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Diagnostic Role of PET CT in Hepatocellular Carcinoma Compaired with Triphasic CT Imaging

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Abstract

Background: Hepatocellular carcinoma (HCC) is one of the leading causes of death from cancer world wide. Proper detection of malignant liver diseases of great value for patient management. Non invasive diagnosis of HCC depends on ultrasound (US), triphasic CT, magnetic resonance imaging (MRI), positron emission tomography (PET/CT). This study will assess the value of PET/CT in diagnosis of HCC in comparison with triphasic CT.

Aim of Study: To assess the added value of PET/CT compaired with triphasic CT for improving tumor detection and ultimately modifying treatment strategies in patients with HCC.

Patients and Methods: The study was carried out on forty patients for primary diagnosis and staging of HCC patients referred to the Nuclear Medicine Unit in the Radiodiagnosis Department of Ain Shams University Hospital for PET/CT assessment in the period from January 2020 till March 2021.

Results: This findings showed that PET/CT is more sensitive than Triphasic CT in HCC diagnosis with sensitivity, specificity, PPV, and NPV of 100%, 33.3%, 89.5% and 100% respectively.

Conclusion: We concluded that PET/CT is as sensitive as the triphasic CT for diagnosis of HCC.

Key Words: *Hepatocellular carcinoma – Positron emission tomography – Magnetic resonance imaging.*

Introduction

HCC is the fifth most common cancer and the third cause of mortality in the world according to WHO, Risk factors for the development of HCC include chronic hepatitis (B and C), alcohol consumption, hepatic steatosis, genetic factors and other causes of liver inflammation or injury **[1]**.

Prognosis of patients with HCC is usually poor, and predicting life expectancy is difficult because of variable factors such as portal vein thrombosis, tumor stage and high recurrence rate of the tumor. Therefore, accurate detection and staging of HCC is crucial to patient management **[2]**.

Many international society guidelines allow the non invasive imaging diagnosis of HCC in at risk patients without the requirement of histologic confirmation **[1]**.

US, triphasic CT, MRI as well as Molecular imaging techniques can be applied in diagnosis of HCC **[3]**.

Residual, recurrent, and metastatic lesions of HCC are not detected well by traditional radiography such as MRI or CT because these modalities detect morphologic changes, which can occur quite slowly in HCC. A more effective modality seems to be PET/CT using the exogenous contrast agent ^{18}F-fludeoxyglucose (^{18}F-FDG) can scan the whole body **[4]**.

PET is an imaging modality using positron-emitting markers. The most commonly used marker in evaluating cancer patients is ^{18}F-FDG, an analogue of glucose, used in processes of glucose metabolism. Glucose metabolism increases rapidly in dividing and growing cells causing an increased uptake of ^{18}F-FDG. In some cancers, ^{18}F-FDG-PET, especially when merged with CT, is highly sensitive in the staging of the malignancies, and can be used in management of individual patients. This modality has been established as a diagnostic tool of various cancers **[2]**.

^{18}F-FDG PET emerged as a highly effective nuclear imaging tool for diagnostic setup, treatment allocation, and assessment of post-interventional tumor response in medical and surgical oncology **[5]**.

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Aim of the study:

The aim of our study is to assess the added value of PET/CT compaired with triphasic CT for improving tumor detection and ultimately modifying treatment strategies in patients with HCC.

Patients and Methods

Patients:

A retrospective study was done after approval of Ethical comitte of our institution, it was carried out on 40 patients 26 males (65%) and 14 females (35%), their ages ranged between 54 and 75 years old with mean 63.10 for primary diagnosis and staging of HCC in patients referred to the Nuclear Medicine Department in the Radiodiagnosis Department of Ain Shams University Hospital for PET/CT assessment in the period from January 2020 till March 2021.

Methods:

Patients were subjected to the following: Obtaining informed consent, explaining the procedure details, risks and complications. Full history taking and clinical examination. Obtaining their previous examinations. Triphasic CT scan. PET/CT examination.

Study population:

Inclusion criteria: Patients with non treated HCC in triphasic CT. Patients have history of HCC and suspected for new HCC. Patients with high Alpha fetoprotein.

Exclusion criteria: Patients with renal impairment. Patients known to have an allergy to contrast medium. Patients with uncontrolled DM. Patients with a bad general condition needing life support.

Imaging protocol:

Patient preparation:

All patients were asked to fast for six hours prior to the scan. All metallic items were removed from the patients and they were given a gown to wear. Patients were asked to empty their bladders before the procedure. An IV cannula was inserted in the patient's arm for administration of ^{18}F-FDG. The patients were instructed to avoid any kind of strenuous activity before the examination and following injection of the radioisotope to avoid physiologic muscle uptake of FDG.

Serum glucose was routinely measured prior to ^{18}F-FDG injection, and fasting levels were 70-140mg/dl. In breastfeeding women, it was recommended that breastfeeding was discontinued for approximately 24 hours after the ^{18}F-FDG injection because of ^{18}F-FDG accumulation in breast milk. The strategies for decreasing brown fat were providing a controlled-temperature (warm) environment for patients before ^{18}F-FDG injection and high-fat, low-carbohydrate, protein-permitted diet before the examination.

Dosage administration of FDG:

A dose of 0.1mCi/kg of ^{18}F-FDG IV injected 45-90 minutes before the examination was administered. This period is referred to as the uptake phase and it is the necessary amount of time for the FDG to be adequately bio-distributed and transported into the patient's cells. Patients were asked to rest in a quiet room, devoid of distractions, and they were also asked to keep their movements, including talking, at an absolute minimum. This minimizes physiologic uptake of FDG into skeletal muscle, which can confound interpretation of the scan. Patients should be comfortable and relaxed.

Patient position:

The patients were positioned supine in a comfortable position with fixed head and arms up.

Scanning technique machine:

GE Discovery IQ PET/CT scanners.

i- CT Technique:

Helical CT was performed following injection of about 125mL of a non-iodinated contrast medium at a rate of 4mL/sec using a power injector. For a typical whole-body PET/CT study (neck, chest, abdomen, and pelvis), scanning began at the level of the skull base and extended caudally to the level of the upper thighs. The total length of CT coverage was an integral number of bed positions scanned during the acquisition of PET data. The study was performed with the patient breathing quietly. Scanning parameters are collimation width of 5.0mm, pitch of 1.5, and gantry rotation time of 0.8 second and field of view of 50cm. The helical data are retrospectively reconstructed at one mm intervals.

ii- PET Technique:

PET was performed following the CT study without moving the patient. Approximately 9 to 11 bed positions are planned in the three-dimensional acquisition mode for scanning the entire patient with 3-5 minute acquisition at each bed position.

iii- PET/CT Fusion:

Hundreds of trans-axial PET and CT images were first reconstructed. These were then reformatted into coronal and sagittal images to facilitate image interpretation. For each of these sets of PET

and CT images, corresponding fusion images, combining the two types of data, also were generated. The whole acquisition time for an integrated PET/CT scan was approximately 25-30mins. PET image data sets were reconstructed using CT data for attenuation correction and co-registered images were displayed using special software.

PET/CT Interpretation:

All PET/CT examinations were analyzed by a consensus of two experienced observers of nuclear medicine radiologists. The PET images and the volume of CT scans were evaluated for the presence and extent of the ^{18}F-FDG-positive hepatic lesion and the presence of extra-hepatic lesions.

Abnormal ^{18}F-FDG uptake was defined as radiotracer accumulation outside the normal anatomic structures and of greater intensity than background activity, excluding normal areas of physiological uptake. In all cases estimation of ^{18}F-FDG uptake was done using SUVmax values for each hepatic mass and metastasis away from the liver.

Triphasic CT technique:

Multi-detector spiral CT used with scanning parameters 120kVp, 180mAs, 7-mm section collimation, and 7mm/sec table speed during a single breath-hold helical acquisition of 25-30sec, depending on liver size. Images were obtained in a craniocaudal direction and reconstructed every 7mm to provide contiguous or overlapping sections.

Patient Position: The patient is positioned supine, with arms up.

Phases of triphasic CT were, Arterial phase (after 25-30s delay) to obtain excellent hepatic arterial opacification with minimal contrast in the portal vein, Portal venous phase (65-70s delay) to show portal vein opacification. And delayed Phase (150-200s delay) starting from the top of the liver to the bottom of the kidneys.

125-150ml of non-ionic iodinated contrast media according to the patient's weight was injected. The volume of contrast medium delivered was 2mL per kilogram of body weight.

Each patient received a contrast medium (Ultravist 300) at a rate of 5mL/s through an IV catheter by using a dual syringe power injector. A saline chaser was used by injection 40cc after contrast after the injection of intravenous contrast material, the liver scanned at the arterial, portal, and delayed phases.

Triphasic CT Interpretation:

All triphasic CT examinations were analyzed by a consensus of two experienced observers of radiologists. The triphasic images were evaluated for the presence and extent of hepatic lesions and the presence of extra-hepatic lesions.

Statistical analysis: Appropriate descriptive and inferential statistical tests were used.

Statistical package: Statistical analyses and graphing were performed using Microsoft Excel version 2016 and SPSS for windows version 20.0.

Results

This study was carried out on 40 patients 26 males (65%) and 14 females (35%) and their ages ranged between 54 and 75 years old with mean 63.1 (Table 1).

When active HCC was identified on PET/CT, it was positive in 95% of cases. The location of tumors was variable in all liver segments, the largest ratio was in segment VIII (40%). Tumor size measured ranged between 1 and 9cm with median 3cm. SUV max ranged between 1.9 and 14 with median 5.4 (Table 2). And when HCC was identified on triphasic CT, it was positive in 85% of patients. Tumor size ranged from 2 to 11 cm with median 5.5cm (Table 3).

Comparison between PET/CT scan and triphasic CT results found that the number of positive patients was 38 (95%) and 34 (85%) and the number of negative patients was 2 (5%) and 6 (15%) regarding PET/CT and triphasic CT respectively (p-value 0.136). Size of tumors ranged between 1 and 9cm with median 3cm and ranged between 2 to 1 1cm with median 5.5 cm regarding PET/CT and triphasic CT respectively (p-value <0.001) (Table 4). Comparison between triphasic CT and PET/CT show sensitivity of PET/CT was 100%, specificity 33.3%, PPV 89.5%, NPV 100% and accuracy 90% respectively (Table 5). SUV max in positive tumors ranged between 2 and 14 with median 5.5 and in negative tumors ranged between 1.9 and 2.4 with median 2.1 (p-value 0.001) (Table 6).

Follow-up of patients by AFP and CT for 3-6 months proved that there were 2 negative patients, biopsies were taken from 20 patients later on and proved to have HCC, and the other 18 patients followed-up by AFP that achieved very high results (doupled in 6 months), where biopsies not needed to prove HCC. So results of our study regarding PET/CT matched with final diagnosis of patients.

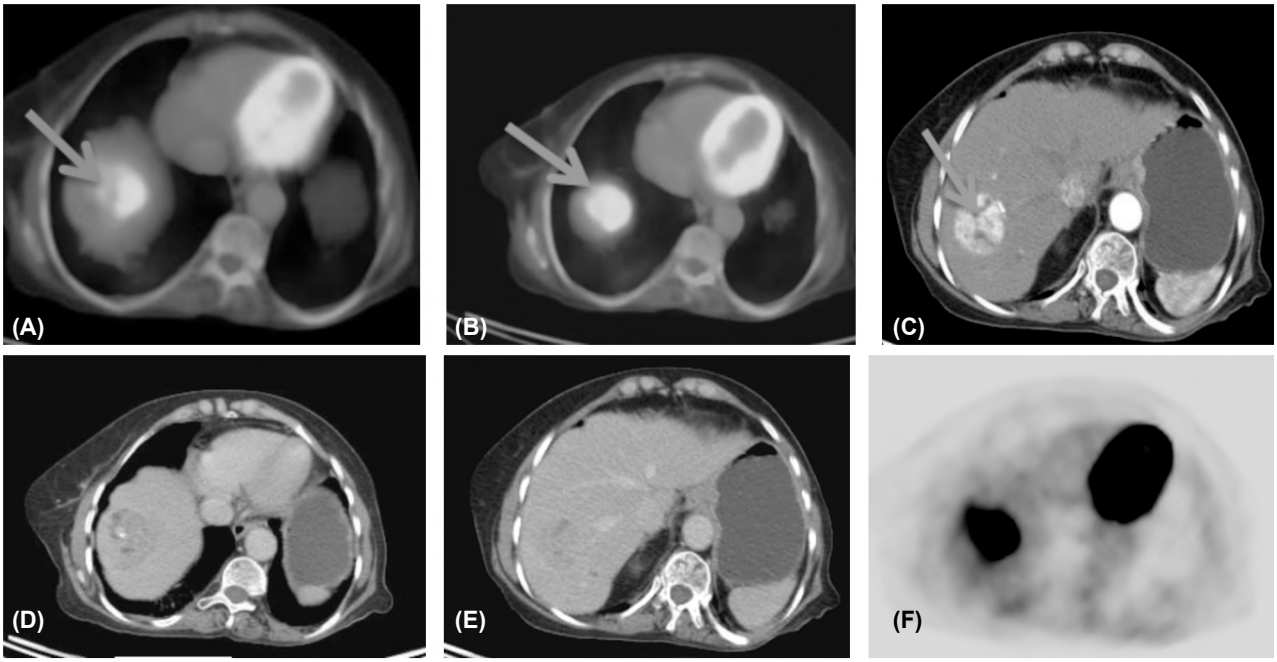

Fig. (1): PET/CT and triphasic CT images of 67 years old female patient show (A,B,F) PET/CT images showing a metabolically active lesion (red arrow) measuring about 5x5.5 cm, achieving SUVmax of 14.08 and SUVratio of 1.62, (C) triphasic CT showing lesion with early arterial heterogenous enhancement (blue arrow), (D,E) The lesion shows rapid washout in portovenous and delayed images.

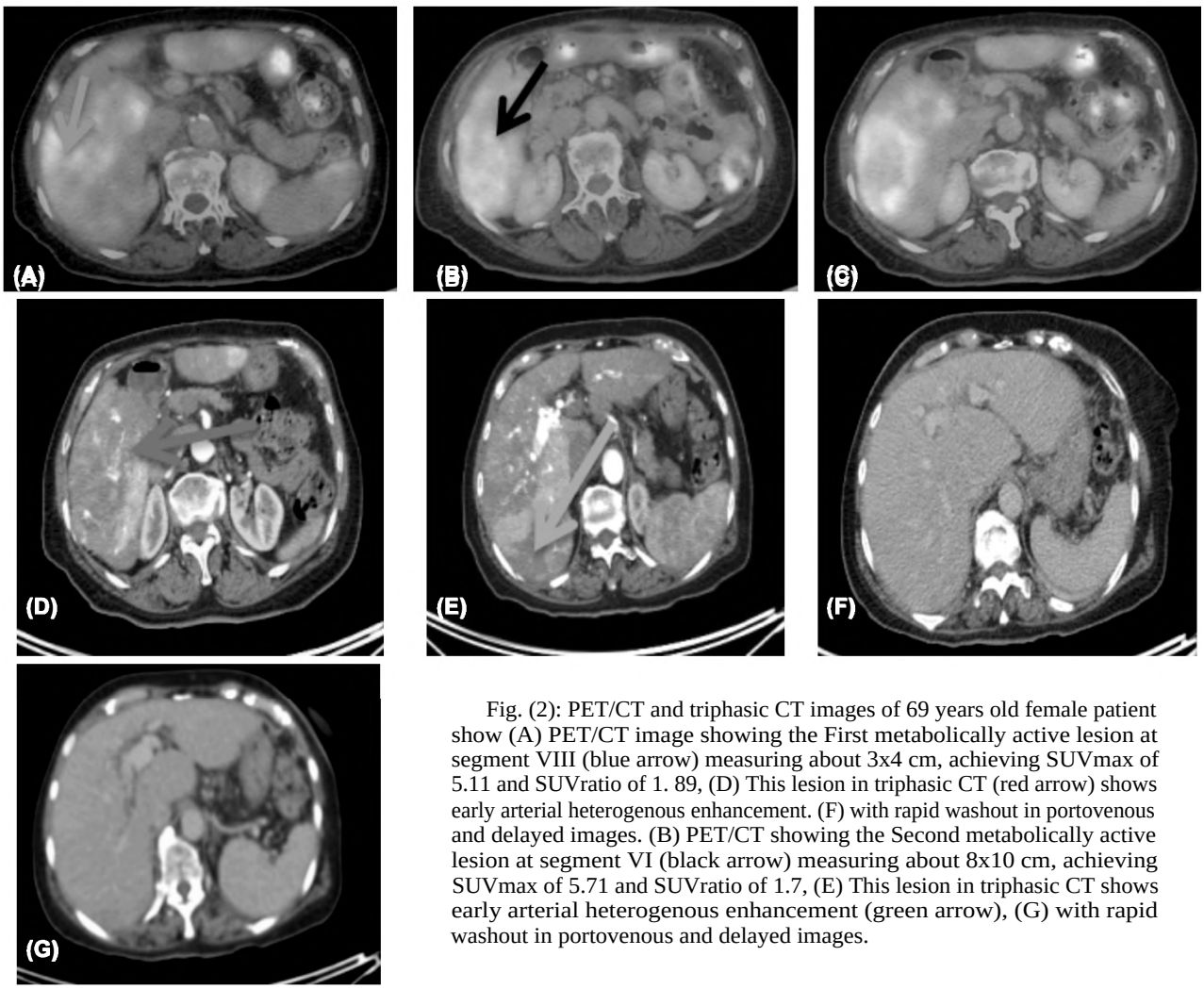

Fig. (2): PET/CT and triphasic CT images of 69 years old female patient show (A) PET/CT image showing the First metabolically active lesion at segment VIII (blue arrow) measuring about 3x4 cm, achieving SUVmax of 5.11 and SUVratio of 1. 89, (D) This lesion in triphasic CT (red arrow) shows early arterial heterogenous enhancement. (F) with rapid washout in portovenous and delayed images. (B) PET/CT showing the Second metabolically active lesion at segment VI (black arrow) measuring about 8x10 cm, achieving SUVmax of 5.71 and SUVratio of 1.7, (E) This lesion in triphasic CT shows early arterial heterogenous enhancement (green arrow), (G) with rapid washout in portovenous and delayed images.

Table (1): Demographic data of the studied patients.

	No.=40
Age (years):	
Mean ± SD	63.10±6.18
Range	54-75
Gender:	
Females	14 (35.0%)
Males	26 (65.0%)

Table (2): Results of PET/CT.

PET scan results	No.=56 tumor
No. of positive pts:	
Negative	2 (5.0%)
Positive	38 (95.0%)
Segments:	
I	0 (0%)
II	6 (15%)
III	2 (5%)
IV	4 (10%)
V	2 (5%)
VI	4 (10%)
VII	6 (15%)
VIII	16 (40%)
Size (cm):	
Median (IQR)	3 (2-4)
Range	1-9
SUV max:	
Median (IQR)	5.4 (3-8.3)
Range	1.9-14

Table (3): Results of triphasic CT scan.

Triphasic CT result	No.=56
No. of positive pts:	
Negative	6 (15.0%)
Positive	34 (85.0%)
Size (cm):	
Median (IQR)	5.5 (3.8-9.5)
Range	2-11

Table (4): Showing Comparison between PET/CT scan and triphasic CT results.

	PET scan	Triphasic CT	Test value	*p*-value	Sig.
No. of positive pts:					
Negative	2 (5.0%)	6 (15.0%)	2.222	0.136	NS
Positive	38 (95.0%)	34 (85.0%)			
Size (cm):					
Median (IQR)	3 (2-4)	5.5 (3.8-9.5)	5.804	<0.001	HS
Range	1-9	2-11			

Table (5): Shows comparison between PET/CT and triphasic CT regarding tumors.

	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
PET scan	34	2	4	0	100%	33.3%	89.5%	100%	90%

Table (6): Shows comparison between PET/CT SUV in positive and negative patient.

	Negative	Positive	Test-value	*p*-value	Sig.
SUV max:					
- Median (IQR)	2.1 (2-2.1)	5.5 (3.6-8.3)	–3.340	0.001	HS
- Range	1.9-2.4	2-14			

Discussion

The current study was carried on 40 patients 26 males (65%) and 14 females (35%), and their ages ranged between 54 and 75 years old. PET/CT scan was positive in 95% and negative in 5% of patients, However triphasic CT was positive in 85% and negative in 15% of patients.

It was found that PET/CT had a sensitivity of 100%, specificity of 33.3%, positive predictive value (PPV) of 89.5%, negative predictive value (NPV) of 100%, and accuracy of 90% that matches with Abdelhalim et al., **[8]** (2020) study showed that the sensitivity of PET/CT was 100%, specificity was 35% and NPV was 100%, PPV was 85% and accuracy was 81 %. And differs from Lee et al., **[9]** (2018) study showed that the sensitivity of PET/CT was 70%.

The SUV of hepatic focal lesion in the current study was significantly higher in patient with HCC than in patient with negative HCC, similar result was also noted in study done by Abdelhalim et al., **[8]**.

And regarding HCC metastases, PET/CT had a sensitivity of 100%, specificity of 100%, PPV 100 of %, NPV of 100%, and accuracy of 100% that matches with Bienz & Saad **[10]** (2015) study.

Comparison between staging of HCC by PET/CT and triphasic CT according to Barcelona clinic liver cancer (BCLC) staging showed that, regarding triphasic CT; stage A, 14 patients (41.2%); stge B, 12 patients (35.3%); stage C, 8 patients (33.5%) and regarding to PET/CT stage A, 12 patients (31.6%); stage B, 13 patients (34.2%); stage C, 13 patients (34.2%). That means that PET/CT disagreed with triphasic CT in 8 cases, where PET/CT

upstage 6 cases and downstage 2 cases, with p-value 0.558. These findings show that PET/CT is better than triphasic CT in HCC staging, but not statistically significant due to lower number of patients.

Cut off point of SUV max was >2.23 with sensitivity 92%, specificity 100%, PPV 100%, NPV 60%, p-value 0.000 that matches with Abdelhalim et al., [8] study showed that cut off point 2.5.

Cut off point of SUV ratio was >1.01 with sensitivity 100%, specificity 100%, PPV 100%, NPV 100%, p-value 0.000.

Our study matches also with Hetta and Attia, [11] (2020) study to compare between PET/CT and triphasic CT in early follow-up of HCC after trans arterial chemoembolization proved that sensetivity, specificity, and accuracy of PET/CT were 96.3%, 66.7%, and 93.3%, respectively. And those of triphasic CT were about 74%, 100%, 76.7%, respectively.

Results of all above mentioned studies match with our data which showed that PET/CT scan is better than triphasic CT in diagnosis and staging of HCC. Neverthless, the high cost of the investigation limits its universal use in HCC patients, making cost effectiveness the main issue in implementation of PET/CT in the standard care of the patient.

Conclusion:

We concluded PET/CT is more sensitive than triphasic CT in diagnosis and staging of HCC thus it is important especially in HCC staging.

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دور التصوير المقطعى بالاصدار البوزيترونى فى تشخيص سرطان الكبد بالمقارنة مع التصوير المقطعى ثلاثى الطور

سرطان الخلايا الكبدية أحد أكثر الأورام الخبيثة شيوعاً فى جميع أنحاء العالم، ويلعب التصوير بالأشعة دوراً مهماً فى الكشف المبكر، والتخطيط الدقيق للعلاج.

كان الهدف من هذا العمل هو تقييم القيمة المضافة للتصوير المقطعى بالاصدار البوزيترونى مقارنة بالتصوير المقطعى ثلاثى الطور.

أجريت هذه الدراسة على ٤٠ مريض ٢٦ ذكر (٦٥٪) و١٤ أنثى (٣٥٪) وتراوحت أعمارهم بين ٥٤ و ٧٥ سنة.

أظهرت المقارنة بين نتائج التصوير المقطعى بالإصدار البوزيترونى ونتائج التصوير المقطعى ثلاثى الطور (على أساس عدد المرضى) أن عدد المرضى الايجابيين كان ٣٨ (٩٥٪) و٣٤ (٨٥٪) وكان عدد المرضى السلبيين ٢ (٥٪) و ٦ (١٥٪) بالنسبة للتصوير المقطعى بالإصدار البوزيترونى التصوير المقطعى ثلاثى الطور على التوالى (قيمة 0.136 *p*) وعلى أساس الورم يظهر أن الأورام الإيجابية كانت ٥٠ (٨٩.٣٪) و٤٨ (٨٥.٧٪) والأورام السالبة كانت ٦ (١٠.٧٪) و ٨ (١٤.٣٪) بخصوص التصوير المقطعى بالإصدار البوزيترونى والتصوير المقطعى ثلاثى الطور على التوالى (قيمة 0.567 *p*).

أظهرت المقارنة بين التصوير المقطعى بالإصدار البوزيترونى التصوير المقطعى ثلاثى الطور بخصوص الثانويات أن عدد الثانويات الإيجابية كان ٣٨ (٥٤.٣٪) و ٢٤ (٣٤.٣٪) وأن عدد الثانويات السلبية كان ٣٢ (٤٥.٧٪) و ٤٦ (٦٥.٧٪) p على التوالى (قيمة 0.017 *p*).

أظهرت المقارنة بين مراحل سرطان الكبد بواسطة التصوير المقطعى بالإصدار البوزيترونى والتصوير المقطعى ثلاثى الطور وفقاً لمراحل BCLC أنه، فيما يتعلق بالتصوير المقطعى ثلاثى الطور، المرحلة أ، ١٤ مريضاً (٤١.٢٪)، المرحلة ب، ١٢ مريضاً (٣٥.٣٪)، المرحلة ج، ٨ مرضى (٣٣.٥٪)، بالنسبة للتصوير المقطعى بالإصدار البوزيترونى: المرحلة أ، ١٢ مريضاً (٣١.٦٪)، المرحلة ب، ١٣ مريضاً (٣٤.٢٪)، المرحلة ج، ١٣ مريضاً (٣٤.٢٪) وهذا يعنى عدم موافقة التصوير المقطعى بالاصدار البوزيترونى مع التصوير المقطعى ثلاثى الطور فى ٨ الحالات، حيث أن التصوير المقطعى بالاصدار البوزيترونى أعلى من تدريج ٦ حالات وقلل من تدريج حالتين، بقيمة (0.567 *p*).

أظهرت هذه النتائج أن التصوير المقطعى بالاصدار البوزيترونى أكثر حساسية من التصوير المقطعى ثلاثى الطور فى تشخيص سرطان الكبد وتحديد المراحل، ولكنها ليست ذات دلالة إحصائية بسبب انخفاض عدد المرضى.

فى دراستنا حول التصوير المقطعى بالاصدار البوزيترونى لسرطان الكبد، تراوحت نسبة SUVmax بحد أقصى بين ٢.١ و ١٢.٤٧ مع تغيير كبير للغاية (قيمة 0.001 *p*) وتراوحت نسبة SUVratio بين ١.١٩ و٢.٧ مع تغيير كبير للغاية (قيمة 0.000 *p*) أثبتت إحصائياً فعاليتها فى التشخيص الأولى لأورام الكبد و اكتشاف الثانويات.