DOI: 10.24996/ijs.2026.67.9.17

ISSN: 0067-2904

Evaluation of Age and Body Mass Index-Related Changes in Standardized Uptake Values in the Normal Liver on ^{18}F-FDG Positron Emission Tomography

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Received: 10/5/2025 Accepted: 23/ 10/2025 Published: xx

Abstract

The physiological level of 2-[18F]-fluoro-2-deoxy-D-glucose (^{18}F-FDG) absorption in the liver varies. Before interpreting whole-body positron emission tomography-computed tomography (PET-CT) imaging for cancer detection. It is critical to understand the different levels of FDG accumulation in the liver, which are indicative of physiological changes and normal distribution of ^{18}F-FDG. the aim of this study is to monitor the possible variables that influence the level of physiological FDG uptake in the liver as seen by FDG PET-CT imaging. A total of two hundred participants underwent ^{18}F-FDG PET/CT tests between March to July 2024 and were categorized into seven age groups. Demographic information was obtained from chart records. The maximum Standard Uptake Values (SUVs) and the Body Mass Index (BMI) of the liver were computed for each subject. It was noted that BMI has an effect on FDG uptake. FDG uptake differed significantly across the low and high BMI groups, as did liver SUV_{max} and FDG uptake with age. The most significant predictor of SUV_{max} was age. The subjects were divided into seven age groups. SUVs experienced a significant increase up to the age group 48-58 year. The study concluded that differences in liver SUVs are significantly influenced by age. Our research revealed the alterations in SUVs with age. The determined normal range of SUVs in the liver may assist physicians in the more precise detection of malignancies. Further, the uptake of hepatic FDG is influenced by, and correlated with BMI.

Key words: Body mass index; standardized uptake value (SUV); liver; whole-body PET/CT imaging

تقييم التغيرات المرتبطة بالعمر وكتلة مؤشر الجسم في قيم الامتصاص المعيارية في الكبد السليم باستخدام التصوير المقطعي بالإصدار البوزيتروني ^{18}F–FDG

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الخلاصة

يتذبذب مستوى امتصاص الكبد الفسيولوجي لـ ^{18}F–FDG . من الضروري فهم المستويات المختلفة لتراكم FDG في الكبد، والتي تشير إلى تغيرات فسيولوجية وتوزيع طبيعي لـ ^{18}F–FDG، قبل تفسير تصوير الجسم الكامل بالتصوير المقطعي بالإصدار البوزيتروني – التصوير المقطعي المحوسب (PET–CT) للكشف عن السرطان. يهدف هذا البحث إلى دراسة العوامل المحتملة التي تؤثر على درجة امتصاص FDG الفسيولوجي في الكبد، كما لوحظ فيالتصوير المقطعي بالإصدار البوزيتروني – التصوير المقطعي المحوسب. خضع مئتا مشارك لاختبارات التصوير المقطعي بالإصدار البوزيتروني باستخدام ^{18}F–FDG بين اذار – تموز 2024، وصُنفوا إلى سبع فئات عمرية. تم الحصول على المعلومات الديموغرافية من سجلات المخططات البيانية. وحُسبت قيم الامتصاص المعياري القصوى (SUVs) ومؤشر كتلة الجسم للكبد لكل مشارك. اشارت النتائج الى ان مؤشر كتلة الجسم على امتصاص FDG. اختلف امتصاص FDG بشكل كبير بين المجموعتين ذات مؤشر كتلة الجسم المنخفضة والمرتفعة، كما اختلف الحد الأقصى لقيمة الامتصاص القياسية في الكبد وامتصاص FDG مع التقدم في العمر. كان أهم مؤشر لقيمة الامتصاص القياسية القصوى في الكبد هو العمر. قسّم البحث المشاركين إلى سبع فئات عمرية فيما يتعلق بالكبد. شهدت قيم الامتصاص القياسية القصوى زيادة كبيرة حتى سن 48 عامًا. استنتجت الدراسة ان تتأثر الفروق في قيم الامتصاص القياسية للكبد بشكل كبير بالعمر. كما تم تحديد النطاق الطبيعي لقيم الامتصاص القياسية في الكبد، مما قد يساعد الأطباء في الكشف الدقيق عن الأورام الخبيثة. علاوة على ذلك، يتأثر امتصاص FDG الكبدي بمؤشر كتلة الجسم ويرتبط به.

1. Introduction

Nowadays, 2-[18F]-fluoro-2-deoxy-D-glucose(^{18}F-FDG) Positron-Emission Tomography/Computed Tomography (PET/CT) is used for staging, restaging, recurrence detection, and therapy response monitoring by integrating metabolic and anatomical information. PET/CT detects regions with increased glycolytic metabolism and membrane glucose transporter (GLUT) protein to detect cancerous tumors [1-2]. Nevertheless, the enhanced retention of FDG is not exclusive to cancerous tissue alone [3-6]. Physiological FDG-uptake in a normal liver exhibits varying degrees of intensity. Familiarity with the different levels of FDG normal accumulation, that indicate normal distribution of ^{18}F-FDG, and the physiological changes as well as the Standardized Uptake Values (SUVs) of this organ(liver) are crucial to be studied before interpreting PET-CT scans for the identification of cancer [7].

SUVs provide a semi-quantitative analysis of the PET data. It is often used to measure the static accumulation of FDG in target tissues and to quantify radiopharmaceutical concentration in tissues, helping to distinguish tumors from normal tissue or track changes in metabolic activity over time. The SUV is frequently described as a semi-quantitative factor since it is not a true kinetic rate constant. As a normalized target-to-background metric, the SUV analyzes variables for body weight, lean body mass, and body surface area [8-10]. In this work, the widely accepted method of calculating. SUV is defined as activity concentration (MBq/ml) in a chosen region of interest (ROI) or volume of interest (VOI) relative to the injected activity ID (MBq) corrected for decay of the radionuclide multiplied by the body weight (g) and can be calculated by the following equation [11]:

$$SVU\left(\frac{g}{ml}\right) = \frac{average\ activity\ in\ ROI(\frac{MBq}{ml})}{injected\ dose\ (MBq)} \times body\ weight\ (g) \ldots\ldots\ldots (1)$$

It should be noted that the buildup of physiological ^{18}F-FDG can be substantial in certain organs, and that this might sometimes imitate pathological conditions. Identification of this physiological activity is crucial for the precise analysis of a whole-body ^{18}F-FDG-PET study

[12, 13]. In addition to its application in research on glucose metabolism [14], hepatic FDG uptake serves as the benchmark for diagnosis, quality control, treatment evaluation, and prognosis. Previous studies have indicated that liver FDG uptake is influenced by age, blood glucose level, body mass index (BMI), incubation period, and hepatic steatosis [15-17].
the aim of this study is to assess the many variables that can influence the liver's physiological absorption of FDG during FDG PET imaging.

2. Materials and methods

The study comprised a total of 200 participants (72 males and 128 females), aged between 18 and 87 (mean age 54.73 ± 14.06 years), with body weights ranging from 31 to 124 kg (mean weight of 75.53 ± 16.72 kg). Participants were from Al-Safeer Hospital, Baghdad. Clinical PET/CT examinations for oncological indications were done between March and July 2024. This study does not require ethical approval. Patients who had undergone chemotherapy or radiotherapy within 4 weeks before the examination were excluded from the study.

The patients were instructed not to perform any heavy muscular activity 24 hours prior to the exam to prevent unnecessary uptake and minimize the imaging background. They were advised to consume 1 liter of water within two hours prior to FDG administration to ascertain whether the concentration of ^{18}F-FDG was within the standard range (< 120 mg/dl for non-diabetics). Both European and American recommendations for PET/CT imaging advise measuring blood glucose levels before the scanning, postponing the test if the level is above 200 mg/dl [18].

A comprehensive patient history was obtained encompassing information regarding prior chemotherapy and/or radiotherapy. The ^{18}F-FDG injection dose (mCi), blood glucose level (mg/dl), the age of the patients (years), and their height (cm) and weight (kg) at the time of the exam were reported. Their body mass index (BMI) was then computed via the following formula [18]:

$$BMI = \frac{Weight\ (Kg)}{Height(m)^2} \dots\dots\dots (2)$$

The patients' nutritional state was categorized based on World Health Organization criteria [18]. Based on the calculated BMI, patients were classified into four nutritional status categories, as shown in Table 1.

Table 1: Classification of participants based on BMI [18]

BMI (kg/ m^2)	Weight Status
Below 18.4	Underweight
18.5 – 24.9	Normal
25.0 – 29.9	Overweight
30.0 – 43.9	Obese grade I
35-39.9	Obese grade II
Greater than or to 40	Obese grade III

Before entering the PET examination room, patients were provided with instructions to empty their bladders. They were positioned in a supine posture, elevating their arms and anteriorly positioning their heads. The bed shuttle was arranged to begin the PET phase of the treatment after a CT scan for attenuation correction. Throughout the PET/CT procedure, patients were

instructed to remain motionless and engage in shallow breathing. Spacing was deliberately maintained between artifacts, metals, and other objects that can cause attenuation to maintain a good quality image and avoid any reduction in resolution. Emission data were gathered over a timeframe of 45 to 90 minutes following the administration of ^{18}F-FDG.

2.1 PET/CT examinations

The study was performed with a GEMINI TF PET/CT system (Philips Medical Systems, Cleveland, OH, USA). The scanner's detector used lutetium-yttrium oxyorthosilicate (LYSO) crystals measuring 4 × 4 × 22 millimeters. A CT facility outfitted with a 64-slice scanner was used, with a stable tube voltage of 90, 120, or 140 kilovolts peak (kVp). The tube current time product (mAs) varied between 20 and 500 mAs.

An FDG dose at a concentration of (0.1-0.2) mCi per kg of body weight was administered intravenously through an IV line inserted in the patient's arm or hand. The PET scan was performed immediately thereafter, followed by a diagnostic CT scan. A low-dose CT scan was conducted to adjust for attenuation and scatter. The diagnostic CT exams were conducted using a tube peak voltage of 120 kV and a rotation speed of 0.44 seconds.

Typically, the scan encompassed the area from the middle of the cranium to the upper part of the thigh. Images were acquired at 45-90 minutes' post-injection of FDG. Three-dimensional PET data were acquired for 1-4 minutes at each bed position while the subject was breathing normally. Furthermore, apart from accounting for attenuation and scatter, all the data underwent correction for dead time and random coincidences.

2.2 Statistical Analysis

The data were reported using the mean and standard deviation (SD). Microsoft Office Excel 2016 was used for all statistical analyses. For comparison purposes a paired and unpaired Student's t-test was done, a result was considered statistically significant if $P < 0.05$.

3. Results

The patients' height (m), weight (kg), glycemia at study time (mg/dl), age (years), and the delivered dose of ^{18}F-FDG (mCi) were recorded. Equation 2 was then used to calculate the BMI.

All participants underwent ^{18}F-FDG PET examinations with a mean of 7.77 ± 1.25 mCi. The mean ± SD dose injected/weight was 0.10 ± 0.01mCi/kg. Average body weight was 75.53 ± 16.72 kg, and average height was 1.62 ± 0.09 m. Blood glucose level was measured for all patients prior to injection. The demographic data recorded for the patients are reported in Table 2.

Table 2: Characteristics of participants included in the study

Parameters	Normal cases (n=200) Mean ±SD
Age (years)	54.73 ± 14.06
Body mass (kg)	75.53 ± 16.72
Height (m)	1.62 ± 0.09
BMI (Kg/m^2)	28.62 ± 7.01
^{18}F-FDG (mCi)	7.77 ± 1.25
Dose injected /weight (mci/kg)	0.10 ± 0.01
SUV_{max} (g/ml)	2.38 ± 0.61

3.1 Relation between injection dose and BMI

Table 3 displays the average maximal ^{18}F-FDG uptake (injection dose) of the examined tissues across the four BMI groups. The increase in ^{18}F-FDG uptake with higher BMI was noted to be statistically significant.

The study evaluated the FDG PET/CT whole-body images of 200 patients. Mean ± SD injected ^{18}F-FDG activity was 6.88 ± 0.47 mCi for patients with low weight, 7.01 ± 0.96 mCi for those of normal weight, 7.70 ± 0.91 for those who were overweight, and 8.55 ± 1.27 for those who were obese.
Comparisons between the four groups of BMI were then obtained, revealing a statistically significant difference between all groups, as reported in Table 3.

Table 3: Results of the administration of ^{18}F-FDG

Groups	Mean ± SD					
	Weight (kg)	Height (m)	BMI kg/(m)^2	Injection dose (mCi)	Dose/weight (mCi/kg)	p-value
Low weight	43.42 ± 6.67	1.67 ± 0.10	15.47 ± 0.12	6.88 ± 0.47	0.12 ± 0.01	< 0.05
Normal weight	62.58 ± 8.43	1.64 ± 0.08	23.03 ± 1.52	7.01 ± 0.96	0.11 ± 0.01	< 0.05
Overweight	73.01 ± 8.30	1.64 ± 0.08	26.97 ± 1.27	7.70 ± 0.91	0.10 ± 0.01	< 0.05
Obese	90.83 ± 14.06	1.60 ± 0.08	35.06 ± 4.6	8.55 ± 1.27	0.09 ± 0.01	< 0.05

3.2 Relation between SUV_{max} with BMI

Upon examining the average liver SUV values based on BMI, as reported in Table 4, a significantly high value of SUV_{max} was observed among obese individuals.
The mean values of BMI SUV_{max} were 2.07 ± 0.53, 2.11 ± 0.47, 2.38 ± 0.65, and 2.56± 0.47, for low weight, normal weight, overweight, and obese patients, respectively. The results showed a significant change between SUV_{max} and BMI for the liver, p-value < 0.05.

Table 4: SUV_{max} values according to BMI

Groups	**Mean ± SD**		
	BMI kg/(m)^2	**SUV_{max} (g/ml)**	**p-value**
Low weight	15.47 ± 0.12	2.07 ± 0.53	< 0.05
Normal weight	23.03 ± 1.52	2.11 ± 0.47	< 0.05
Overweight	26.97 ± 1.27	2.38 ± 0.65	< 0.05
Obese	35.06 ± 4.6	2.56 ± 0.47	< 0.05

3.3 Relation between age, SUV_{max}, and FDG uptake

The subjects were grouped into seven age groups (18–28, 28–38, 38–48, 48–58, 58–68, 68–78, and 78–88 years). Overall, the liver SUV_{max} (from 2.72±0.57 to 2.83±0.72) showed a significant increase until the age group 48-58, as can be seen in Table 5.

Table 5: Mean SUVs and ^{18}F-FDG uptake of normal liver in different subject age groups.

Age (years)	SUV_{max} (g/ml)	p-value	^{18}F-FDG uptake (mCi)	p -value
18-28	2.72 ± 0.57	<0.05	7.65 ± 1.14	<0.05
28-38	2.76 ± 0.81	>0.05	7.99 ± 1.32	>0.05
38-48	2.79 ± 0.62	<0.05	8.15 ± 1.44	<0.05
48-58	2.83 ± 0.72	<0.05	8.32 ± 1.19	<0.05
58-68	2.79 ± 0.83	<0.05	8.43 ± 1.23	<0.05
68-78	2.75 ± 0.80	<0.05	7.62 ± 1.29	<0.05
78-88	2.66 ± 0.75	<0.05	7.18 ± 0.68	<0.05

4. Discussion

Observing, characterizing, and measuring biological events at the molecular and cellular levels within a living creature is known as molecular imaging.

One of the medical imaging modalities that is rapidly growing in use for the clinical management of cancer patients is PET [19]. Inaccurate physiological FDG uptake recordings might cause a PET scan to be misinterpreted, which can reduce the effectiveness of the procedure and produce false diagnostic results [20]. Numerous studies have shown the reasons behind the physiological variation in the distribution of FDG [21].

This study aimed to determine the impact of patient-and procedure-related variables, specifically SUV_{max} and FDG uptake, on liver metrics. It was found that age and BMI are important determinants of liver SUV_{max}. Establishing a reference range of SUVs with ^{18}F-FDG PET/CT across a range of age groups is clinically valuable, as prior research has identified a correlation between age and SUVs [22-23].

In this five-month retrospective study of 200 people, it was found that the liver's SUV_{max} rose until the age group 48-58; after that, it decreased.

Seven age groups were studied in this investigation to determine a normative range of baseline SUVs. When treating cancer patients of different ages, this can help physicians select appropriate SUVs based on the reference background. The age-related SUV patterns found in our study have several reasonable biological explanations. Organ metabolism, organ degeneration, and molecular transport provide insight into the relevant mechanisms. At the cellular level, the volume of hepatocytes increases with age, whereas the quantity of hepatocytes and their functional volume both significantly decrease [24]. Moreover, there is a favorable correlation between hepatic metabolic activity and age in adults [25]. According to earlier studies, the increase in FDG uptake with age may suggest changes in liver volume and hepatocyte amount as well as age-related metabolic activity [26]. Cao et al. suggested that there might be age-related hepatotoxins causing cumulative inflammatory changes [25]. The trends in blood pool SUV may be explained by the organ's metabolic rate, which is regulated by ageing [27]. The similarities between previous research and our own analysis indicate that our results have a high degree of scientific validity.

The effects of age, BMI, and dose on ^{18}F-FDG uptake in the liver have been documented in numerous studies [28, 29]. These effects were examined in 51 patients (28 males and 23 females) in a study conducted by Mahmud et al. [30].

Our data showed no discernible positive correlation between age and liver SUV_{max}, which could be because of the small sample size, the inclusion of elderly patients, and differences in SUV_{max}. Lin et al. conducted a study of 339 asymptomatic subjects [31], examining the correlations between liver SUVs and sex, age, and HBV and HCV infection status. The authors

reported that liver SUVs were significantly positively correlated with age. The other factors did not exhibit any significant associations with SUVs [23].

In the current study, a statistically significant and positive correlation was observed between the liver's SUV and age. This suggests that the physiological uptake of FDG in the liver may be higher in elderly individuals than in younger adults. High levels of physiological background could potentially reduce the diagnostic sensitivity and accuracy of FDG PET imaging in the identification of malignant lesions. This could cause false negatives in liver tests in older people.

Finally, age has a considerable and beneficial impact on the liver's maximal and mean SUV in FDG PET imaging. The high physiological baseline FDG uptake will reduce the diagnostic sensitivity and accuracy of liver cancer detection. Previous research has documented the influence of body weight and BMI on the delivery of FDG to tissue and circulation [32]. Our research has verified that individuals with a higher body mass index (BMI) exhibit a higher level of normal blood and tissue FDG absorption than those with a lower BMI. This is most likely due to the fact that fat accumulates minimal amounts of FDG during a fasting state, resulting in a higher absorption of FDG by non-fatty tissue.

5. Conclusion

1. When calculating liver SUV_{max}, age is probably a major factor. As people age, their liver's physiological uptake of FDG can change significantly. Before analyzing whole-body PET/CT images the liver background SUV_{max} changes with age should be determined to follow the progress of the disease.
2. SUV_{max} overestimates all patients' metabolic activity, and to a more significant extent in obese individuals than in those with a normal BMI.

6. Recommendations

1. Reducing patient radiation exposure is an essential objective. Patients must be protected from excessive exposure to radiation in the course of ^{18}F-FDG whole-body PET/CT investigations while still preserving or enhancing diagnostic quality. Our research indicates that this objective is attainable when BMI is used as the criterion for dose modification. Within our department, BMI has emerged as a significant factor in ^{18}F-FDG whole-body PET/CT studies and has the potential to be similarly utilized in any department where it is adopted.
2. To support the current study and ensure the accuracy of the results, it is essential to conduct additional studies with a larger patient population and across different organs. This will enable a more comprehensive statistical analysis and more accurate results.

7. Acknowledgments

The author expresses gratitude to the University of Baghdad/ College of Medicine. Gratitude is extended to AL-Safeer Hospital/Nuclear Medicine Department, Baghdad, for their assistance and counsel throughout this endeavor.

8. Limitations of the study

Since our study only included one organ and the sample size was small, more individuals would be needed to obtain more precise and trustworthy results. Additionally, a variety of cancer types should be studied in order to determine the maximum SUV for each organ.

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