Role of FDG PET/CT in Hepatocellular carcinoma in Cirrhotic patients

Thesis

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By

Ekram Ali Ahmed

(M.NM)Under Supervision Of

Prof. Dr. Hosna Mohamed Mohamed Moustafa

Professor of Nuclear Medicine

Faculty of medicine-Cairo University

Prof. Dr. Eman Abd-Elhady Hassan

Professor of Clinical Oncology

Faculty of medicine-Cairo University

Dr. Mahasen Amin Abo-Gabal

Assistant professor of Nuclear Medicine

Faculty of medicine

Cairo University

Dr. Mohamed Mohamed Houseni

Lecturer of Radiology Department

National Liver Institute

Minoufiya University

Faculty of medicine

Cairo University

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اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ (١) خَلَقَ الْإِنسَانَ مِنْ عَلَقٍ (٢) اقْرَأْ وَرَبُّكَ الْأَكْرَمُ (٣) الَّذِي عَلَّمَ بِالْقَلَمِ (٤) عَلَّمَ الْإِنسَانَ مَا لَمْ يَعْلَمْ(٥)

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List of abbreviations

3D-CRT	*Three dimention cathode ray tube*
AFB	*Aflatoxin B*
AFP	*α-Fetoprotein*
APS	*Aarterioportal shunts*
AJCC	*American Joint Committee on Cancer*
BCLC	*The Barcelona Clinic Liver Cancer*
ce-CT	*Contrast enhanced Computed Tomography*
EBRT	*External Beam Radio Therapy*
FDG	*Fluro-2-Deoxy-Glucose*
FNH	*Fine nodular hyperplasia*
GIT	*Gastro Intestinal Tract*
Gy	*Gray is a derived unit of ionizing radiation*
GSO	*Gadolinium Orthosilicate*
HBV/HDV	*Hepatitis B/D virus*
HCC	*Hepatocellular Carcinoma*
HCV	*Hepatitis C virus*
LEL	*Lympho-Epithelial-Like Carcinoma (LEL)*
mCi	*Microcuries*
MDCT	*Multidetector CT*
MELD	*Model for End-Stage Liver Disease*
MRI	*Magnetic Resonance Imaging*
P53	*A Tumor Suppressor Gene*
PCT	*Porphyria cutanea tarda (PCT)*

PEI	*Percutaneous ethanol injection*
PET	*Positron Emission Tomography*
PVT	*portal vein thrombosis*
RFA	*Radiofrequency ablation (RFA)*
ROS	*Reactive oxygen species*
SPECT	*Single Photon Emission Computed Tomography*
SUV	*Standardized uptake value*
^{99m}Tc	*Technetium 99m*
TCA	*Tricarboxylic acid*
TACE	*Trans arterial chemoembolization*
US	*Ultrasound*
VIP	*Vasoactive Intestinal Peptide*
Y90	*Yttrium-90*

Introduction

Hepatocellular carcinoma (HCC) is the commonest primary liver cancer (80–90%) and represents 4% of all cancer deaths and the 5th cause of death from cancer ***(Jemal et al 2011).*** Chronic infection with hepatitis C virus (HCV) is one of the factors for HCC occurrence ***(Ibrahim et al., 2010).***

Due to late diagnosis and advanced underlying liver cirrhosis, only limited treatment options with marginal clinical benefits have been available in up to 70% of patients ***(Wörns and Galle, 2010).***

The current ability to increase survival of patients with HCC relies upon the surveillance of cirrhotic patients. Surveillance allows HCC precursors (dysplastic nodules) and malignant tumors to be recognized at an early stage making cure possible.

Radiology plays a major role in HCC diagnosis because HCC is characterized by neo-arterial vascularization with a typical imaging pattern. Current international guidelines have restricted the use of the liver biopsy to the characterization of hepatocellular nodules which remain diagnostically equivocal after imaging. Thus pathologists are facing very challenging and often well differentiated lesions, leading to difficulties in distinguishing high grade dysplasia and well differentiated HCC ***(Roncalli et al., 2011).***

Accurate diagnosis and staging are essential for the optimal management of cancer patients. 18 F-FDG PET/CT has an important role in the detection of

various cancers. The combined acquisition of PET and CT has synergistic advantages over PET or CT alone and minimizes their individual limitations. PET/CT is a valuable tool for staging and restaging of tumors and has an important role in the detection of recurrence in asymptomatic patients with rising tumor marker levels and patients with negative or equivocal findings on conventional imaging techniques ***(Almuhaideb et al., 2011).***

About 45%-50% of cases with hepatocellular carcinoma demonstrate FDG uptake higher than the liver parenchyma, whereas 50%-55% of cases show FDG uptake similar to that of liver parenchyma **.**This is because well and moderately differentiated HCC has a rate of gluconeogenesis comparable with normal liver tissue, resulting in similar uptake of 18F-FDG ***(Verhoef et al., 2002).***

Major advantage of 18F-FDG PET/CT is the capability to perform full-body examinations and the potential to detect intrahepatic involvement and extra hepatic metastases in one single examination and the possibility of distinguishing new active disease from scar or necrotic tissue ***(Langenhoff et al., 2002)***. HCC may be amenable to potentially curative resection, early detection of intra hepatic recurrence and/or extra hepatic metastases are extremely important and can facilitate successful retreatment at an early stage. Late diagnosis makes retreatment difficult ***(Sun et al., 2009).***

18F-FDG PET /CT has superior accuracy in identification of lymph node tumor metastases with the advantage of whole body scanning and high sensitivity for tumor detection **(*Xin et al., 2006).***

Aim of the study

The aim of this work is to evaluate the role of the whole body FDG PET/CT scan with ^{18}F-fluorodeoxyglucose (FDG) in patients with hepatocellular carcinoma.

This aim will be fulfilled through the following objectives:

- Assessing the role of FDG-PET/CT imaging in the initial diagnosis of hepatocellular carcinoma, specially evaluating the aggressiveness and extent of the lesion.
- Assessment of extra-hepatic metastatic spread.

Anatomy of the liver

The knowledge of normal morphology is basic to the understanding of pathologic processes ***(Wanless , 2006) .***

The liver is the largest visceral organ, It occupies most of the right hypochondrium and epigastrium, and frequently extends into the left hypochondrium ***(Gray and Standring et al, 2000) .*** In the male it weighs from 1.4 to 1.6 kilogram, accounts for 2% of the body weight of the adult and about 5% of the body weight of a newborn ***(Angelica and Fong, 2004)***

Segments of the liver:

The sectors of the liver are made up of between one and three segments: right lateral sector = segments VI and VII; right medial sector = segments V and VIII; left medial sector = segments III and IV (and part of I); left lateral sector = segment II. Segments are numbered in an ante-clockwise spiral centered on the portal vein with the liver viewed from beneath, starting with segment I up to segment VI, and then back clockwise for the most cranial two segments VII and VIII (Fig. 1).

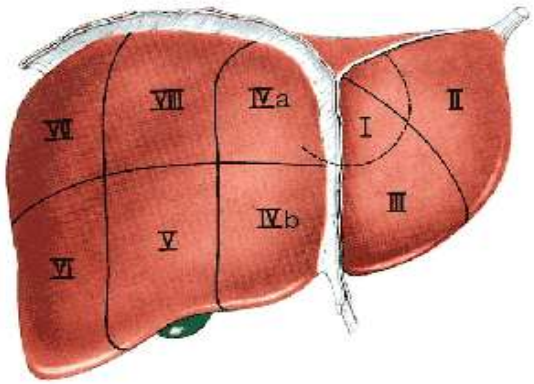

Figure 1: Segmental anatomy of the liver

Segment I: It corresponds to the anatomical caudate lobe and lies posterior (dorsal) to segment IV with its left half directly posterior to segments II and II and its medial half surrounded by major vascular branches.

Segment II: It is the only segment in the left lateral sector of the liver and lies postero-lateral to the left fissure. It often has only one Glissonian sheath and drains into the left hepatic vein. Rarely, a separate vein drains directly into the inferior vena cava.

Segment III: It lies between the umbilical fissure and the left fissure and is often supplied by one to three Glissonian sheaths: it drains into the left hepatic vein. The vein of the falciform ligament can provide an alternative drainage route for segment III.

Segment IV: It lies between the umbilical fissure and the main fissure, anterior to the dorsal fissure and segment I. Segment IV is supplied by three to five Glissonian sheaths, of which the majority arises in the umbilical fissure; their origins are often close to those that supply to segments II and III. Occasionally segment IV is supplied by branches from the main left pedicle. The main venous drainage segment is into the middle hepatic vein; the segment can also drain into the left hepatic vein through the vein of the falciform ligament.

Segment V: It is the inferior segment of the right medial sector and lies between the middle and the right hepatic veins. Its size is variable, as are the number of Glissonian sheaths that supply it. Venous drainage is into the right and middle hepatic veins.

Segment VI: It forms the inferior part of the right lateral sector posterior to the right portal fissure. It is often supplied by two to three branches from the right posterior Glisson's sheath, but occasionally the Glisson's sheath to segment VI can arise directly from the right pedicle. Venous drainage is normally into the right hepatic vein, but may be via the right inferior hepatic vein directly into the inferior vena cava.

Segment VII: It forms the superior part of the posterior sector and lies behind the right hepatic vein. The sheaths to segment VII are often single. The venous drainage is into the right hepatic vein; occasionally the segment can drain through the right middle hepatic vein directly into the inferior vena cava.

Segment VIII: It is the superior part of the right anterior sector. The right anterior sectoral sheaths end in segment VIII and supply it after giving off branches to segment V. The venous drainage is to the right and middle hepatic veins.

Segment IX: It is a recent subdivision of segment I, and describes that part of the segment that lies posterior to segment VIII.

Pathology of Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the fifth most frequent tumor worldwide, and the incidence of HCC in western countries has risen considerably in recent years ***(Jemal et al., 2011).***This increase can be attributed on one hand to the growing number of patients with hepatitis B and C, and on the other to the constantly high number of cases of alcohol-related liver disease***(Ferlay et al., 2010).***

Risk factors

The risk factors which are most important vary widely from country to country. In countries where Hepatitis B is endemic, such as China, Hepatitis B will be the predominant cause of Hepatocellular Carcinoma ***(Donadon et al.,2009).***Whereas in countries, such as the United States, where Hepatitis B is rare because of high vaccination rates, the major cause of HCC is Cirrhosis (due to alcohol abuse).

The main risk factors for hepatocellular carcinoma are: Cirrhosis of the liver, Hepatitis-B, Hepatitis-C, Alcoholism, Aflatoxin, Hemochromatosis,Wilson's disease and Type 2 diabetes.

Cirrhosis

Cirrhosis is the most important risk factor for the development of HCC, regardless of the cause ***(Zakim and Boyer, 2012).***Cirrhosis, irrespective of its etiology, is a risk factor for the development of hepatocellular carcinoma. The risk is 3–4 times higher in patients with cirrhosis compared to those with chronic hepatitis in a given population. An increase in hepatocellular proliferation may