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Variations of the liver standardized uptake value in relation to background blood metabolism

An 2-[^{18}F]Fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography study in a large population from China

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Abstract

To investigate the influence of background blood metabolism on liver uptake of 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}F-FDG) and search for an appropriate corrective method.

Positron emission tomography/computed tomography (PET/CT) and common serological biochemical tests of 633 healthy people were collected retrospectively. The mean standardized uptake value (SUV) of the liver, liver artery, and portal vein (i.e., SUV_L, SUV_A, and SUV_P) were measured. $SUV_{L/A}$ was calculated as SUV_L/SUV_A, while $SUV_{L/P}$ was calculated as SUV_L/SUV_P. SUV of liver parenchyma (SUV_{LP}) was calculated as $SUV_L - .3 \times (.75 \times SUV_P + .25 \times SUV_A)$. The coefficients of variation (CV) of SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} were compared to assess their interindividual variations. Univariate and multivariate analyses were performed to identify vulnerabilities of these SUV indexes to common factors assessed using serological liver functional tests.

SUV_{LP} was significantly larger than SUV_L (2.19 ± .497 vs 1.88 ± .495, $P < .001$), while $SUV_{L/P}$ was significantly smaller than SUV_L (1.72 ± .454 vs 1.88 ± .495, $P < .001$). The difference between $SUV_{L/A}$ and SUV_L was not significant (1.83 ± .500 vs 1.88 ± .495, $P = .130$). The CV of SUV_{LP} (22.7%) was significantly smaller than that of SUV_L (22.7%:26.3%, $P < .001$), while the CVs of $SUV_{L/A}$ (27.2%) and $SUV_{L/P}$ (26.4%) were not different from that of SUV_L ($P = .429$ and .929, respectively). Fewer variables independently influenced SUV_{LP} than influenced SUV_L, $SUV_{L/A}$, and $SUV_{L/P}$; Only aspartate aminotransferase, body mass index, and total cholesterol, all P-values <.05.

The activity of background blood influences the variation of liver SUV. SUV_{LP} might be an alternative corrective method to reduce this influence, as its interindividual variation and vulnerability to effects from common factors of serological liver functional tests are relatively lower than the commonly used SUV_L.

Abbreviations: ^{18}F-FDG = 2-[^{18}F]fluoro-2-deoxy-D-glucose, CV = coefficient of variation, ICC = intraclass correlation coefficient, PET/CT = positron emission tomography/computed tomography, SUV = standardized uptake value, SUV_A = SUV of liver artery, SUV_L = SUV of liver, $SUV_{L/A}$ = SUV_L divide SUV_A, $SUV_{L/P}$ = SUV_L divide SUV_P, SUV_{LP} = SUV of liver parenchyma, SUV_P = SUV of portal vein, VOI = volume of interest.

Keywords: 2-fluoro-2-deoxy-D-glucose (^{18}F-FDG), computed tomography (CT), liver, positron emission tomography (PET), standardized uptake value (SUV)

1. Introduction

The clinical use of 2-[^{18}F]Fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) is growing rapidly because of its usefulness in cancer diagnosis, staging, and treatment-response evaluation.[1–4] Commonly, the determination of liver ^{18}F-FDG uptake is essential for diagnosis, treatment-response assessment, and prognosis of diseases.[1,2] Numerous authors have used the standardized uptake value (SUV) to compare the uptake of ^{18}F-FDG in lesions with the expected normal liver as a reference.[5,6]

^{18}F-FDG uptake is often monitored by measuring the SUV because of its simplicity. However, it has been reported that the liver SUV is vulnerable to variations of many plasma biochemical parameters, such as blood glucose, serological liver enzymes, and serological lipids.[7–11] Another method, where liver activity is corrected by the plasma FDG activity, might be an important alternative, and theoretically, might be more suitable for hepatic tissue, because of its high blood flow.[12] Hunter et al[13] originally described this kind of method by including the total blood volume to obtain an estimate of the arterial input curve,

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which showed a significantly improved value compared with the SUV. A more simple method was proposed by Kanstrup et al[14] who divided the liver SUV by the plasma SUV to generate a tissue-to-background (T/B) ratio, which was identified as largely comparable to the SUVs, but not superior in homogeneous subjects. The liver always demonstrates a heterogeneous ^{18}F-FDG uptake pattern and sometimes shows abnormally increased uptake, even in the absence of a malignant tumor; therefore, the T/B method may be theoretically superior in a nonhomogeneous population or when using different scanners. All these approaches imply, at least in part, the necessity to determine a more suitable SUV index that is free from effect of plasma activity.

About 25% to 30% of the hepatic volume in vivo is made up of blood.[15] Therefore, we assumed that the liver SUV (SUV_L) = (.7 × SUV of the liver parenchyma ($SUV_{L/P}$)) + (.3 × hepatic blood metabolism). The portal (P) vein provides approximately 75% of the blood flow to the liver and the hepatic artery (A) provides the other 25%;[16] therefore, the hepatic blood metabolism can be calculated as $.75 \times SUV_P + .25 \times SUV_A$. Thus, we propose that $SUV_L = (.7 \times SUV_{LP}) + [.3 \times (.75 \times SUV_P + .25 \times SUV_A)]$. Consequently, the blood-free hepatic metabolism-SUV_{LP}-can be calculated as $[SUV_L - .3 \times (.75 \times SUV_P + .25 \times SUV_A)]/.7$. We hypothesized that this index might reflect the metabolism of the hepatic parenchyma more accurately, and might be less influenced by plasma metabolism than SUV_L. To verify this hypothesis, we attempted to compare this corrected index with SUV_L, $SUV_{L/A}$, and $SUV_{L/P}$ with regard to their variations in relation to common factors of plasma biochemical liver functional tests.

2. Materials and methods

2.1. Study population

This study was approved by the institutional ethics committee of our hospital. Informed consent for possible use of data in the future was obtained from all subjects included in this study at the time of initial examinations.

We retrospectively searched the electronic registry system of the PET/CT center in our hospital. A total of 633 patients admitted for cancer screening with PET/CT performed between May, 2011 and October, 2014, who were shown to be free of active disease, were included. The inclusion criteria were: PET/CT covers whole body; clinical reports of PET/CT images had not indicated any meaningful finding except some old and inactive abnormalities, such as calcification, small calculus, small hepatic, or renal cysts. Any patients with any one of the following findings in their medical records that might impact liver metabolic activity were excluded: Malignancy or metastasis, in a status of acute inflammation, hyperthyroidism or hyperparathyroidism, abnormal serological liver enzymes, liver cirrhosis or deposit diseases, liver segmentectomy or transplantation, splenectomy, diabetes with blood glucose > 120 mg/dL, and acute or chronic renal/heart failure. In addition, patients with any laboratory test item (performed within 1 week) beyond the normal range were also excluded.

For all included subjects, data were collected by 2 researchers to avoid errors during data recording. Each patient's height, weight, and main laboratory tests were recorded. All laboratory tests were performed within 1 week of the PET/CT examinations. The body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

2.2. Imaging technique

Before the PET/CT examination, height, weight, and blood glucose were tested and recorded. All patients had fasted for at least 6 hours before the injection of ^{18}F-FDG (4.44 MBq/kg). The amount of injected radioactivity was routinely calculated by measuring the radioactivity of the syringe before and after injection. The mean injected ^{18}F-FDG dose was 347.8 MBq (SD 70.3; range 192.4–599.4 MBq). PET/CT scanning was started 1 hour after intravenous injection of ^{18}F-FDG on a GE Discovery VCT 64 (General Electric, Milwaukee, WI) PET/CT scanner from the skull vertex to the mid-thigh level, in a supine position, and in a caudal-cranial direction with the arms above the head. Helical CT acquisition with no contrast media was performed first using the following parameters: tube current, 200 mAs; tube voltage, 120 to 140 kV; collimation configuration, 64 × .6 mm; pitch, .516; matrix size, 512 × 512; scanning time, .33 second per rotation. For review, the CT images were reconstructed with a slice thickness of 1.5 mm and an increment of 1.25 mm. PET scanning was performed using a three-dimensional (3D) imaging mode with emission scans of 2 min per bed position. Images were reconstructed using the 3D iterative reconstruction method.

2.3. Imaging analysis

All PET/CT images were retrieved from the institutional electronic archival system and reviewed on a GE Advantage Workstation (Mim Vista, Version 4.4; Cleveland, OH). For each patient, 3 different spherical volumes of interest (VOIs) were drawn to measure the SUV of liver (SUV_L), SUV of liver portal vein (SUV_P), and SUV of liver artery (SUV_A) by GL and YH, both of whom had experience of more than 2 years in reading PET/CT images. To measure SUV_L, the VOI was set identically 3 cm in diameter and was placed in the right lobe of the liver at the level of bifurcation of the portal vein, avoiding any obvious vessels (Fig. 1A and B). When measuring SUV_P, a VOI was drawn to cover, but not exceed, the trunk of the portal vein as much as possible (Fig. 1C and D). As the hepatic artery is too small to draw a VOI in it, we chose the area of the abdominal aortic artery at the level of coeliac trunk instead (Fig. 1E and F), considering that liver artery is one of the branches of the coeliac trunk. Based on these SUV indexes, 3 more SUV indexes were calculated. The first one was the liver-to-artery ratio of the SUV (namely $SUV_{L/A}$), calculated as SUV_L/SUV_A. The second one was the liver-to-portal vein ratio ($SUV_{L/P}$), calculated as SUV_L/SUV_P. The third index was the blood-free hepatic parenchymal SUV (SUV_{LP}), which was calculated as $[SUV_L - .3 \times (.75 \times SUV_P + .25 \times SUV_A)]$. For all VOIs, the mean values of SUV indexes were selected for analysis.

2.4. Statistical analysis

The continuous variables were summarized as the mean ± standard deviation (SD), while categorical variables were expressed as frequencies or percentages. Interobserver agreement between the 2 observers (LG and HY) and intraobserver agreements between 2 times of measurements from one reader (LG) were analyzed by calculating intraclass correlation coefficients (ICCs). An ICC >.75 indicated good agreement.[17] The coefficients of variations (CVs) were calculated to compare interindividual variations of SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP}, with the Miller test being performed to test the significance of the difference. Paired *t* tests were performed to compare SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} among the groups of categorical variables.

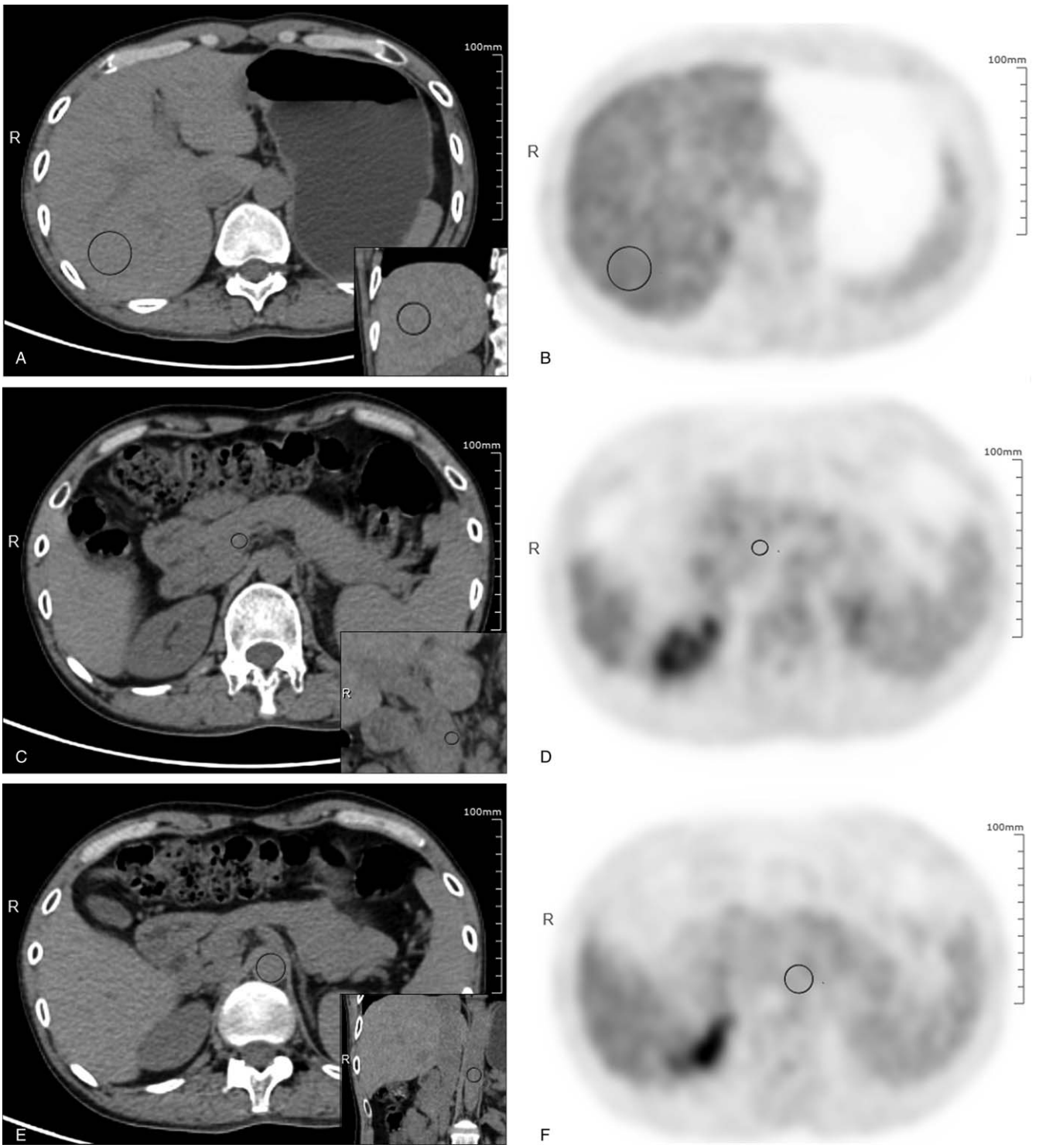

Figure 1. Transverse unenhanced computed tomography (CT) (A, C, E) and positron emission tomography (PET) images (B, D, F) of hybrid PET/CT from a healthy individual at the level of bifurcation of the portal vein, the trunk of the portal vein, and the truncus coeliacus, respectively. Areas in circles denote the volumes of interest (VOIs) to measure the standardized uptake value (SUV) of the liver (SEV_L, the SUV of portal vein (SUV_P), and the SUV of liver artery (SUV_A), respectively. Pictures inserted in A, C, and E correspond to coronal CT images that help to show the exact positions of the VOIs.

The Kolmogorow–Smirnow test was performed to test the normal distribution of the variables. General linear model univariate analyses were performed to investigate associations between clinicoserological items and SUV indexes. Partial correlations were established between covariates and SUV indexes, after adjusting for other covariates. The significances of the crude and adjusted effects were tested. Only when both crude and adjusted effects were significant could the variable be included for multivariate analysis. Then, multivariate stepwise linear regressions were conducted to identify independent factors of common serological biochemical tests that influenced the variations of SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP}. All statistical

Table 1

Intra- and interobserver agreements of SUV measurements expressed as intra/interclass correlation coefficients.

Agreements	SUV_L	SUV_A	SUV_P
Intraobserver	.899 (.863–.926)	.934 (.909–.952)	0.941 (.921–.958)
Interobserver	.920 (.907–.931)	.882 (.864–.898)	0.949 (.941–.956)

Note: Data in parentheses are 95% confidential intervals.
A = liver artery, L = liver, P = portal vein, SUV = standardized uptake value.

analyses were performed using SPSS 20 (IBM SPSS Inc., Chicago, IL), with 2-sided *P*-value < .05 indicating statistical significance.

3. Results

3.1. Reliability and reproducibility of data collection

The intraobserver and interobserver ICCs calculated for the SUV measurements were good, with the former ranging from .899 for SUV_L to .941 for SUV_P, and the latter ranging from .882 for SUV_A to .949 for SUV_P (Table 1).

3.2. Distributions of SUV indexes between categorical variables

Of the 633 patients included, 489 (77.3%) were male and 144 were female (22.7%). The intergender differences in SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} were identified as not significant (Table 2). Among all subjects, 377 patients had HBsAg tests, in which 45 were HBsAg positive, while 332 were HBsAg negative. The differences in SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} between HBsAg positive and HBsAg negative individuals were not significant (Table 2). In contrast, 351 patients underwent HCAb tests, among which 231 were positive and 120 were negative, with no difference in the SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, or SUV_{LP} between the HCAb positive and negative groups being demonstrated (Table 2).

3.3. Comparisons of variations of SUV indexes

The SUV indexes-SUV_L, SUV_P, and SUV_A-were measured as 1.88 ± .465, 1.10 ± .369, and 1.18 ± .537, respectively. Based on these indexes, the $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} were calculated as 1.83 ± .512, 1.72 ± .454, and 2.19 ± .497, respectively. SUV_{LP} was identified as significantly larger than SUV_L ($P < .001$; Table 3), while $SUV_{L/P}$ was significantly smaller than SUV_L ($P < .001$; Table 3). Differences between $SUV_{L/A}$ and SUV_L were not significant ($P = .130$; Table 3). The CVs of SUV_L, SUV_P, SUV_A, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} were 26.3%, 33.5%, 45.5%, 27.2%, 26.4%, and 22.7%, respectively, with SUV_{LP} having the smallest CV. The difference in the CV between SUV_L and SUV_{LP} was significant ($P < .001$; Table 3), while the CVs of $SUV_{L/A}$ and $SUV_{L/P}$ were not different from the CV of SUV_L (Table 3).

3.4. Summary of univariate analyses

Although SUV_A and SUV_P were tested and did not show not a normal distribution, it did not influence the following univariate and multivariate analysis as SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} all obeyed a normal distribution (Table 3). The results of univariate analyses are summarized in Table 4. For SUV_L, it was necessary to include age, BMI, aspartate aminotransferase (AST), total cholesterol (TC), and high-density lipoprotein (HDL) in the multivariate analysis, because both the crude and adjusted effects of these variables on SUV_L were significant. In contrast, age, BMI,

Table 2

Distributions of SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP} among categorical variables.

Variables	Frequency (%)	SUV_L	*P* values	$SUV_{L/A}$	*P* values	$SUV_{L/P}$	*P* values	SUV_{LP}	*P* values
Gender			.129		.060		.071		.639
Male	489 (77.3%)	1.87 ± 0.513		1.90 ± 0.524		1.76 ± 0.479		2.19 ± 0.542	
Female	144 (22.7%)	1.94 ± 0.381		1.81 ± 0.423		1.68 ± 0.417		2.21 ± 0.446	
HBsAg			.707		.150		.169		.864
Positive	45 (11.9%)	1.80 ± 0.397		1.87 ± 0.440		1.71 ± 0.422		2.10 ± 0.484	
Negative	332 (88.1%)	1.77 ± 0.514		1.99 ± 0.534		1.82 ± 0.509		2.08 ± 0.522	
HCAb			.707		.561		.055		.421
Positive	231 (65.8%)	1.76 ± 0.506		1.98 ± 0.462		1.81 ± 0.541		2.08 ± 0.535	
Negative	120 (34.2%)	1.74 ± 0.400		2.02 ± 0.637		1.70 ± 0.435		2.04 ± 0.478	

Numerical data were expressed as mean ± standard deviation.
A = liver artery, L = liver, LP = liver parenchyma, P = portal vein, SUV = standardized uptake value.

Table 3

Comparisons among SUV indexes in relation to interpatient variations.

SUV	Mean ± SD	95% CI	K–S test*	*P* values#	CV (%)	*P* values‡
SUV_L	1.88 ± 0.495	1.85–1.92	.053	NA	26.3	NA
SUV_A	1.10 ± 0.369	1.07–1.13	.036	<.001	33.5	<.001
SUV_P	1.18 ± 0.537	1.14–1.22	.039	<.001	45.5	<.001
$SUV_{L/A}$	1.83 ± 0.500	1.80–1.87	.220	.130	27.2	.429
$SUV_{L/P}$	1.72 ± 0.454	1.69–1.76	.112	<.001	26.4	.929
SUV_{LP}	2.19 ± 0.497	2.16–2.23	.959	<.001	22.7	<.001

A = liver artery, CI = confidential interval, CV = coefficient of variation, L = liver, LP = liver parenchyma, P = portal vein, SD = standard deviation, SUV = standard uptake value.
* Kolmogorow–Smirnow test for normal distribution.
# Paired *t* test in comparison with SUV_L.
‡ The Miller test for comparing CVs of SUV indexes with those of SUV_L; NA, not associated.

Table 4

Univariate analyses demonstrating associations between common plasma laboratory measures and SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP}.

		SUV_L		$SUV_{L/A}$		$SUV_{L/P}$		SUV_{LP}	
Variables	Mean ± SD	Crude *P*	Adjusted *P*	Crude *P*	Adjusted *P*	Crude *P*	Adjusted *P*	Crude *P*	Adjusted *P*
Age	47.7 ± 8.71	.011	.039	.048	.009	.231	.912	.129	.344
BMI	25.0 ± 3.74	<.001	<.001	<.001	<.001	<.001	.018	<.001	<.001
ALT	26.8 ± 11.68	.046	.406	<.001	<.001	.005	.001	.015	.318
AST	24.2 ± 7.70	<.001	.021	.014	.024	.553	.006	<.001	.028
TG	2.2 ± 1.71	.018	.252	.279	.128	.032	.399	.004	.320
TC	4.2 ± 0.58	.031	.023	.001	.042	.018	.035	.028	.016
TB	6.9 ± 6.75	.112	.401	.914	.030	.102	.001	.017	.153
HDL	1.2 ± 0.34	.044	.009	.005	.927	<.001	.015	.658	.130
LDL	2.8 ± 0.81	.845	.724	.579	.455	.149	.085	.527	.504
BGlu	5.7 ± 1.24	.045	.142	.104	.750	.089	.388	.028	.116

β = β coefficients, A = liver artery, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BGlu = blood glucose, BMI = body mass index, HDL = high-density lipoprotein, L = liver, LDL = low-density lipoprotein, LP = liver parenchyma, P = portal vein, SD = standard deviation, SUV = standardized uptake value, TB = total bilirubin, TC = total cholesterol, TG = triglyceride.

alanine aminotransferase (ALT), AST, and TC for $SUV_{L/A}$; BMI, ALT, TC, and HDL for $SUV_{L/P}$; and BMI, AST, and TC for SUV_{LP}, had to be included for the corresponding multivariate analysis.

3.5. Summary of multivariate analyses

The statistics of the multivariate analyses are summarized in Table 5. The number of variables that independently influenced SUV_{LP} was the smallest compared with those that influenced SUV_L $SUV_{L/A}$, and $SUV_{L/P}$: Only BMI, TC, and AST. With other variables controlled similarly, an increase in each kg/m^2 of BMI, in each mmol/L of TC, and in each U/L of AST indicated a .028 ($P = .010$), .089 ($P < .001$), and .007 ($P = .013$) increase in SUV_{LP}, respectively.

4. Discussion

In the present study, based on a large healthy population undergoing PET/CT examination for cancer screening, we found that the commonly used liver semiquantitative index, SUV_L, was influenced by concentrations of serological AST, BMI, TC, age, and HDL. In contrast, the blood-free SUV index, SUV_{LP}, exhibited lower interindividual variation and was less influenced by common serological factors of liver functional tests. Thus, SUV_{LP} might represent an alternative semi-quantitative index to assess liver ^{18}F-FDG uptake because of the reduced influence of background blood activity. In addition, SUV_{LP} might reflect the metabolism of the liver parenchyma more accurately. As for the formula proposed in this study, we think it is robust, as evidenced by the study done by Park et al,[18] who used it to calculate the CT attenuation of the liver parenchyma in 2006.

The findings of this study have some implications for clinical practice. Ideally, the ^{18}F-FDG uptake of a hepatic tumor should not influenced by the background liver metabolism. However, the ^{18}F-FDG uptake of the liver background is always large enough to influence the contrast between a hepatic tumor and its surrounding normal liver parenchyma, especially when the metabolic activity of the tumor is not high.[19,20] The commonly used semiquantitative index, SUV_L, to assess liver ^{18}F-FDG is, to a great extent, influenced by background metabolism of liver blood; therefore, it is necessary to take account of the infusion status of liver blood and its metabolic activity when using SUV_L to semiquantitatively assess liver metabolism. For example, when facing a patient with congestive heart failure or stagnation of the hepatic venous system, the influence of background blood metabolism on the liver SUV_L will inevitably increase because of the increased blood volume in the liver. By contrast, in a patient with diffused cirrhosis, whose liver blood infusion is dramatically decreased because of the reduced hepatic sinusoid, the influence of background blood metabolism on the liver SUV_L would decrease. These 2 pathological statuses are among the various factors that cause interindividual variation of liver SUV_L. In addition, in clinical practice, the metabolic status of the liver is often used as reference to assess lesions in other organs.[5,21] Therefore, it is also important to know the status of blood infusing into the liver before comparing liver metabolism with those of lesions. The blood-free SUV index, SUV_{LP}, proposed in

Table 5

Multivariate linear stepwise regressions demonstrating influences of common plasma laboratory measures on SUV_L, $SUV_{L/A}$, $SUV_{L/P}$, and SUV_{LP}.

		SUV_L		$SUV_{L/A}$		$SUV_{L/P}$		SUV_{LP}	
Variables	Mean ± SD	β	*P*	β	*P*	β	*P*	β	*P*
BMI	25.0 ± 3.74	.021	<.001	.033	<.001	.034	<.001	.028	<.001
TC	4.2 ± 0.58	.068	.023	−.023	.040	−.029	.041	.089	.015
AST	24.2 ± 7.70	.006	.006	−.007	.048		NS	.007	.008
Age	47.7 ± 8.71	.005	.021	.006	.014		NS		NS
HDL	1.2 ± 0.34	.138	.011		NS	−.035	.029		NS
ALT	26.8 ± 11.68		NS	.008	.001	.004	.033		NS

β = β coefficients, A = liver artery, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, HDL = high density lipoprotein, L = liver, LP = liver parenchyma, NS = not significant, P = portal vein, SUV = standardized uptake value, TC = total cholesterol.

this study avoids the above-mentioned problems. The clinical validation of SUV_{LP} in specific clinical conditions is underway and the results will be shared in the near future.

The liver is highly infused with blood. This means that the liver uptake of ^{18}F-FDG will be inevitably influenced by background blood activity compared to organs with a poor blood supply.[12,14] Therefore, it is necessary to construct an SUV index that can accurately reflect the metabolism of the liver parenchyma. In this study, the metabolism of background blood, measured as SUV_A and SUV_P, presented relatively larger CVs (33.5% and 45.5%, respectively) compared with that of the commonly used SUV_L (26.3%), while the blood-free index, SUV_{LP}, had a significantly smaller CV than SUV_L (22.7%:26.3%; Table 3). Thus, we speculated that the interindividual variation of SUV_L might, to a large extent, originate from variation in the background blood metabolism. The interindividual variation of the liver parenchyma may be small (just as the CV of SUV_{LP} measured in this study was only 22.7%); however, when mixed with the infused blood, its variation would be neutralized into a relatively larger one (CV of SUV_L, 26.3%). Another SUV index proposed in this study, namely $SUV_{L/A}$, may not be a suitable index to reduce the influence of background blood activity on liver metabolism, as both $SUV_{L/A}$ and its CV were not significantly different from SUV_L and its CV (Table 3). This finding is consistent with the study conducted by Kanstrup et al,[14] who advocated that $SUV_{L/A}$ was not superior over SUV_L, because they had similar interindividual variations. Likewise, $SUV_{L/P}$ is not an appropriate corrective method, as its CV did not significantly decrease either, as compared with those of SUV_L ($P = .929$, Table 3).

Furthermore, the number of factors in the liver functional tests that independently influenced the variation of SUV_{LP} was less than those of SUV_L, $SUV_{L/A}$, and $SUV_{L/P}$. This indicated that SUV_{LP} is more stable as an index to semiquantitatively assess the liver uptake of ^{18}F-FDG. SUV_L, $SUV_{L/A}$, and SUV_{LP} were influenced by AST, BMI, and TC, indicating that they might truly be independent factors that are associated with liver metabolism. ALT and AST are sensitive liver enzymes that reflect the functional status of hepatic cells, with the former being more associated with acute injury of hepatic cells, while the latter is more associated with chronic injury of hepatic cells.[22,23] In the present study, the subjects included were almost all healthy and thus free of acute injury of hepatic cells. This may explain why AST, but not ALT, was identified as independently associated with liver FDG metabolism, given the potential for chronic injury of hepatic cells caused by some chronic inflammation of the liver parenchyma, which might result in increased activity of Kupffer cells and the corresponding increased uptake of ^{18}F-FDG.[24] For BMI and TC, their positive associations with background liver uptake of ^{18}F-FDG have been reported previously.[11,25,26] The theoretical basis may be related to the increased chronic inflammation in people with obesity or hyperlipidemia causing an increase in background liver uptake of ^{18}F-FDG because of the response of the liver parenchyma to chronic inflammation.[27]

Several limitations of this study should be mentioned. First, we used the mean SUV instead of the maximum SUV as an index to assess liver uptake of ^{18}F-FDG, although the latter was the most common index used clinically. However, the mean SUV is more robust and more suitable to assess background liver ^{18}F-FDG metabolism, and in general, foci are compared with liver uptake as a whole, rather than as specific voxels. Second, our results need to be interpreted within this study, as we did not investigate all factors that could possibly influence liver ^{18}F-FDG uptake, such as diabetic status and blood glucose. However, we excluded subjects with diabetes or blood glucose more than 120 mg/dL when performing the population selection. We believe that confounding effects from these factors are weak.

5. Conclusions

Liver SUV is vulnerable to influence from the background blood metabolism. The corrected blood-free index, SUV_{LP}, might be a suitable alternative index to reduce metabolic influence of infused blood, because its interindividual variation and vulnerability to influences from common serological examination factors were relatively lower than those of the commonly used index SUV_L.

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