

Impact of age on FDG uptake in the liver on PET scan

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Abstract

Purpose: The intensity of physiological 18F-2-deoxy-D-glucose (FDG) uptake in the liver varies. It is important to be familiar with the varying degree of FDG accumulation in the liver that represents normal distribution and physiological changes, before attempting to interpret whole-body positron emission tomography (PET) imaging for malignancy detection. The aim of this study is to evaluate the possible factors influencing the intensity of physiological FDG uptake in the liver on FDG PET imaging. **Materials and Methods:** From 2005 to 2007, a total of 339 consecutive healthy subjects, referred from the Department of Community Medicine and Health Examination Center of our hospital for health screening, were retrospectively recruited for analysis. Demographic data were collected from chart records. Whole body FDG PET imaging and serologic determination of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection status were performed on all subjects. The mean and maximum standard uptake values (SUVs) of the liver were calculated. The relationships between sex, age, HBV and HCV infection status, and SUVmax and SUVmean of the liver on FDG PET imaging were evaluated. **Results:** There was no statistically significant relationship between sex, HBV and HCV infection status and maximum standard uptake value (SUVmax) or mean standard uptake value (SUVmean) of the liver. After adjusting for covariables, age was a statistically significant predictor of SUVmax ($B=0.18$; $P=.001$) and SUVmean ($B=0.16$; $P=.004$) of the liver on FDG PET imaging. **Conclusion:** Age has a significant and positive impact on both maximum and mean standard uptake values of the liver on FDG PET imaging. High physiological background FDG uptake will reduce diagnostic sensitivity and accuracy for malignancy detection in the liver.

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Keywords: Whole-body PET imaging; Standard uptake values

1. Introduction

Clinical use of positron emission tomography (PET) has grown rapidly due to its usefulness in cancer diagnosis, staging, and management. 18F-2-deoxy-D-glucose (FDG) PET is a functional imaging modality, which reflects cellular

glucose metabolism. Accumulation and trapping of FDG allow the visualization of increased uptake in most malignant cells compared to normal cells. FDG is the most commonly used radiopharmaceutical for positron emission tomography studies in oncology and the tracer is a substrate of energy metabolism [1,2]. However, increased FDG uptake is not limited to malignant tissue alone [3–7]. The intensity of physiological FDG uptake in the liver varies. It is important to be familiar with the varying degree of FDG accumulation that represents normal distribution and physiological changes, before attempting to interpret whole-body PET imaging for malignancy detection. The aim of this study is to evaluate the

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possible factors influencing the intensity of physiological FDG uptake in the liver on FDG PET imaging.

2. Materials and methods

2.1. Subjects

From 2005 to 2007, a total of 339 consecutive healthy subjects, referred from the Department of Community Medicine and Health Examination Center of our hospital for health screening, were retrospectively recruited for analysis. Demographic data were collected from chart records. Whole body FDG PET imaging and serologic determination of hepatitis B virus (HBV) and hepatic C virus infection status were performed on all subjects. Infections with HBV and hepatitis C virus (HCV) were defined as positive serum tests for HBsAg and anti-HCV antibody, respectively. The mean and maximum standard uptake values (SUV) of the liver were calculated. The relationships between sex, age, HBV and HCV infection status, and SUVmax and SUVmean of the liver on FDG PET imaging were evaluated. The SPSS statistical package version 13.0 was used for statistical analysis, and the conventional *P* value of .05 was used as the cutoff for statistical significance.

2.2. FDG-PET imaging

Whole body PET images were acquired on a GE Advance NXi scanner (35 image planes, 4.30 mm/slice, 15 cm axial-field-of-view), 40 min–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 minutes 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.

The SUV, 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.

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

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

3. Results

A total of 339 subjects, 134 male and 205 female, were recruited in the study. The mean age of the subjects was 54.09 ± 9.96 years. The mean of the maximum standard uptake value (SUVmax) of the liver was 2.89 ± 0.56 . The

Table 1
Demographic data of subjects

	No.	
Sex (male; female)	134; 205	
	Mean	S.D.
Age (year)	54.09	9.96
SUVmax of liver	2.89	0.56
SUVmean of liver	2.37	0.45

mean of the mean standard uptake value (SUVmean) of the liver was 2.37 ± 0.45 (Table 1). There was no statistically significant relationship between sex, HBV and HCV infection status, and SUVmax or SUVmean of the liver. After adjusting for covariables, age was a statistically significant predictor of SUVmax ($B=0.18$; $P=.001$) (Table 2) and SUVmean ($B=0.16$; $P=.004$) of the liver on FDG PET imaging (Table 3).

4. Discussion

Molecular imaging is the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in a living system. PET is one of the most rapidly growing areas of medical imaging in the clinical management of patients with cancer [8]. However, some physiological FDG uptake can cause misinterpretation of a PET scan and, as a consequence, may lead to false-positive or false-negative reports, thus reducing the accuracy of the technique [9–12]. The causes of physiological variation in FDG distribution have been reported in articles [7,13–15]. It has been reported that there was positive relationship in age and mean SUV of the liver on FDG PET imaging, but the relationship between age and maximal SUV of the liver on FDG PET was not assessed [16]. In this study, we found that age was a significant predictor in the both SUVmax and SUVmean of the liver on FDG PET imaging.

HBV infects more than 350 million people worldwide [17]. Hepatitis B infection is a leading cause of chronic hepatitis, liver cirrhosis, and hepatoma in Taiwan. Today, approximately 2.5 million people in Taiwan are carriers of the HBV, and the serum HBsAg-positive carrier rate in the general population is 20.2% in Taiwan [18]. HCV infection is a global health problem. HCV infection is becoming the

Table 2
Relationship between sex, age, HBV, and HCV infection status, and SUVmax of the liver by multiple linear regression analysis

	Beta coefficient	<i>P</i> value
Sex	.003	.96
Age	.182	.001*
HBV infection	.042	.434
HCV infection	-.1	.067

Dependent variable: SUVmax of the liver.

* $P < .05$.

Table 3
Relationship between sex, age, HBV and HCV infection status, and SUVmean of the liver by multiple linear regression analysis

	Beta coefficient	P value
Sex	-.038	.49
Age	.16	.004*
HBV infection	.042	.443
HCV infection	-.095	.083

Dependent variable: SUVmean of the liver.

* $P < .05$.

second most common chronic viral infection in the world with a global prevalence of about 180 million people [19]. Approximately 700,000 people are afflicted with hepatitis C in Taiwan. The prevalence of positive serum test for anti-HCV antibody in the general population in Taiwan is 4% [20]. HBV and HCV infections are the leading risk factors of hepatoma in Taiwan. Nevertheless, FDG PET imaging plays only a limited role in detecting hepatoma, because only 50% of the patients with hepatoma can be detected by FDG PET imaging [21,22].

In this study, we found a statistically significant and positive relationship between age and SUV of the liver. This indicates that older people may have higher physiological FDG uptake in the liver than younger adults. High physiological background FDG uptake may reduce diagnostic sensitivity and accuracy for detecting malignant lesions, and, in an aging population, may result in false negative findings in the liver on FDG PET imaging. In conclusion, age has a significant and positive impact on both maximum and mean SUV of the liver on FDG PET imaging. High physiological background FDG uptake will reduce diagnostic sensitivity and accuracy for malignancy detection in the liver.

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References

- [1] Răileanu I, Rusu V, Ștefănescu C, Cinotti L, Hountis D. 18F FDG PET-applications in oncology. *Rev Med Chir Soc Med Nat Iasi* 2002; 106(1):14–23.
- [2] Son HB, Han CJ, Kim BI, Kim J, Jeong SH, Kim YC, Lee JO, Choi CY, Im SM. Evaluation of various hepatic lesions with positron emission tomography. *Taehan Kan Hakhoe Chi* 2002;8(4):472–80.
- [3] Truong MT, Pan T, Erasmus JJ. Pitfalls in integrated CT-PET of the thorax: implications in oncologic imaging. *J Thorac Imaging* 2006;21(2):111–22.
- [4] Gorospe L, Raman S, Echeveste J, Avril N, Herrero Y, Hernandez S. Whole-body PET/CT: spectrum of physiological variants, artifacts and interpretative pitfalls in cancer patients. *Nucl Med Commun* 2005;26(8):671–87.
- [5] Cook GJ. Pitfalls in PET/CT interpretation. *Q J Nucl Med Mol Imaging* 2007;51(3):235–43.
- [6] Cook GJ, Wegner EA, Fogelman I. Pitfalls and artifacts in 18FDG PET and PET/CT oncologic imaging. *Semin Nucl Med* 2004;34(2):122–33.
- [7] Lin CY, Ding HJ, Liu CS, Chen YK, Lin CC, Kao CH. Correlation between the intensity of breast FDG uptake and menstrual cycle. *Acad Radiol* 2007;14(8):940–4.
- [8] Vallabhajosula S. (18)F-labeled positron emission tomographic radiopharmaceuticals in oncology: an overview of radiochemistry and mechanisms of tumor localization. *Semin Nucl Med* 2007;37(6):400–19.
- [9] Dong MJ, Lin XT, Zhao J, Guan YH, Zuo CT, Chen X, Dai JZ, Jiang BD. Malignant tumor with false negative 18F-FDG PET image. *Zhonghua Zhong Liu Za Zhi* 2006;28(9):713–7.
- [10] Mahmood S, Martinez de Llano SR. Paget disease of the humerus mimicking metastatic disease in a patient with metastatic malignant mesothelioma on whole body F-18 FDG PET/CT. *Clin Nucl Med* 2008;33(7):510–2.
- [11] Acar C, Akkas BE, Sen I, Sen I, Kitapci MT. False positive 18F-FDG PET scan in adrenal oncocytoma. *Urol Int* 2008;80(4):444–7.
- [12] Roarke MC, Nguyen BD, Pockaj BA. Desmoplastic melanoma: true positive and false negative findings on F-18 FDG-PET/CT. *Clin Nucl Med* 2008;33(8):562–4.
- [13] Thie JA, Hubner KF, Isidoro FP, Smith GT. A weight index for the standardized uptake value in 2-deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography. *Mol Imaging Biol* 2007;9(2):91–8.
- [14] Kitajima K, Murakami K, Yamasaki E, Kaji Y, Sugimura K. Standardized uptake values of uterine leiomyoma with 18F-FDG PET/CT: variation with age, size, degeneration, and contrast enhancement on MRI. *Ann Nucl Med* 2008;22(6):505–12.
- [15] Chin BB, Green ED, Turkington TG, Hawk TC, Coleman RE. Increasing uptake time in FDG-PET: standardized uptake values in normal tissues at 1 versus 3 h. *Mol Imaging Biol* 2009;11(2):118–22.
- [16] Meier JM, Alavi A, Iruvuri S, Alzeair S, Parker R, Houseni M, Hernandez-Pampaloni M, Mong A, Torigian DA. Assessment of age-related changes in abdominal organ structure and function with computed tomography and positron emission tomography. *Semin Nucl Med* 2007;37(3):154–72.
- [17] Custer B, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL, Knowlley KV. Global epidemiology of hepatitis B virus. *J Clin Gastroenterol* 2004;38(10 Suppl 3):S158–68.
- [18] Lu JN, Chen CJ. Prevalence of hepatitis B surface antigen carrier status among residents in the endemic area of chronic arsenicism in Taiwan. *Anticancer Res* 1991;11(1):229–33.
- [19] Craxi A, Laffi G, Zignego AL. Hepatitis C virus (HCV) infection: a systemic disease. *Mol Aspects Med* 2008;29(1-2):85–95 [Epub 2007 Nov 21].
- [20] Sun CA, Chen HC, Lu CF, You SL, Mau YC, Ho MS, Lin SH, Chen CJ. Transmission of hepatitis C virus in Taiwan: prevalence and risk factors based on a nationwide survey. *J Med Virol* 1999;59(3):290–6.
- [21] Eastman RC, Carson RE, Orloff DG, Cochran CS, Perdue JF, Rechler MM, Lanau F, Roberts Jr CT, Shapiro J, Roth J, et al. Glucose utilization in a patient with hepatoma and hypoglycemia. Assessment by a positron emission tomography. *J Clin Invest* 1992;89(6):1958–63.
- [22] Enomoto K, Fukunaga T, Okazumi S, Asano T, Kikuchi T, Yamamoto H, Nagashima T, Isono K, Itoh H, Imazeki K, et al. Can fluorodeoxyglucose-positron emission tomography evaluate the functional differentiation of hepatocellular carcinoma. *Kaku Igaku* 1991;28(11):1353–6.