stage Liver Disease
METAVIR	Meta-analysis of Histological Data in Viral Hepatitis
MMF	Mycophenolate mofetil
MPAP	Mean pulmonary artery pressure
MR	Magnetic resonance
MSAFP	Maternal serum AFP
NAFLD	Nonalcoholic fatty liver disease
NASH	Nonalcoholic steatohepatitis
NMR	Nuclear magnetic resonance
NUCs	Nucleos(t)ide analogues
OLT	Orthotopic liver transplantation
PBC	Primary biliary cholangitis
PDGFRs	Platelet-derived growth factor receptor
PegIFN	Peginterferon
PEI	Percutaneous ethanol injection
PET	Positron emission tomography
PH1	Primary hyperoxaluria type 1
PIKCA	Phosphatidylinositol 3-kinase catalytic subunit
PIVKA II	Prothrombin induced by Vitamin K Absence II
PPD	Purified protein derivative
PPHTN	Portopulmonary hypertension
PROM	premature rupture of membranes
PSC	Primary sclerosing cholangitis
PT	Prothrombin Time
PTLD	Post-transplant lymphoproliferative disorders
PVT	Portal vein thrombosis

List of Abbreviations (Cont...)

Abb.	Full term
QoL	Quality of life
RBV	Ribavirin
RCT	Randomized controlled trial
RFA	Radiofrequency ablation
RNA	Ribonucleic acid
SRL	Sirolimus
SVR	Sustained virological response
T bili	Total bilirubin
Tac	Tacrolimus
TACE	Transcatheter arterial chemoembolization
TE	Elastography
TGF-β	Transforming growth factor **beta**
TIPS	Transjugular intrahepatic portosystemic shunt
UCSF	University of California San Francisco criteria
UNOS	United Network for Organ Sharing
US	Ultrasonography
VDRL	Venereal disease research laboratory
VEGFRs	Vascular endothelial growth factor receptors
VZV	Varicella zoster virus

INTRODUCTION

Liver cancer is currently one of the leading causes of cancer death worldwide. Hepatocellular carcinoma (HCC) accounts for approximately 90% of all primary liver cancers and it is the fifth most common cancer worldwide **(*Torre et al., 2012).***

Cirrhosis is the main risk factor for developing HCC, with chronic hepatitis B virus and C virus (HCV) infection and, more recently, non- alcoholic fatty liver disease as the major causes of cirrhosis ***(Alexander et al., 2013).***

The American Association for the Study of Liver Diseases recommends that patients with cirrhosis undergo abdominal ultrasound every 6 months for surveillance of HCC ***(Bruix and Sherman, 2011).***

Currently, the observation of isolated alpha-fetoprotein (AFP) levels is considered unsuitable for HCC screening, surveillance, and diagnosis because of its low sensitivity and specificity ***(Biselli et al., 2015).***

Liver transplantation (LT) is the best available treatment modality for HCC. Patients who meet the Milan criteria and undergo transplantation have an estimated 5-year recurrence-free survival rate of approximately 83% ***(Mazzaferro et al., 1996).***

The primary objective of patient selection criteria is to detect advanced disease, which causes early recurrence and treatment failure. The best predictors for tumor staging can only be obtained after OLT by histologic examination of the explanted liver for vascular invasion, degree of differ- entiation, and the presence of satellite nodules ***(Parfitt et al., 2007).***

The value of an elevated pretransplantation AFP level as a predictor of poor prognosis has been increasingly recognized in recent studies ***(Hakeem et al., 2014)***.

Therefore, although the significance of AFP levels in nontransplanted patients remains debatable, support is mounting for the utility of this marker in transplant candidates with HCC and for its impact on transplant outcomes ***(Vibert et al., 2012).***

Aim of the Study

The aim of this study is to assess pretransplantation AFP level as a risk factor for post-transplant HCC recurrence.