The value of α-Fetoprotein (AFP)-L3 and Transforming Growth Factor B1 (TGFB1) as Prognostic markers of Hepatocellular Carcinoma after Radiofrequency Ablation

Thesis

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List of Abbreviations

3D-CRT	3-dimensional conformal technique
AASLD	American Association of Study of the Liver Disease
AFP	Alpha fetoprotein
AFPL3	Alpha fetoprotein L3
ALP	Alkaline phosphatase
ALT	Alanine transaminase
AST	Aspartate transaminase
BCLC	Barcelona Clinic Liver Cancer
BMI	Body mass index
CLD	Chronic liver disease
CLIP	Cancer of the Liver Italian Program
CT	Computed tomography
DAP-kinase1	Death associated protein kinase1
DAXX	Death associated protein 6
DCP	Des-gamma-carboxy prothrombin
DMD	Duchenne muscular dystrophy
EASL	European Association of Study of Liver

ECM	Extracellular matrix
EGFR	Epidermal growth factor receptors
GDP	Guanosine 5 – Diphosphate
GP 73	Golgi protein-73
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HIV	Human immunodefiency virus
ILK	Integrin-linked kinase
INR	International randomized ratio
ITAS	Micro total analysis system
JIS	Japan Integrate Staging
LAP	Latency associated peptide
LCA	Lens calinaris agglutinin
MELD	Model for End-Stage Liver Disease
PEI	Percutaneous ethanol injection
PMCT	Percutaneous microwave coagulation therapy
POAG	Primary open angle glaucoma
PODs	PML oncogenic domains

RUQ	Right upper quadrant
SD	Standard deviation
Smads	Mothers against decapentaplegic homolog
SPSS	Statistical Program for Social Science
SVR	Sustained virological response
T Bilirubin	Total bilirubin
T.AFP	Total alpha fetoprotein
TACE	Transarterial chemoembolization
TbR	TGFB1 receptor
TNF-α	Tumor necrosis factor-alpha
U/S	Ultrasound

INTRODUCTION

Liver cancer in men is the fifth most frequently diagnosed cancer worldwide, and is the second leading cause of cancer-related death in the world. In women, it is the seventh most commonly diagnosed cancer and the sixth leading cause of cancer death **(Jemal et al., 2011).**

Early detection of hepatocellular carcinoma (HCC) is important as the treatment of HCC with surgical resection, liver transplantation or percutaneous ablation can be curative at early stage **(Izumi, 2010)**.

The recommended screening strategy for hepatocellular carcinoma includes measurement of serum α-fetoprotein (AFP) levels and an abdominal ultrasound every 3-6 mo for the detection of HCC at an earlier stage **(Bruix and Sherman, 2011)**. However, serum AFP level has a high false negative rate for the detection of small or early stage tumors **(Saffroy et al., 2007)** and it is often markedly elevated in patients with either cirrhosis or those with exacerbated chronic hepatitis without HCC **(Bae et al., 2005)**.

AFP-L3 is an isoform of alphafetoprotein (AFP), has been reported to be highly specific for HCC **(Durazo et al., 2008)** and the surveillance program with this marker have

been mostly organized by Japanese study groups **(Izumi., 2010)**.

TGF-β1 is a family of disulfide-linked polypeptides with a molecular weight of 25kD. There are three isoforms of TGF-β expressed in mammals; TGF-β-1, TGF-β-2 and TGF-β-3. Understanding the mechanism of TGF-β has been the focus of recent studies in separating the pathogenesis of many human cancers **(Elliott and Blobe, 2005)**.

TGF-β-1 is the predominant and universally expressed isoform found in human liver. It has been implicated to play a role as a potent inhibitor of both normal and neoplastic rat hepatocyte proliferation as well as in the development of liver fibrosis. TGF-β-1 has also been found to be elevated in serum, urine and tissues of patients with HCC **(Sacco et al., 2000)**.

Radiofrequency ablation (RFA) is a localized thermal treatment technique designed to induce tumor destruction by heating the tumor tissue to temperatures that exceed 60°C **(McGahan et al., 1992).** Radiofrequency ablation (RFA) has been used as the most popular method for treating early stage HCC and during the past two decades, many clinical studies have confirmed the safety and therapeutic efficacy of radiofrequency **(Yan et al., 2008).**

AIM OF THE WORK

To asses the value of α-fetoprotein (AFP)-L3 combined with transforming growth factor B1 (TGFB1) as prognostic markers in the hepatocellular carcinoma after radiofrequency.

HEPATOCELLULAR CARCINOMA (HCC)

Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignant tumor and is derived from hepatocytes. The most common causes are chronic viral infection (hepatitis B and C), aflatoxin B1 ingestion, and chronic alcoholic abuse **(Ayman Abdo et al., 2011)**.

It is a fatal disease, with a life expectancy of about 6 months from the time of diagnosis and exhibits striking differences related to age, gender, ethnic group, and geographic region, and is rising even in countries with relatively low incidence **(Olivier Seror et al., 2014)**.

It has poor prognosis and ranks third as the cause of cancer deaths in East Asia and sub-Saharan Africa and second as the cause of male cancer deaths in China. **(YasunoriMinami and Masatoshi Kudo, 2011)**.

The majority of HCC patients present with an advanced stage for which chemotherapy and radiotherapy have limited efficacy **(Ryota Masuzaki and Masao Omata, 2008)**.