RESEARCH PAPER

Impact of Advanced Liver Cirrhosis on Hepatic Metabolic Parameters and Volumetric Measurements Using 18F-FDG PET/CT

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ABSTRACT

Background: Liver cirrhosis alters hepatic metabolism and FDG uptake, which may affect the reliability of using the liver as a reference in PET/CT interpretation. Aim: To assess hepatic metabolic and volumetric parameters on 18F-FDG PET/CT in advanced cirrhosis versus normal liver, identify key differences, and propose correction factors for accurate semiquantitative analysis. Patients and methods: This was prospective comparative research involving 114 adult patients with different extrahepatic malignancies who presented for PET/CT for staging or restaging of their malignant process to Kasr Al-Ainy Hospital, Cairo University, in the period from October 2022 to August 2024. Patients were divided into two groups: Group I included individuals with no liver disease history and normal liver appearance on CT; Group II included patients with a long-standing history of cirrhosis and CT features of advanced liver disease, regardless of cause. Results: Cirrhotic cases had a mean age of 63.9 years and were mostly female. CT confirmed advanced cirrhosis features, with splenomegaly in 60%. Using the whole liver ROI, SUVmean was significantly lower in cirrhotics (1.82 ± 0.3) vs. controls (2.4 ± 0.51), $p < 0.001$, while SUVmax illustrated insignificant variance. Cirrhotics also had significantly lower functional liver volume, GHG, and HU. Blood pool SUVmean was similar between groups, but the liver/BP SUVmean ratio was lower in cirrhotics. Suggested correction factors for SUVmean are 1.89 (<1.5), 1.33 (1.5–2), and 1.09 (>2). Conclusion: In advanced cirrhosis, whole liver ROI is more accurate. SUVmean is lower, other liver measures reduced, especially with ascites. Correction factors are advised for SUVmean.

Keywords: Liver cirrhosis, FDG PET/CT, SUVmean, Semiquantitative analysis

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INTRODUCTION

18F-FDG PET/CT has incorporated metabolic tumor function with anatomic localization, allowing more accurate staging, restaging, assessment of response to therapy, and follow-up of different malignancies (1). Interpretation of PET/CT studies is done by both qualitative and semiquantitative assessment of different lesions. The latter is standardized through the use of reference organs, mainly the liver and blood pool, reported to have a stable activity over time. Normal liver is used in clinical practice and popularized in literature as the most common tissue background used for this purpose (2, 3). The usefulness of the liver as a reference organ was reported to be compromised by many physical, individual patient, technical, and pathological factors (4, 5).

The liver demonstrates a heterogeneous 18F-FDG uptake pattern with variable SUV figures in different benign and malignant disorders, including diffuse parenchymal liver diseases, mainly steatosis and cirrhosis. Additionally, much research has illustrated that hepatic FDG uptake and metabolic parameters also reflect hepatic function in these disorders because hepatic glycolysis is decreased in various genetic and metabolic diseases (6, 7).

Liver cirrhosis is the end stage of progressive liver fibrosis and is considered one of the most challenging health problems, representing an enormous burden on the economy of healthcare services worldwide. In the initial stages, cirrhosis is compensated, which is usually discovered incidentally, as most patients in this stage are asymptomatic. Decompensation in cases with compensated cirrhosis is usually described as the 1st occurrence of ascites, hepatic encephalopathy, esophageal variceal bleeding, and, in some individuals, increased bilirubin concentration (8). Nasr et al. (9) stated that the estimated number of people with compensated cirrhosis all over the world was 112 million, corresponding to an age-standardized global occurrence of 1,395 cases per 100,000 population (9). They reported that cirrhosis is accused of rising in both morbidity and mortality from liver diseases all over the world, including Egypt. There are various

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etiological factors of cirrhosis, including infectious, autoimmune, vascular, hereditary, or alcohol intake. Alcoholic liver disease and hepatitis C are the predominant causes of cirrhosis in affluent nations, while hepatitis B is the primary cause in many regions of Asia and sub-Saharan Africa.

Viral hepatitis, including HCV, was considered the most common etiology for chronic liver diseases in Egypt (10).

The goal of this research was to assess hepatic metabolic and volumetric parameters using 18F-FDG PET/CT in advanced cirrhosis cases versus those with normal liver function, identify significant differences, and develop correction factors for accurate liver-based semiquantitative analysis in cirrhotic patients.

PATIENTS AND METHODS

This was a prospective comparative study that included 114 adult cases with different extrahepatic malignancies presented for PET/CT for staging or restaging of their malignant process to Kasr Al-Ainy Hospital, Cairo University, in the period from October 2022 to August 2024. Patients were separated into two groups: Group I included individuals with no liver disease history and normal liver appearance on CT; Group II involved cases with a long-standing history of cirrhosis and CT features of advanced liver disease, regardless of cause.

Inclusion criteria for group I: Adult patients (>18 years) scheduled to undergo ^18F FDG-PET/CT for staging or restaging of extrahepatic malignancy, with no history of alcoholism, hepatitis C virus, or hepatitis B virus; normal liver function tests and hepatic sonography if available; and normal hepatic appearance on the CT component of the FDG-PET/CT study.

Inclusion criteria for group II: Adult patients (>18 years) undergoing ^18F FDG-PET/CT for staging or restaging of extrahepatic malignancy, with confirmed advanced liver cirrhosis of any cause (hepatitis B or C, chronic alcoholism, or fatty liver), based on imaging or biopsy if available. CT findings suggestive of cirrhosis should be present, such as caudate lobe and left lateral segment hypertrophy, right posterior and left medial segment atrophy, liver surface nodularity, heterogeneous parenchyma, and possible signs of portal hypertension like varices, ascites, splenomegaly, bowel wall edema, or intrahepatic vascular shunts.

Exclusion criteria for both groups: Cases were excluded if they were pregnant, had a Karnofsky score below 60%, or had hepatocellular carcinoma (HCC), cholangiocarcinoma, or solitary/multiple liver deposits. Other exclusion factors included any prior or recent medications affecting liver function, features of early or severely decompensated cirrhosis, hepatic steatosis on sonography or CT, coexisting liver diseases, prior hepatic surgery, bulky malignant tumors, a history of radiotherapy or hepatotoxic chemotherapy within the last six months, or uncontrolled diabetes with persistently high blood glucose levels.

Methods

Demographic data were gathered involving age, gender, height, weight, and BMI. Clinical data included primary tumor site, prior surgery, purpose of PET/CT (e.g., staging, restaging, follow-up), recent anticancer therapy, and comorbidities such as diabetes or hypertension. In Group I, patients with any hepatic insult, liver-affecting medications, or prior liver surgery were excluded. Liver function tests and abdominal sonography were reviewed if available. In Group II, data on the cause and duration of cirrhosis, related symptoms, liver function, and sonographic findings were recorded. Patient preparation and imaging protocols followed EANM guidelines for 18F-FDG PET/CT imaging (11). Patients avoided strenuous activity for 1–2 days, fasted for 6 hours, avoided carbohydrates for ~24 hours, and refrained from caffeine. Blood glucose was checked to ensure levels <200 mg/dL. After resting in a quiet, warm environment, patients received IV 18F-FDG (3.7 MBq/kg, max 370 MBq). Imaging was done ~60 minutes post-injection using an Ingenuity TF 64 PET/CT scanner (Philips Healthcare, USA). The system operated in 3D mode with TOF-OSEM reconstruction. Scanning was performed from skull to thighs, with arms raised, and involved both CT and PET components. Calibration was performed quarterly, and SUV validation bimonthly. When not contraindicated, contrast-enhanced CT was acquired at 120 kV, 300 mA, with 1.5 mL/kg of contrast. PET/CT images were assessed both qualitatively and quantitatively. A radiologist and nuclear medicine consultant reviewed images to confirm the absence of liver pathology in Group I and to assess cirrhotic features in Group II. Hepatic volume was measured using automated segmentation on the PHILIPS IntelliSpace Portal, excluding hilar structures for functional volume (FHV). SUVmean and SUVmax were calculated using two methods: fixed-size circular ROI in segment VI and whole-liver 3D ROI using OsiriX software, excluding hilum, IVC, and gallbladder. SUVmean represented average uptake; SUVmax represented peak activity. Mediastinal SUVmean was measured using a 1.2 cm ROI in the aortic arch or descending aorta, excluding vessel wall and plaques. Global hepatic glycolysis (GHG) was calculated as GHG = SUVmean × HV (12, 13). Hounsfield units (HU) were measured manually in segment VII on non-enhanced CT using ±2.5 cm ROIs across multiple axial slices to calculate average HU values (14).

Ethical Approval: All procedures used in research, including human subjects, were in conformity with the institutional research committee's ethical standards as well as the 1964 Helsinki statement and its subsequent amendments.

Statistical Analysis

Data were coded and analyzed utilizing SPSS version 28 (IBM Corp., Armonk, NY, United States of America).

Quantitative data were summarized as standard deviation, median, mean, minimum, and maximum, while categorical data were presented as frequencies and percentages. Group comparisons have been carried out utilizing unpaired t-tests for two groups and ANOVA with post hoc tests for more than two groups. The chi-square test has been applied for categorical variables, and the exact test was applied when expected frequencies were below 5. ROC curve analysis has been applied to determine the optimal SUV cutoff for detecting advanced cirrhosis. A p-value < 0.05 has been considered statistically significant.

RESULTS

Table (1): Age, Gender, and BMI of Cases Involved in the Two Groups

Normal		Cirrhotics	P value
Age: **-Mean** **-Range**	59.5±12.9 29-78	63.9± 9.6 44-83	0.126
Group II patients: **-With ascites: Mean/median** **-Withoutascites: Mean/median**	------	65.1± 12.61/ 67 63.4± 8.35 / 64	0.214
Gender: **-Females** **-Males**	39(66.1%) 20(33.9%)	34(61.8%) 21(38.2%)	0.189
BMI: **-Mean** **-Median**	27.73±6.39 27.37	26.58±5.39 27.04	0.279

Table 1 found that patients with advanced cirrhosis had a mean age of 63.9 years, slightly older than those without ascites. Females accounted for 61.8% of cirrhotic patients compared to 66.1% of controls. The control group had a similar BMI to those with advanced cirrhosis.

Table (2): CT features of advanced cirrhosis in group II.

Cirrhotics (55 patients)		
CT features	**Number**	**%**
Three main features of cirrhosis	55	100
Splenomegaly	33	60
Ascites and splenomegaly	15	27.3

Table 2 showed that, out of the 55 cirrhotic patients, the CT component of PET/CT showed the main three CT features of advanced cirrhosis. Additionally, splenomegaly was reported in a CT study in 33 patients (60%), being associated with ascites in 15 patients (27.3%).

Table (3): Comparison between SUVmean and SUVmax of the two groups using small right hepatic ROI

	Cirrhotic					Normal					P value
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	
SUVmean	2.34	0.39	2.30	1.60	3.70	2.40	0.51	2.40	1.40	3.60	**0.533**
SUVmax	2.82	0.48	2.80	1.90	4.40	2.82	0.58	2.80	1.70	4.30	**0.994**

Table 3 showed that, using this ROI, the mean and median figures of SUVmax were almost equal in both groups. On the other hand, the SUVmean figure in cirrhotic patients is 2.34 ± 0.39, which was relatively less than that of normal controls (2.4 ± 0.51), yet the difference was statistically insignificant.

Table (4): Comparison between SUVmean and SUVmax of the two groups using the whole liver ROI.

	Cirrhotic					Normal					P value
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	
SUVmean	1.82	0.31	1.90	1.10	2.21	2.40	0.51	2.40	1.70	3.60	**<0.001**
SUVmax	2.72	0.46	2.70	1.40	3.70	2.82	0.58	2.80	1.70	4.30	**0.288**

Table 4 showed that, upon applying the whole liver ROI, SUVmean was significantly lower in cirrhotic patients (1.82 ± 0.3; median: 1.9) compared to controls (2.4 ± 0.51; median: 2.4), $p < 0.001$ (Table 7, Fig. 23). SUVmax was also lower in cirrhotics (2.72 ± 0.46; median: 2.7) vs. controls (2.82 ± 0.58; median: 2.8), but the variance was insignificant ($p = 0.288$). Notably, SUVmax exceeded SUVmean by 49.5% and 42.1% in cirrhotics and by 17.5% and 16.7% in controls.

Table (5): Comparison between GHG, FHV, and HU between patients with advanced cirrhosis and normal controls using the whole liver ROI

	Cirrhotic					Normal					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
GHG	1991.56	633.48	1953.81	743.84	3719.73	3764.44	1400.89	3570.42	1771.98	7990.34	< 0.001
FHV	1091.26	283.32	1045.70	464.90	1885.90	1558.24	406.98	1492.50	945.50	2474.80	< 0.001
HF units	44.02	11.04	46.4	30.20	65.50	53.54	7.22	53.60	32.10	75.00	0.015

Table 5 showed that patients with cirrhosis had mean and median figures of functional hepatic volume (FHV), global hepatic glycolysis (GHG), and CT Hounsfield units (HU) less than those reported for the normal control group, with a statistically significant variance in favor of the latter.

Table (6): Comparison between Bp SUVmean figures between cirrhotics and normal controls.

	Cirrhotic					Normal					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Bp mean	1.68	0.43	1.70	0.80	3.60	1.72	0.45	1.70	1.00	3.10	0.639

Table 6 showed that blood pool (Bp) SUVmean figures were comparable between cirrhotic patients and the normal control group, with a statistically insignificant variance (p:0.639) between both group

Table (7): Comparison of hepatic SUVmean/Bp SUVmean between cirrhotics and normal controls.

	Cirrhotics			Normal			
	Mean	SD	Median	Mean	SD	Median	
Liver SUVmean	1.82	0.30	1.90	2.40	0.51	2.40	< 0.001
Bp mean	1.68	0.43	1.70	1.72	0.45	1.70	0.639
Ratio Liver mean /Bp mean	1.08	0.71	1.12	1.41	0.69	1.42	< 0.001

Table 7 showed that there was significant variance in the liver SUVmean/Bp SUVmean ratio between those with advanced cirrhosis and normal controls in favor of the latter (p-value < 0.001).

Table (8): Suggested correction factors for different mean SUV in patients with advanced cirrhosis.

	In case SUVmean		
	<1.5	1.5 to 2	>2
Mean SUVmean	1.27	1.81	2.21
Correction factor	1.89	1.33	1.09

Table 8 showed that, on using the liver SUVmean as a standard reference in PET/CT performed for patients with advanced cirrhosis, applying the whole liver ROI, we can suggest a correction factor to be used to avoid the pathological effect of cirrhosis on hepatic SUVmean, especially with deterioration of the cirrhotic process on follow-up studies. In a PET/CT study using the whole liver as an ROI for SUVmean measurement, advanced cirrhotic patients with a mean figure of SUVmean <1.5, SUVmean from 1.5 to 2, and SUVmean >2, the suggested correction factors are 1.89, 1.33, and 1.09, respectively.

Case presentation

Case (1)

A 44-year-old female patient, her BMI = 22.19, presented with pathologically proven Hodgkin lymphoma (HL) and was referred for initial staging, with qualitative analysis that confirmed the presence of all CT criteria of advanced cirrhosis on the CT image series with no bulky disease as seen on her MIP image. While quantitative assessment was done by

Automated method was used to measure total and functional hepatic volume (HV) using a dedicated PHILIPS IntelliSpace Portal Workstation. FHV=1142.4 cc and THV=1370.8 cc.

Semi-automated method: Mediastinal SUVmean ~ 0.9.

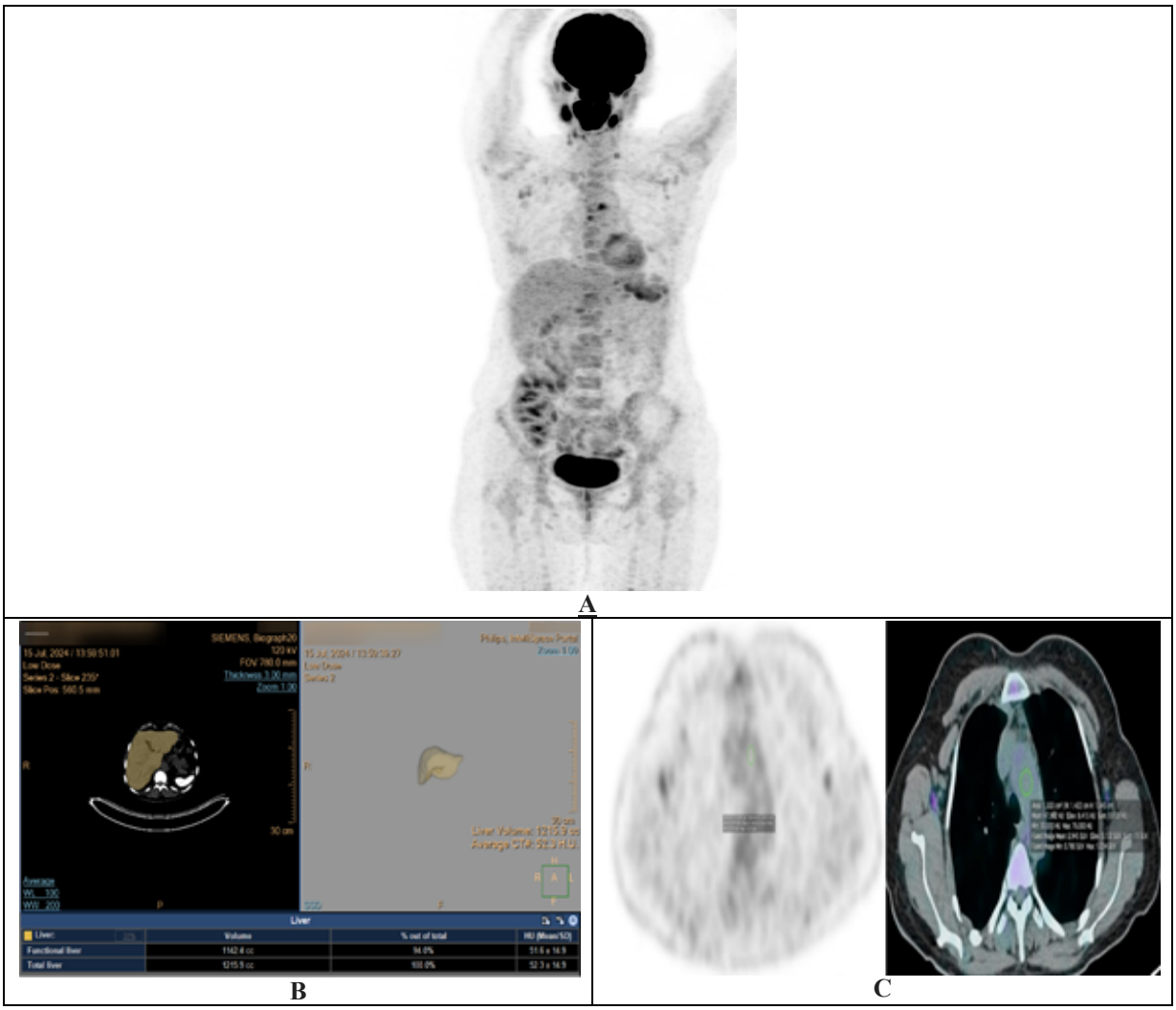

Figure (1): (A): MIP image of initial staging of HL patient with advanced cirrhosis. (B): shows total and functional hepatic volume of an advanced cirrhotic case, with 1215.9 and 1142.4 cc. respectively. (C): Shows circular ROI within the aortic arch on axial PET and fused PET/CT images, with SUVmean ~0.9.

Calculating SUVmean and SUVmax is done by: On using the whole liver ROI: SUVmean 1.3 and SUVmax 2.1.

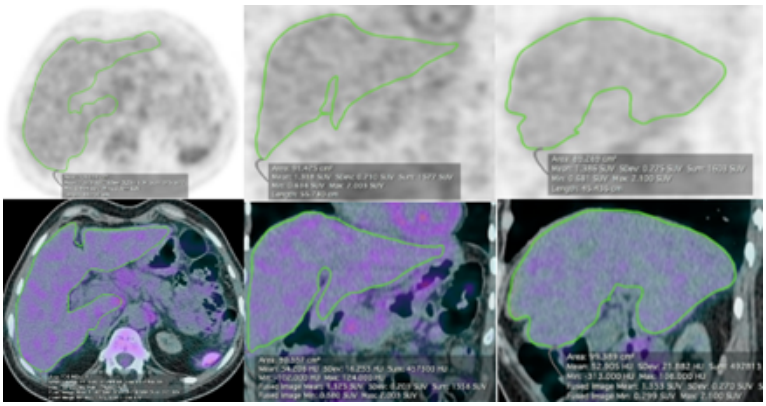

Figure (2): Axial, coronal, and sagittal views of regions of interest (ROIs) are drawn manually to calculate SUVmean (~1.3) and SUVmax (~2.1) in a whole cirrhotic liver. The first row is (18F-FDG PET) of the liver, and the second row is fused images of PET/CT.

Using a small rounded ±2.5 cm ROI drawn on the right hepatic lobe segment VI shows an SUVmean of 1.5 and an SUVmax of 2.0.

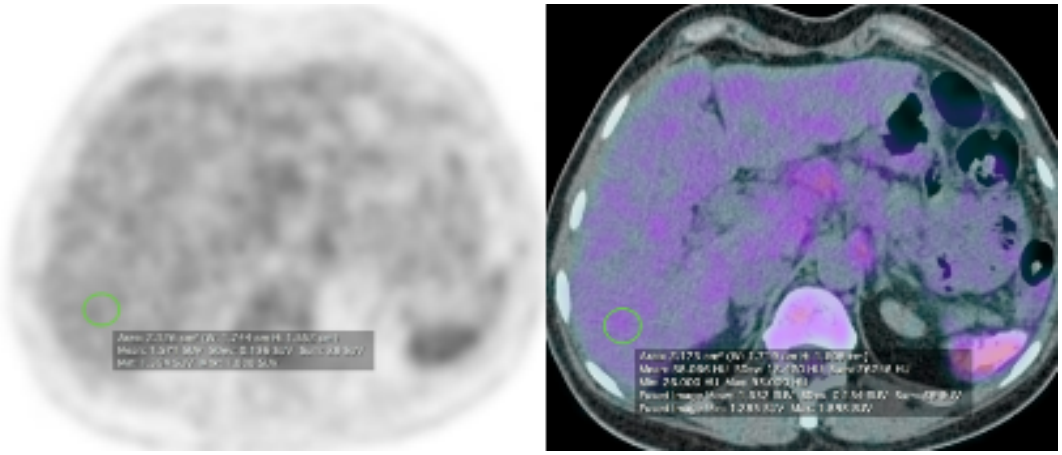

Figure (3): small ROI within the right hepatic lobe, with SUVmean~1.5 and SUVmax~2.0 ~2.0 axial fused PET/CT image (right) and PET image (left).

Global hepatic glycolysis (GHG) is based on the whole liver ROI, applying the following equation:
Hounsfield units (HU) = 48.5

GHG = SUVmean x HV = 1.3 x 1142.4 = 1485.12

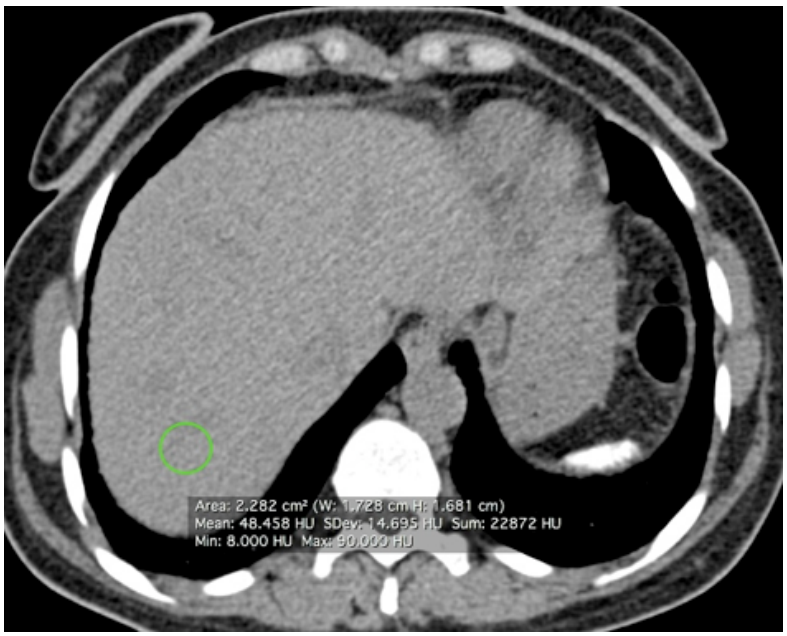

Figure (4): shows the average Hounsfield unit (HU) in an advanced cirrhotic patient by placing ROI on segment VII, HU=48.5.

Case 2

A 70-year-old male patient, with a history of treated colon cancer, presented 2 years post-treatment for follow-up, with a BMI of 26.7, and underwent an 18FDG-PET/CT study that revealed no hypermetabolic lesions distinctive for active neoplastic lesions, a "negative study," as seen on the MIP image. The study also shows moderate ascites with CT features of advanced cirrhosis. Quantitative assessment was done by

Automated method was used to measure total and functional hepatic volume (HV) using a dedicated PHILIPS IntelliSpace Portal Workstation. FHV=1218.1 cc and THV=1252.2 cc.

Semi-automated method: Mediastinal SUVmean ~ 1.4.

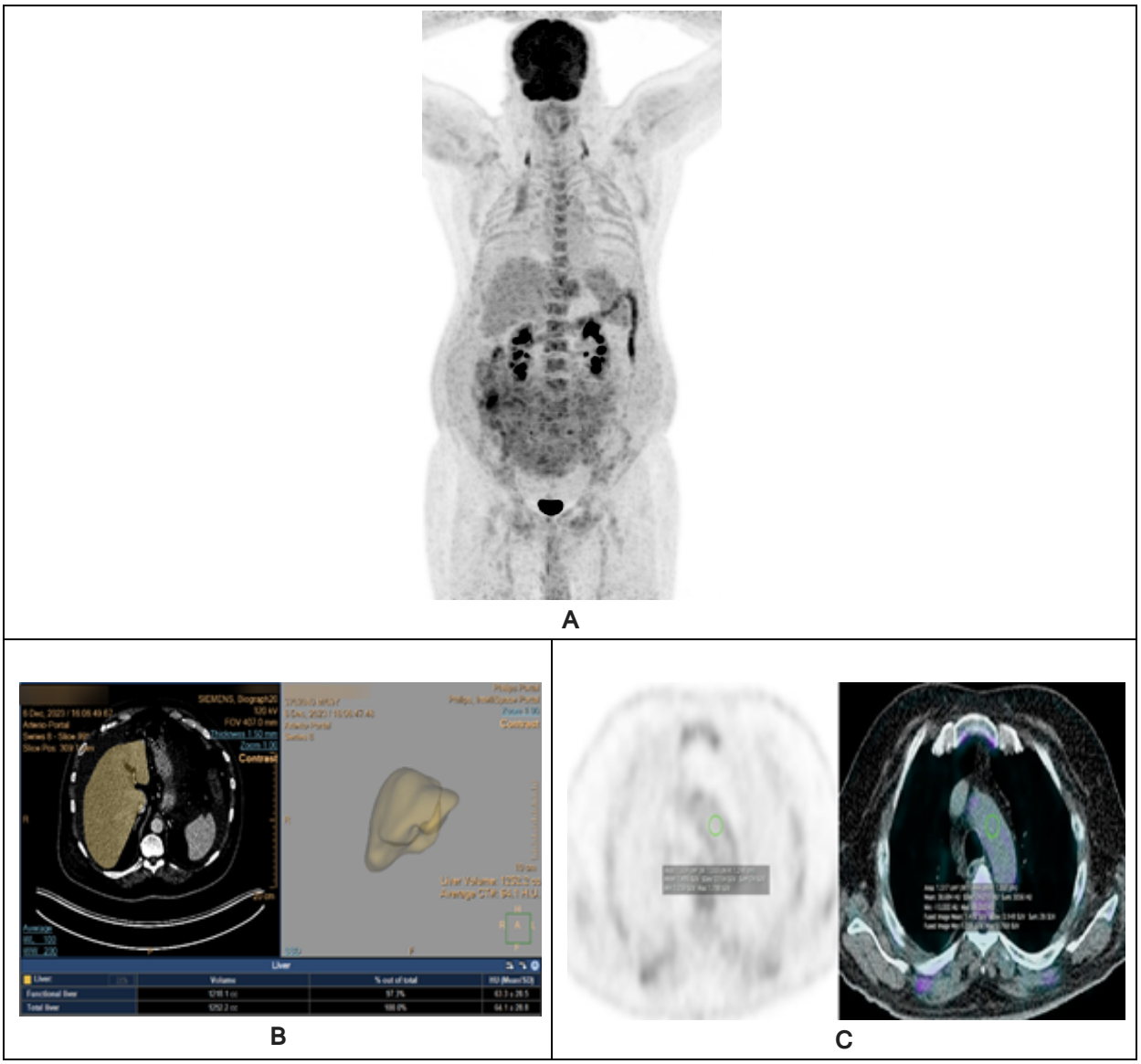

Figure (5): (A): MIP image of negative study scan showing no hypermetabolic lesions with abdominal distension "ascites. (B): shows total and functional hepatic volume of an advanced cirrhotic case with ascites, with 1252.2 and 1218.1 cc, respectively. (C): shows circular ROI within the aortic arch on axial PET and fused PET/CT images, with SUVmean ~1.4.

Calculating SUVmean and SUVmax is done by: On using the whole liver ROI: SUVmean 1.8 and SUVmax 3.2

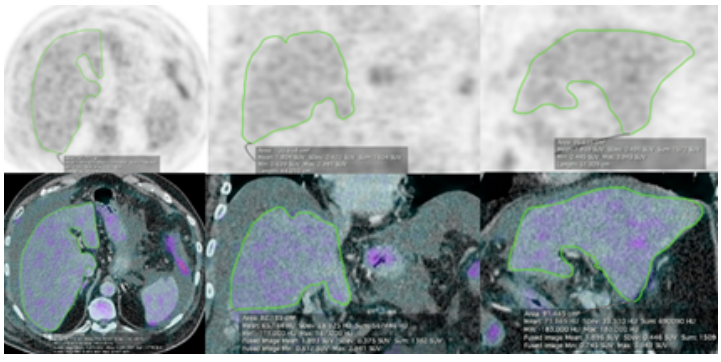

Figure (6): Axial, coronal, and sagittal views of regions of interest (ROIs) are drawn manually to calculate SUVmean (~1.8) and SUVmax (~3.2) in a whole cirrhotic liver with abdominal ascites. The first row is (18F-FDG PET) of the liver, and the second row is fused images of PET/CT.

On using small rounded ±2.5 cm ROI drawn on right hepatic lobe segment VI shows: SUVmean 2.1 and SUVmax 2.5

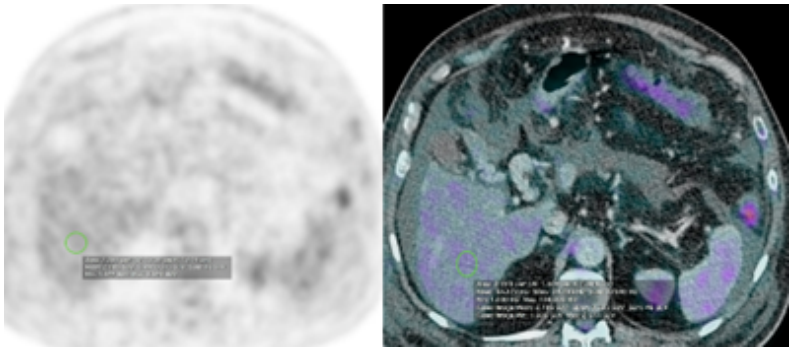

Figure (7): small ROI within the right hepatic lobe, with SUVmean~2.1 and SUVmax~2.5 ~2.5 axial fused PET/CT image (right) and PET image (left).

Global hepatic glycolysis (GHG) is based on the whole liver ROI, applying the following equation:

GHG = SUVmean x HV = 1.8 x 1218.1 = 2192.6

Hounsfield units (HU) = 47.6

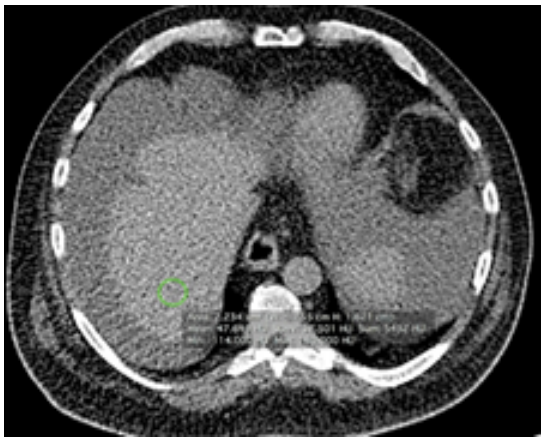

Figure (8): Shows average Hounsfield unit (HU) in advanced cirrhotic patient with ascites by placing ROI on segment VII, HU=47.6

DISCUSSION

Yet, age and gender are a bit different between both groups. Age was relatively higher in those with advanced cirrhosis compared to the control group, with a slightly older age in those with ascites. Body mass index (BMI) is mildly higher in the control group compared to those with advanced cirrhosis, with mean and median figures of 27.73±6.39 & 27.37 and 26.58±5.39 & 27.04, respectively, with a non-significant statistical difference.

In advanced liver cirrhosis, a CT scan shows a nodular hepatic contour... In the current work, the three main features of advanced cirrhosis are found in all 55 cirrhotic patients, splenomegaly in 33 patients, and ascites in 15 patients.

While, for group I patients with normal liver, there is no difference in SUV figures on using small or whole liver ROIs in the current work. This is consistent with Kanstrup et al. (15), who reported that in normal subjects the mean FDG uptake in small hepatic ROI is representative of whole liver FDG uptake. On the other hand, as regards patients with advanced cirrhosis, when we use a single rounded right hepatic lobe ROI, the SUV figures differ on changing the position of the small ROI in the right hepatic lobe of the same patient. Besides, the SUV figures on using small ROI are relatively higher, more evident in SUVmean figures, compared to applying the whole liver ROI. This was explained by the fact that cirrhosis as a chronic liver disease is a heterogeneous condition regarding scarring pattern, rates of progression, and the potential for regression, with variable SUV figures in different right hepatic lobe areas. Also, it was stated by Sorensen et al. (16), that liver histology exhibits considerable heterogeneity when affected by parenchymal illness in

spite of an etiology when compared with controls. This focal heterogeneity in liver FDG uptake is elevated in patients with hepatic cirrhosis, being responsible for variability in hepatic SUV figures in different hepatic regions in our study on using small rounded right hepatic ROI. So, we decided to employ the whole liver as an ROI in the current study, being more useful in the evaluation of global hepatic metabolic activity and giving more realistic figures. Also, this has a great value to minimize errors of small ROIs and to provide more accurate data about hepatic metabolic activity in those with advanced cirrhosis as deduced from FDG uptake and liver SUV figures.

In the current study, on applying the whole liver ROI, there is a significant difference in SUVmean between those with advanced cirrhosis and those with normal livers... This difference was lacking when using a fixed small rounded ±2.5 cm ROI due to the heterogenicity of the cirrhotic process.

This difference was lacking when using a fixed small rounded ±2.5 cm ROI due to the heterogenicity of the cirrhotic process. Using the same whole liver ROI, this difference was also significant in the study of Hernandez-Martinez et al (12), who stated that subjects with cirrhosis illustrated a statistically significant lower hepatic SUVmean compared to non-cirrhotic subjects with hepatic SUVmean figures of 1.55 ± 0.29 versus 1.81 ± 0.23 (p: 0.009). Besides, they found that subjects with cirrhosis showed a statistically significant lower average GHG compared to non-cirrhotic subjects, being 2238.29 ± 903.60 for the former versus 2974.67 ± 829.16 for normal subjects with (p:0.024). Yue et al.,(17) also reported SUVmean figures in the cirrhotic group of (2.01 ± 0.36) versus (2.23 ± 0.42) in the control group with a statistically significant difference. Similarly, they also reported a statistically significant variance between global hepatic glycolysis (GHG) in the control group ($2,230.46 \pm 549.47$) and the hepatic cirrhosis group ($1,693.81 \pm 666.21$) in favor of the former. The difference in GHG was also found to be significant in the current study (p-value <0.001), with GHG in the cirrhotic and control groups of 1991.56±633.48 and 3764.44±1400.89, respectively. This figure for the cirrhotic group was evidently lower in our study compared to the figure in Hernandez-Martinez et al study (12), likely due to the inclusion of those with advanced cirrhosis only in our study compared to the inclusion of all cirrhotic patients with different stages in their work, denoting a more evident reduction in GHG in association with advanced cirrhosis as a diffuse hepatic disease globally affecting hepatocytic function and reducing overall hepatic metabolism.

In agreement with our data, Sorensen et al,. (18) also illustrated a significant reduction in hepatic metabolic function in cirrhotic livers compared to normal control livers. They stated that cases with cirrhosis demonstrated a greater degree of intrahepatic metabolic heterogeneity than healthy subjects, thus enforcing the application of total hepatic ROI in patients with cirrhosis, to minimize sampling errors, for the creation of global hepatic PET/CT-based parameters in a correct and precise way.

In our research, the CT hepatic volume in those with advanced cirrhosis is 1091.26±283.32versus 1558.24±406.98 in normal control subjects, with median figures of 1045.7 and 1492.5, respectively, with a statistically significant variance in favor of the latter (p<0.001). In concordance with our results, Patel et al (19), reported that the hepatic volume of cases with cirrhosis was significantly lower compared to that of normal healthy controls, with clear shrinkage of the whole liver observed in cases with advanced cirrhosis. Also, Zhou et al ,.(20), found a significant association between liver volume index as calculated on CT and severity of cirrhosis with regard to the Child classification. In their study, the mean total liver volume of Child A, B, and C cases was 1.156±258 cm^3, 1.054±430 cm^3, and 814±169 cm^3, respectively, of which the Child C group was significantly smaller compared to that of the healthy control subjects. This goes with the relatively lower hepatic volume in the current study in patients with ascites (1056.85±264.71), which is a more advanced stage of cirrhosis, compared to those without ascites (1104±292.17), yet the variance was statistically insignificant. This insignificance may be due to the lower number of patients with ascites in our study, seen in only 15 patients, representing 27% of those with advanced cirrhosis. The volume change ratio of Child-Pugh class C cases in Zhou et al study (20) was 33.72% ± 18.05%, which is significantly greater compared to the volume change ratio of Child-Pugh class A and B patients ($p < 0.05$). Similarly, in our study, a comparable volume change ratio of 30% is found in cases with advanced cirrhosis.

In the current research, there is a significant difference in the liver SUVmean/blood pool SUVmean ratio (L/BR) between patients with cirrhosis compared to the control group, with this ratio's mean and median figures of 1.08±0.71and 1.12 for cirrhotic and 1.40±0.69 and 1.41 for the normal controls (P<0.001). In a study by verloh et al. (21) done on 37 patients with variable METAVIR scores of liver fibrosis or cirrhosis, divided into smaller groups, they reported that L/BR elevated up to the advanced stage of liver fibrosis (F2, reaching a value of 2.00 ± 0.40) and reduced until liver cirrhosis is reached (F4, 1.32 ± 0.14).

They stated that this is mostly due to higher GLUT-4 transporter expression in patients with active fibrosis (F2) with a resultant increase in FDG uptake. In contrast, the expression level of GLUT-4 has been observed to decrease in liver cirrhosis. They concluded that functional changes in liver parenchyma during liver fibrosis/cirrhosis affect hepatic glucose metabolism that significantly differ between stages of liver fibrosis and cirrhosis(21). Similarly, Hernandez-Martinez et al. (12)

stated that the reduced FDG uptake in cirrhotic livers can be reflected also in reducing the L/BR compared to normal controls, as found in our work. Ng et al ,. (22), stated that liver/blood pool uptake in 18F-FDG PET/CT can be influenced by many hepatic conditions, including cirrhosis, with a more prominent pathological impact on this ratio with more disease severity. They concluded that radiologists must exercise great caution in the utilization of liver/blood pool uptake as metabolic references in patients with severe hepatic illness, avoiding any significant qualitative and quantitative effects on the diagnostic accuracy of PET/CT interpretation.

In the current study, for cases with advanced cirrhosis using the whole liver as an ROI, we suggest application of 1.89, 1.33, and 1.09 correction factors for hepatic mean SUVmean figures <1.5, from 1.5 to 2, and >2, respectively. These factors are to be applied for correction of mean SUV when the liver is applied as a reference standard. These factors can be applied during PET/CT done for staging and, more importantly, in PET/CT done for restaging and test-retest follow-up studies in patients with extrahepatic malignancy. The idea is to apply different correction factors for different degrees of impairment of metabolic hepatic function. As during follow-up of malignancy, there may be more deterioration in metabolic hepatic function for those with advanced cirrhosis as they may pass from compensated cirrhosis to decompensated cirrhosis with further reduction of FDG uptake and SUVmean figures, so we can apply the appropriate correction factor compatible with more progression of cirrhosis over time.

CONCLUSION

In advanced liver cirrhosis, a small right hepatic ROI does not accurately reflect hepatic metabolic alterations due to intrahepatic heterogeneity, necessitating the use of a whole liver ROI for more reliable SUV assessment. In contrast, normal livers show consistent SUV values between small and whole liver ROIs due to uniform metabolic activity. Patients with advanced cirrhosis demonstrate significantly lower hepatic SUVmean compared to healthy controls, while SUVmax shows no significant difference. Additionally, cirrhotic patients exhibit marked reductions in liver volume, GHG, L/BR, and HU when using whole liver ROI. The presence of ascites is associated with further decline in metabolic and volumetric parameters. Therefore, when using the liver as an internal reference in FDG PET/CT interpretation in cirrhotic patients, correction factors of 1.89 (for SUVmean <1.5), 1.33 (for 1.5–2), and 1.09 (for >2) are recommended to obtain more accurate hepatic SUV values.

RECOMMENDATION

In advanced cirrhosis, we recommend using the whole liver as ROI due to intrahepatic heterogeneity that may distort SUV values when using a small right hepatic ROI. SUVmean should be preferred over SUVmax, as it provides a more accurate reflection of hepatic metabolism. Moreover, when using the liver as a reference organ for semiquantitative analysis, applying correction factors based on individual SUVmean values enhances the accuracy, reliability, and reproducibility of metabolic assessment in this population.

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