The negative impact of fatty liver on maximum standard uptake value of liver on FDG PET

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Abstract

Purpose: The purpose of the study is to evaluate the impact of fatty liver on maximum standard uptake value (SUVmax) of liver on 2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET). **Materials and methods:** A total of 173 consecutive healthy subjects were retrospectively recruited for analysis. Subjects with acute renal disease, chronic renal disease, or malignancy were excluded. Demographic data were collected from chart records. All subjects performed whole-body FDG PET, sonography of liver, and glutamic pyruvic transaminase (GPT) level. The SUVmax of liver on FDG PET was calculated. The relationship between the severity of fatty liver and SUVmax of liver on FDG PET was analyzed. **Results:** There were significant differences in SUVmax of liver on FDG PET in four groups: no fatty liver, mild-degree, moderate-degree, and severe-degree fatty liver on sonography diagnosis ($P=.041$). After adjusting for possible covariates age, sex, body mass index, and GPT, there was a significantly negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET ($\beta=-.20$, $P<.001$). **Conclusion:** Based on the results of this study, the liver cannot be used as a comparator of extrahepatic foci of equivocal increased FDG activity in patients with fatty liver disease.
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Keywords: Fatty liver; Maximum standard uptake value (SUVmax); 2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET)

1. Introduction

Fatty liver is the condition of fat accumulation in liver cell via the process of steatosis (abnormal retention of lipids within a cell). The prevalence of fatty liver disease in the general population ranges from 10% to 24% in various countries [1]. Fatty liver disease is the most common cause of abnormal liver function test in the United States. Despite having multiple causes, fatty liver occurs worldwide in those with excessive alcohol intake and those who are obese. Fatty liver is also associated with other diseases that influence fat metabolism. Accumulation of fat may be accompanied by a progressive inflammation of the liver. With inflammation, cell death, and fibrosis, the steatosis process may result in end-stage liver disease or be a precursor of hepatocellular carcinoma [2–5].

Positron emission tomography (PET) is a nuclear medicine imaging technique that produces a three-dimensional image or picture of functional processes in the body. Clinical use of PET has grown rapidly because of its usefulness in cancer diagnosis, staging, and management. 2-Fluoro-2-deoxy-D-glucose (FDG) PET is a functional imaging modality, which reflects cellular glucose metabolism. FDG is the most commonly used radiopharmaceutical for PET studies in oncology, and the tracer is a substrate of

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energy metabolism. Accumulation and trapping of FDG allow the visualization of increased uptake in most malignant cells compared to normal cells [6,7].

It has been reported that the oral cavity, the liver, the stomach, and the colon could be visualized with various degrees of FDG uptake in normal subjects [8]. FDG accumulates not only in malignancies but also in inflammatory processes [9–11]. It is important to be familiar with the varying degree of FDG accumulation that represents normal distribution, artifacts, and physiological changes before attempting to interpret whole-body PET imaging for malignancy detection [12]. The purpose of the study is to evaluate the impact of fatty liver on maximum standard uptake value (SUVmax) of liver on PET.

2. Materials and methods

A total of 173 consecutive healthy subjects from January, 2009, to December, 2009, referred from the Department of Community Medicine and Health Examination Center of China Medical University Hospital for health screening, were retrospectively recruited for analysis. The study was approved by the local institutional review board (DMR99-IRB-010). Subjects with acute renal disease, chronic renal disease, or malignancy were excluded. Demographic data were collected from chart records. All subjects performed whole-body FDG PET, sonography of liver, and serum liver enzyme level [glutamic pyruvic transaminase (GPT)]. The SUVmax of liver on FDG PET was calculated. After adjusting for possible covariates age, sex, body mass index (BMI), and GPT, the relationship between severity of fatty liver and SUVmax of liver on FDG PET was analyzed.

2.1. Ultrasonographic diagnosis of severity of fatty liver

All subjects were divided into four groups: no fatty liver, mild-degree, moderate-degree, and severe-degree fatty liver. When only the relative brightness of the liver in comparison to the renal parenchyma (L-K contrast) was noted, it was defined as mild-degree fatty liver. When both L-K contrast and blurring of the hepatic vein trunk were noted, it was defined as moderate-degree fatty liver. When deep attenuation (attenuation of the echo-bean in deep portion of the right hepatic lobe) was noted, it was defined as severe-degree fatty liver [13].

2.2. FDG PET

Whole-body PET images were acquired on a GE Advance NXi scanner (35 image planes, 4.30 mm/slice, 15 cm AFOV), 40 min to 1 h after intravenous injection of 370 MBq (10 mCi) of F-18-FDG. Emission PET images of the neck, chest, abdomen, and pelvis were acquired in two-dimensional mode, 4 min per bed position, followed by transmission scans at selected sites. Images were reconstructed using vendor-provided software and formatted into transaxial, coronal, and sagittal image sets. All subjects fasted for at least 4 h before the examination.

2.3. Standard uptake value

The SUVmax, which is defined as the ratio of activity in tissue per milliliter to the activity in the injected dose per patient body weight, has been proposed as a simple useful semiquantitative index for FDG accumulation in tissue.

$$SUVmax = \frac{\text{maximum activity in ROI (kBq)}}{\text{injected dose (MBq)} \times \text{body weight (kg)}}$$

2.4. Statistics

The STATA 11.0 computer package was used to perform all statistical analysis. The statistical significance level was set at .05. Data were described as the mean±S.D. SUVmax of liver on FDG PET in the four groups (no fatty liver, mild-degree, moderate-degree, and severe-degree fatty liver) was compared by analysis of variance (ANOVA). The relationship between severity of fatty liver and SUVmax of liver on FDG PET was analyzed by multiple linear regression analysis.

3. Results

A total of 104 males and 69 females were recruited in this study. The mean age of the subjects was 53.54±9.47 years. The range of GPT values among the subjects was 8–184 IU/L. There were 61 subjects without fatty liver, 49 subjects with mild-degree fatty liver, 42 subjects with moderate-degree fatty liver, and 21 subjects with severe-

Table 1
Number of subjects, sex, mean values of BMI, and SUVmax of liver on FDG PET in four groups: no fatty liver, mild-degree, moderate-degree and severe-degree fatty liver

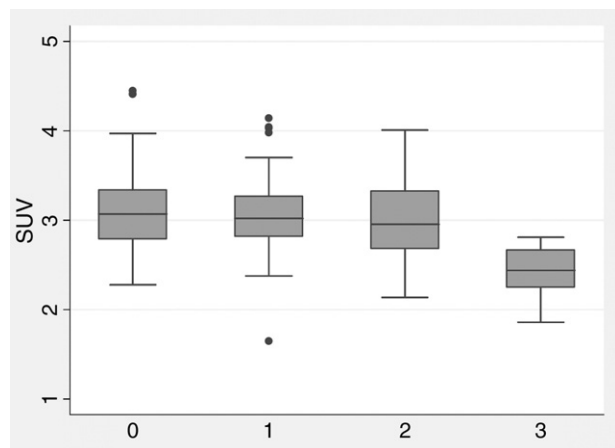| Degree of fatty liver	No	Mild	Moderate	Severe	P
Number of subjects	61	49	42	21	
Male vs. female	31 vs. 30	21 vs. 28	10 vs. 32	7 vs. 14	
BMI	22.10±2.98	24.58±2.48	25.90±3.78	23.70±3.83	<.001
SUVmax	3.13±0.49	3.08±0.45	3.01±0.44	2.43±0.27	.041

Fig. 1. Box plot of SUVmax of liver on FDG PET in four groups: no fatty liver, mild degree, moderate-degree, and severe-degree fatty liver.

Table 3
Relationship between age, sex, fatty liver severity and GPT, and maximum SUV of liver on FDG PET in different levels of BMI by multiple linear regression analysis

SUVmax vs.	Coefficient	P
BMI less than 18.5 (underweight)		
Age	−.03	.005
Sex	.36	.07
Fatty liver severity	−.64	.003
GPT	.13	.01
BMI 18.5–24.9 (optimal)		
Age	.004	.41
Sex	.09	.31
Fatty liver severity	−.21	<.001
GPT	.001	.69
BMI above 25 (overweight)		
Age	.0002	.98
Sex	−.93	.62
Fatty liver severity	−.14	.085
GPT	.002	.48

degree fatty liver. The mean values of BMI in subjects without fatty liver, mild fatty liver, moderate fatty liver, and severe fatty liver were 22.10±2.98, 24.58±2.48, 25.90±3.78, and 23.70±3.83. There were significant differences in BMI in four groups by ANOVA ($P<.001$) (Table 1). The mean SUVmax of liver in subjects without fatty liver, mild degree, moderate-degree and severe-degree fatty liver were 3.13±0.49, 3.08±0.45, 3.01±0.44, and 2.43±0.27. There were significant differences in SUVmax of liver on FDG PET in four groups by ANOVA ($P=.041$) (Table 1) (Fig. 1). After adjusting possible covariates age, sex, BMI, and GPT, there was significantly negative correlation between severity of fatty liver and SUVmax of liver on FDG PET by multiple linear regression analysis ($\beta=-.20$, $P<.001$) (Table 2). There was a significantly positive correlation between BMI and SUVmax of liver on FDG PET by multiple linear regression analysis ($\beta=.035$, $P=.002$).

There was a significantly positive correlation between BMI and the severity of fatty liver by Pearson correlation ($\beta=.30$, $P<.001$). Since BMI was the significant predictor for SUVmax of liver on FDG PET, the subjects were stratified by BMI values. According to the World Health Organization classification, a BMI of 18.5 to 24.9 indicates optimal weight [14]. Thus, the subjects were divided into three groups by BMI values: a BMI lower than 18.5 (an underweight person), 18.5 to 24.9 (person with optimal

Table 2
Relationship between age, sex, BMI, fatty liver severity and GPT, and SUVmax of liver on FDG PET by multiple linear regression analysis

SUVmax vs.	Coefficient	P
Age	.002	.59
Sex	.025	.75
BMI	.035	.002
Fatty liver severity	−.20	<.001
GPT	.002	.3

weight), and above 25 (an overweight person). When a BMI was lower than 18.5, there was a significantly negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET by multiple linear regression analysis ($\beta=-.64$, $P=.003$). When a BMI was 18.5 to 24.9, there was a significantly negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET by multiple linear regression analysis ($\beta=-.21$, $P<.001$). When a BMI was above 25, there was a trend of negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET by multiple linear regression analysis ($\beta=-.14$, $P=.085$) (Table 3).

4. Discussion

The SUV is a quantitative parameter of the glucose metabolic rate. The intensity of physiological FDG uptake in the liver varies. One study showed that there is positive correlation between serum liver enzyme levels and standard uptake values of liver on FDG-PET [15]. A significant correlation between SUV of the liver and BMI, triglycerides, and HDL cholesterol [16] has been reported. A significantly positive correlation between SUVmax of the liver and BMI was also noted in the present study.

Fatty liver is commonly associated with alcohol or metabolic syndrome (diabetes, obesity, and dyslipidemia). Nonalcoholic fatty liver disease is recognized as an important cause of decompensated liver disease and is frequently associated with insulin resistance. Liver with extensive inflammation and high degree of steatosis often progress to a more severe form of the disease. Hepatocyte ballooning and hepatocyte necrosis of varying degree are often present at the advanced stage. Liver cell death and inflammation lead to the hepatic fibrosis. The extent of fibrosis varies widely, which may contribute to low FDG uptake in the liver in fatty liver disease

subjects. Up to 10% of cirrhotic alcoholic fatty liver disease will develop hepatocellular carcinoma. The association of liver cancer in nonalcoholic fatty liver disease is well established [17–21].

In this study, there were significant differences in BMI in subjects without fatty liver, mild fatty liver, moderate fatty liver, and severe fatty liver. There was a significantly positive correlation between BMI and the severity of fatty liver. The findings were compatible with the known association between obesity and hepatic steatosis [18]. The severity of fatty liver was the significant predictor for SUVmax of liver on FDG PET in underweight subjects and subjects with optimal weight. There was a trend of negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET in overweight subjects. When low FDG uptake in the liver was found, the possibility of fatty liver disease might be considered.

Abele et al. [22] reported that hepatic steatosis did not have any significant effect on FDG uptake by the liver as determined by using mean SUV values. Nevertheless, the results of the present study showed the significantly negative correlation between the severity of fatty liver and SUVmax of liver on FDG PET. The possible reasons for the different results were as follows: (a) the subjects were all oncologic patients in the study by Abele et al. However, all subjects in the current study were non-oncologic. The quite different study population may have different results; (b) the diagnostic tools in the assessment of fatty liver were different in the two studies. Unenhanced CT was used in the study of Abele et al., but ultrasonography was used in the current study in assessment of hepatic steatosis. Compared the diagnostic performance in assessment of hepatic steatosis, sensitivity of ultrasonography and unenhanced CT was 65% and 74%, and specificity was 77% and 70%, respectively [23]; (c) the fatty liver case number in the current study was about three times of that in study of Abele et al. Thus, the power of the current study was higher than that of the study by Abele et al.

One potential problem with our study was that no subject had liver biopsy done to confirm the diagnosis of fatty liver and the grading.

5. Conclusion

In conclusion, we observed a significantly negative association between the severity of fatty liver and SUVmax of liver on FDG PET. Specifically, hepatic steatosis had a significantly negative impact on FDG uptake by the liver as determined by using SUVmax. Based on the results of this study, the liver cannot be used as a comparator of extrahepatic foci of equivocal increased FDG activity in patients with fatty liver disease. Whether liver activity is acceptable to use as a stable comparator or not in patients with fatty liver disease needs future studies.

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