Original Article

# Age-related changes of standardized uptake values in the blood pool and liver: a decade-long retrospective study of the outcomes of 2,526 subjects

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**Background:** Background activity on fluorine-18-fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography/computed tomography (PET/CT) is often used as a reference to assess a patient's response to tumor treatment. To produce a suitable background activity reference, we examined the variations in standardized uptake values (SUVs) in the blood pool and liver of a large multi-aged population.

**Methods:** A total of 2,526 subjects underwent $^{18}$F-FDG PET/CT examinations and were divided into 12 age groups. Pearson's partial correlation and multivariate regression analyses were performed to assess the associations between individual factors and SUVs of the blood pool and liver and to identify the factor that most influenced the SUVs. The mean SUVs across the age groups were also determined.

**Results:** Positive correlations were found between individual factors and SUVs. Age appeared to be the most important predictor of SUVs and was significantly associated with the blood pool $SUV_{max}$ (ß=0.466, P=0.000), blood pool $SUV_{mean}$ (ß=0.393, P=0.000), liver $SUV_{max}$ (ß=0.347, P=0.000), and liver $SUV_{mean}$ (ß=0.354, P=0.000). Blood pool and liver SUVs rose rapidly until the age of 20 and then showed a slow upward trend without reaching a plateau.

**Conclusions:** Age is an important factor that influences variations in the blood pool and liver SUVs. Our study clarified this understanding of age-related variations in SUVs and provided a normal range of blood pool and liver SUVs that may aid clinicians in evaluating tumors with greater accuracy.

**Keywords:** Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography ($^{18}$F-FDG-PET/CT); standardized uptake value (SUV); liver; blood pool; age variation

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## Introduction

Fluorine-18-fluorodeoxyglucose ($^{18}$F-FDG) integrated positron emission tomography and computed tomography (PET/CT) is an imaging technique that provides both anatomical and glucometabolic information that guides clinicians in distinguishing benign disease from malignant disease, as well as assessing patient response to cancer treatment (1,2). Standardized uptake values (SUVs) are a useful quality index of FDG PET/CT studies at the PET/CT image interpretation stage (3). A five-point scale (5-PS) model can be used with liver and mediastinal blood pool SUV measurements to differentiate abnormal FDG uptake from physiological FDG uptake. These measurements are often used as reference background values to distinguish tumors and define treatment response for head and neck squamous cell carcinoma and lymphoma (3-6). However, a variety of biological factors can cause errors in liver and blood pool SUVs (7). These factors may give rise to false-positive or false-negative PET/CT reports (8) and include age, sex, weight, serum glucose level, hepatic function, and

hyperthyroidism (6,9-11). Therefore, normal SUVs of the liver and blood pool must be determined before clinicians can interpret PET/CT images. Growing evidence suggests that age has a major impact on SUVs (1,12). However, no studies have focused on variations in SUVs across different ages, possibly because of the limitations of small sample sizes. Therefore, to ensure scientific rigor and enable reproducibility, defining a precise range of blood pool and liver SUVs from $^{18}$F-FDG PET/CT in multi-aged populations is of great importance.

Although a previous study of pediatric patients and adults has explored the impact of age on SUVs (1), it only provided potential associations; the relationship between different ages and the SUVs of blood pool and liver have not been fully explored. To date, there is no clear consensus on the real impact that age has on $^{18}$F-FDG uptake. In addition, the mechanisms related to this association have not been determined. In this study, the mean SUVs ($SUV_{mean}$) and maximum SUVs ($SUV_{max}$) were both applied as indices of $^{18}$F-FDG uptake in the blood pool and liver; the blood pool is a less variable and more robust parameter, while the liver is the most common clinical parameter for illustrating $^{18}$F-FDG accumulation in tumors. We enrolled a cohort of Chinese patients, stratified them into 12 age groups for evaluation, and quantified a normal range of background blood pool and liver SUVs to guide clinicians in more accurately identifying tumors and evaluating cancer treatment response. We present the following article in accordance with the STROBE Statement guidelines. A completed STROBE reporting checklist is available at http://dx.doi.org/10.21037/qims-20-35.

## Methods

### *Selection of participants*

The research procedures in this study were approved by the West China Hospital of Sichuan University Ethics Committee. This is a retrospective study, so no ethical approval or informed consent was obtained. This retrospective study initially included all subjects who underwent $^{18}$F-FDG PET/CT examinations at our institution between January 2009 and January 2019. The inclusion and exclusion criteria included the following. Imaging was performed from the top of the skull to mid-thigh, and PET was performed from the pelvis to the head with the arms elevated and a tracer uptake period of 50–75 minutes. Since this study included subjects that ranged from infant to adult to elderly, there were diverse incubation times. However, the previous study that investigated the impact of age on SUVs determined an incubation time that was within only 5% of the peak value, between 50 and 110 min after the injection (13). Subjects with a fever, diabetes, hematologic disease, abnormal liver or renal function, and primary or secondary hepatic and/or aortic diseases (neoplasms, large-sized cysts, aneurysms, inflammation, viral hepatitis B or C, and hepatic adipose infiltration) were excluded from this study. Subjects with FDG-avid tumors or who had received chemotherapy within eight weeks of imaging, radiotherapy for the liver or mediastinum, or bone marrow colony-stimulating factor treatment within two weeks of imaging were also excluded. The flow diagram of subject selection is shown in *Figure 1*. The following data were recorded: age, sex, weight, $^{18}$F-FDG dose, serum glucose level, and the results of liver function tests. All participant data were collected by two clinicians (YC and KZ) to minimize errors during the data collection process.

### *Imaging technique*

All subjects fasted for at least 6 hours prior to the examination to maintain low glucose and low insulin levels. The $^{18}$F-FDG PET/CT images were acquired after intravenous injection of 5.55 MBq (0.15 mCi) of $^{18}$F-FDG per kilogram of bodyweight via the cubital vein. The scanning parameters were 4 mm/slice for PET and 120 kV, 40 mAs, and 5 mm/slice for low-dose CT. The emission PET images were acquired in 3D mode at 2 minutes per bed position and a bed overlap of 50%. The reconstruction of PET images was performed according to the European Association of Nuclear Medicine Guidelines for tumor PET imaging (6) and used a line-of-response row-action maximum likelihood algorithm (3 iterations and 33 subsets, voxel size of 4 mm × 4 mm × 4 mm, with no additional Gaussian smoothing). Trans-axial, coronal, and sagittal CT and PET/CT fusion images were reconstructed and formatted using vendor-provided software (Phillips EBW Workstation). All scans were acquired using a Gemini GXL PET/CT scanner (Philips, Netherlands).

### *Imaging protocols and analysis*

FDG uptake was represented by SUVs, which were calculated according to the following formula (1):

$$SUV_{max} = \text{maximum activity in region of interest (ROI) (kBq) / injected dose (MBq) × body weight (kg)} \quad [1]$$

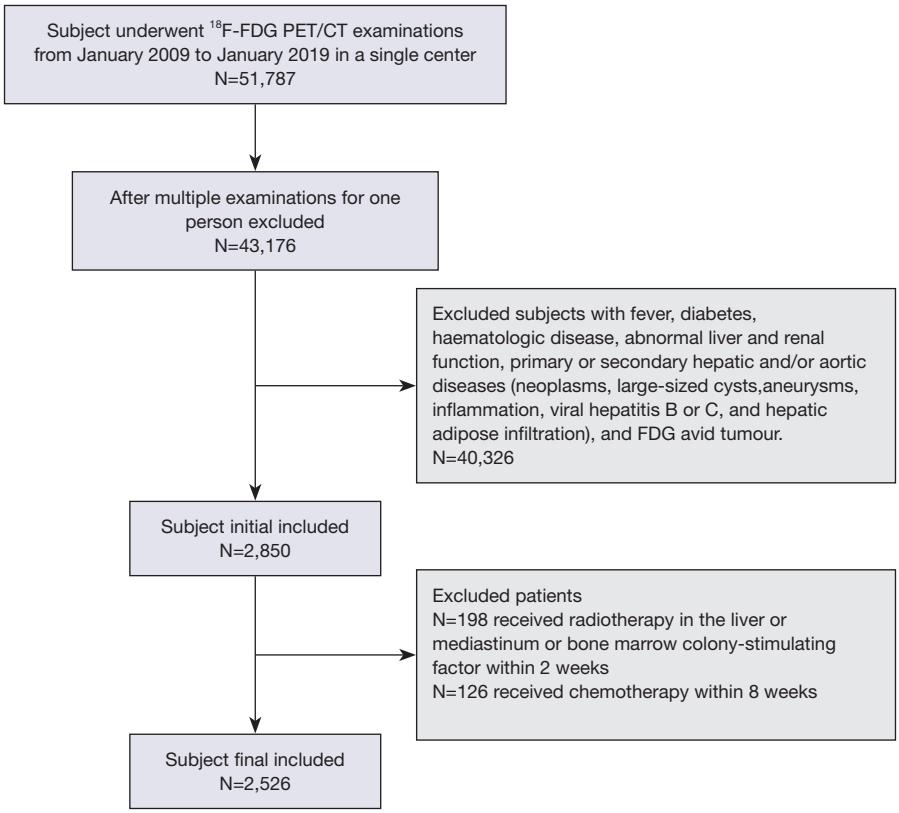


**Figure 1** Flow diagram of subject selection.

$SUV_{mean}$ = mean activity in ROI (kBq) / injected dose (MBq) × body weight (kg) [2]

A quantitative method was performed by placing a spherical volume of interest (VOI) with a diameter of 3 cm in the center of the right lobe of the liver while avoiding visible vessels on the CT (6) (*Figure 2A,B*). The mediastinal blood pool measurements were performed by drawing a combined VOI on three contiguous slices inside the thoracic aorta at the carinal level and measuring uptake within the vessel while avoiding the vessel wall (14,15) (*Figure 2C,D*). The $SUV_{mean}$ and $SUV_{max}$ of the blood pool and liver were recorded (16).

### *Statistical analysis*

All analyzes were performed using SPSS software version 22.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD). Data normality was evaluated by the Kolmogorov-Smirnov test. Pearson's partial correlation coefficients were used to evaluate the relationships of $SUV_{max}$ and $SUV_{mean}$ in the blood pool and liver with age, weight, $^{18}$F-FDG dose, and serum glucose level. A multivariate linear regression model was established to determine the best predictors of liver and blood pool $SUV_{max}$ and $SUV_{mean}$. $P<0.05$ was considered statistically significant.

## Results

Applying exclusion criteria, a total of 2,526 subjects, 1,436 males and 1,090 females, were recruited in this study. The mean $SUV_{max}$ and $SUV_{mean}$ in the blood pool were 1.89±0.36 and 1.55±0.28, respectively, while the mean $SUV_{max}$ and $SUV_{mean}$ in the liver were 2.81±0.46 and 2.26±0.38, respectively. The clinical characteristics of the study populations are shown in *Table 1*.

### *Pearson's partial correlation analysis*

A scatter plot matrix shows the correlations between individual factors and SUVs (*Figure 3*). The blood pool $SUV_{max}$ and $SUV_{mean}$ had statistically significant positive

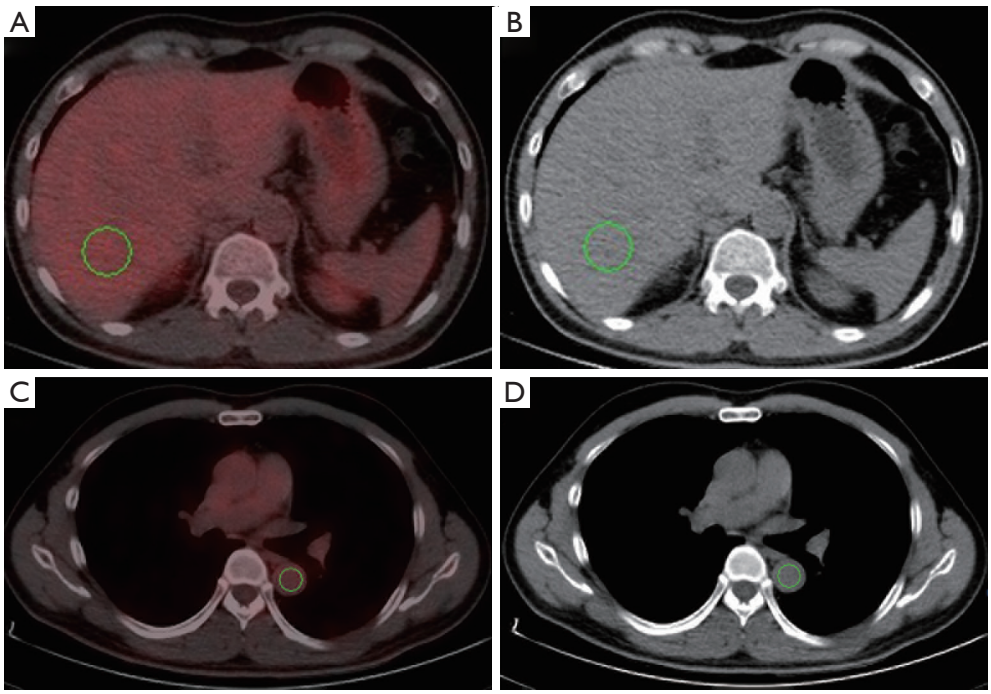


**Figure 2** Images of a 40-year-old man with no cancer history. PET/CT was performed for physical examination. (A) The fusion image showed an ROI with a diameter of 3 cm in the center of the right lobe of the liver. (B) The CT images showed a liver of normal appearance with no sign of abnormalities. (C) The fusion image showed an ROI inside the thoracic aorta at the carinal level. (D) The CT images showed a blood pool of normal appearance with no sign of abnormalities. PET/CT, positron emission tomography/computed tomography; ROI, region of interest.

correlations with age, weight, $^{18}$F-FDG dose, and serum glucose level. Of these, age had the strongest correlation with both $SUV_{max}$ (r=0.466, P=0.000) and $SUV_{mean}$ (r=0.393, P=0.000). The liver $SUV_{max}$ and $SUV_{mean}$ had similar correlations with the abovementioned factors, except serum glucose level (r=0.017, P=0.404 for liver $SUV_{max}$; r=0.03, P=0.136 for liver $SUV_{mean}$). Of these, age also had the strongest positive correlation with liver $SUV_{mean}$ (r=0.347, P=0.000) and liver $SUV_{max}$ (r=0.354, P=0.000) (*Table 2*).

### *Multivariate linear regression analysis*

The multivariate regression analysis suggested that, of the four factors, age had the greatest impact on $SUV_{max}$ and $SUV_{mean}$ in the blood pool (ß=0.462, P=0.000 for $SUV_{max}$; ß=0.385, P=0.000 for $SUV_{mean}$) and in the liver (ß=0.324, P=0.000 for $SUV_{max}$; ß=0.376, P=0.000 for $SUV_{mean}$) (*Table 3*). We grouped the subjects into 12 age groups (1–5, 6–10, 11–15, 16–20, 21–25, 26–30, 31–40, 41–50, 51–60, 61–70, 71–80, and 81–100 years). Overall, the blood pool $SUV_{max}$ (from 1.06±0.24 to 1.62±0.23) and $SUV_{mean}$ (from 0.89±0.18 to 1.35±0.24) increased rapidly until the age of 20. Then the growth trend continued more slowly with age, and no plateau was reached. The liver $SUV_{max}$ (from 1.38±0.25 to 2.60±0.36) and $SUV_{mean}$ (from 1.10±0.20 to 2.08±0.28) showed similar patterns (*Table 4*, *Figure 4*). Similar changes were also found in PET/CT images showing maximum intensity projections (MIPs) of the blood pool and liver at different ages (5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, and 90 years) (*Figure 5*).

### *Subgroup analysis*

According to the above trend, children and adolescents showed more significant growth relationships between age and SUVs. To avoid the influence of a wide age range on the results, particularly the influence of children and adolescents, which may reduce the robustness of the results, we also obtained Pearson's partial correlations and performed multivariate linear regression analysis between individual factors and SUVs in subjects older than 18 years. Similar correlations and trends were obtained in

**Table 1** Demographic data of subjects

| Characteristics | Number of subjects (N=2,526) |
|---|---|
| Gender | |
| Male | 1,436 |
| Female | 1,090 |
| Category | |
| Cancer screening | 1,720 |
| Lymphoma | 341 |
| Lung cancer | 154 |
| HNSCC & NPC | 110 |
| Colorectal cancer | 102 |
| Melanoma | 69 |
| Ewing sarcoma | 30 |
| Liver function test* | |
| Alanine transaminase (serum IU/L) | 19.30±9.36 |
| Aspartate transaminase (serum IU/L) | 22.60±6.07 |
| Bilirubin (μmol/L) | 11.94±5.18 |
| Albumin (g/L) | 46.52±3.30 |
| Weight (kg) | 60.87±14.00 |
| $^{18}$F-FDG dose (mCi) | 9.50±2.08 |
| Blood glucose (mmol/L) | 5.36±0.62 |
| Blood pool $SUV_{max}$ | 1.89±0.36 |
| Blood pool $SUV_{mean}$ | 1.55±0.28 |
| Liver $SUV_{max}$ | 2.81±0.46 |
| Liver $SUV_{mean}$ | 2.26±0.38 |

*The reference range: alanine transaminase (<50 IU/L); aspartate transaminase (<40 IU/L); bilirubin (5–28 μmol/L); albumin (40–55 g/L). HNSCC, head, and neck squamous cell carcinoma; NPC, nasopharyngeal carcinoma; $^{18}$F-FDG, fluorine-18-fluorodeoxyglucose; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value; N, number.

the subgroup analysis, which validated the original results (Tables S1,S2).

## Discussion

Treatment response in patients with head and neck squamous cell carcinoma and lymphoma can be assessed using 5-PS scores; this requires the comparison of SUVs of the $^{18}$F-FDG-positive lesion with that of the mediastinum blood pool and liver (17). Determining a reference range of SUVs using $^{18}$F-FDG PET/CT in multi-aged populations is of great clinical utility, as previous studies have found an association between age and SUVs (1). This study further demonstrated that SUVs of the blood pool and liver were affected by age, even after adjusting for weight, injected a dose of $^{18}$F-FDG, and serum glucose level. Based on this 10-year retrospective study of 2,526 patients, we found that the $SUV_{max}$ and $SUV_{mean}$ of the blood pool and liver increased rapidly until the age of 20. The growth trend then slowed without reaching a plateau. More importantly, this study provided a normal range of background SUVs across 12 age groups. This could assist clinicians in selecting appropriate reference background SUVs when treating oncologic patients of different ages.

Several studies have documented the effects of age, weight, BMI, and $^{18}$F-FDG dose on $^{18}$F-FDG uptake in the blood pool and liver (5,18-20). A study by Mahmud *et al.* (12) investigated these effects in 51 oncology patients, including 28 males and 23 females. In contrast to our results, no significant positive association was found between liver $SUV_{max}$ and age. This may be due to the small sample size, the inclusion of elderly patients, and $SUV_{max}$ variations. Notably, the lack of a significant correlation between serum glucose level and $SUV_{max}$ was consistent with our results. Lin *et al.* (1) investigated the relationships of liver SUVs with sex, age, and HBV and HCV infection status in 339 asymptomatic subjects. The authors reported that age had a significant positive relationship with liver SUVs. No significant associations were observed between the other factors and SUVs. In our study, although no significant correlation was found between liver SUVs and serum glucose levels, we did find weak positive correlations between weight, $^{18}$F-FDG dose, serum glucose level, and the other SUV measurements. Moderate positive correlations between age and the blood pool and liver FDG uptake were found. Even after adjusting for confounding variables, the blood pool and liver SUVs retained a significant correlation with age. To the best of our knowledge, apart from the influence of hyperthyroidism on the liver itself (6,9), there are several potential biological explanations for the age-related trends of SUVs observed in our study. We speculate that the relevant mechanisms may be explained by organ deterioration, organ metabolism, and molecular transport.

On a cellular level, although the volume of hepatocytes grows with age, functional hepatocyte volume, and hepatocyte numbers decrease significantly with age (21,22).

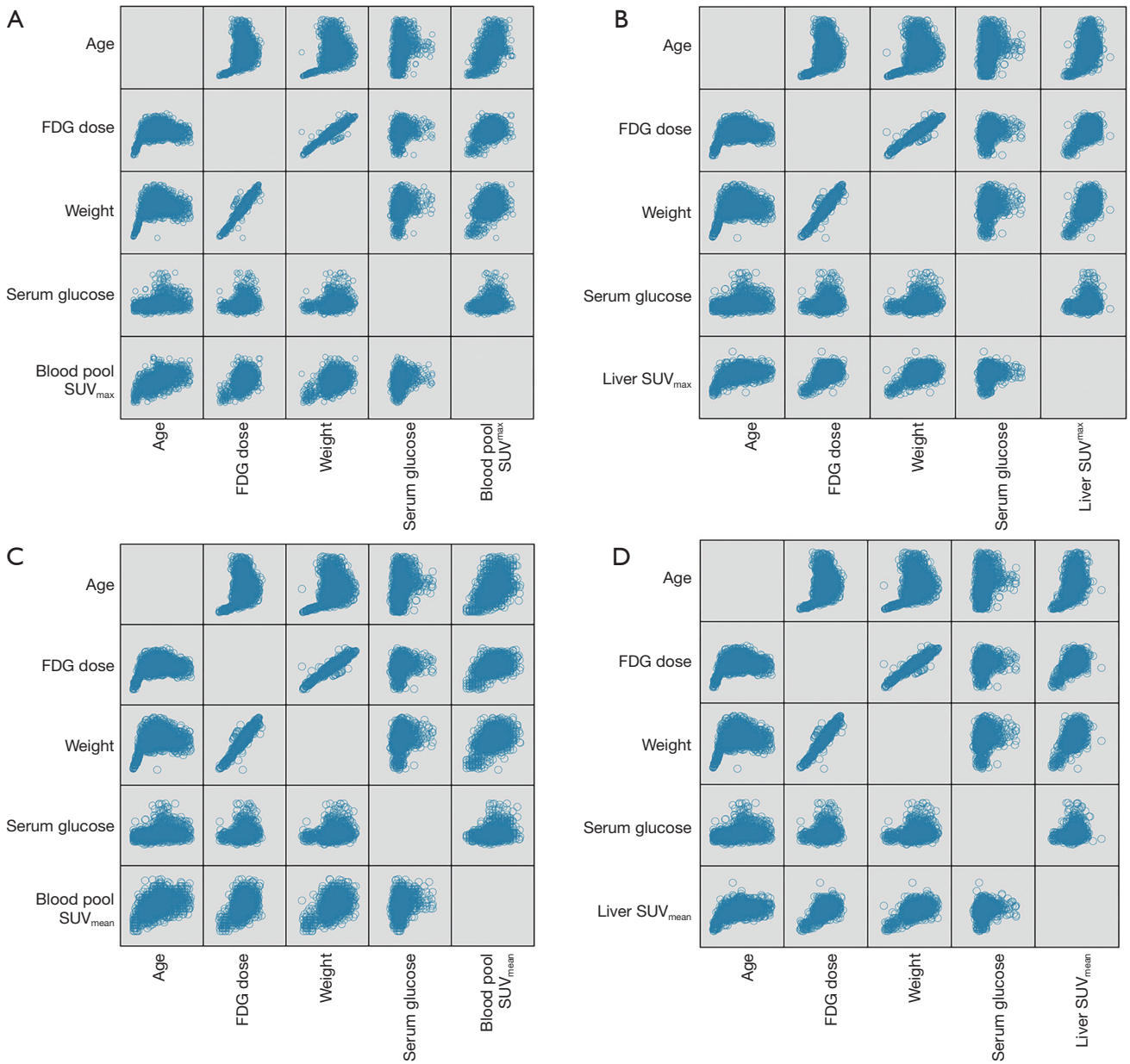


**Figure 3** The correlation between individual factors and SUVs. (A) A scatter plot matrix showing the relationships between different factors and blood pool $SUV_{max}$. (B) A scatter plot matrix showing the relationships between different factors and liver $SUV_{max}$. (C) A scatter plot matrix showing the relationships between different factors and blood pool $SUV_{mean}$. (D). A scatter plot matrix showing the relationships between different factors and liver $SUV_{mean}$. SUV, standardized uptake value.

Additionally, there is a positive association between metabolic activity in the liver and age in adults (23). The increase of FDG uptake with age may also reflect age-related metabolic activity and changes in liver volume and hepatocyte numbers, as noted by previous studies (23,24). However, Meier and colleagues suggested that cumulative inflammatory changes secondary to the release of age-related hepatotoxins may exist (23). The age-related metabolic level of the organ may be one explanation for blood pool SUV trends (25). Overall, the similarities between previous research and our study indicate that our study results are of high scientific integrity.

**Table 2** Correlations between SUVs and related factors

| Parameters | Age | Weight | $^{18}$F-FDG dose | Serum glucose level |
|---|---|---|---|---|
| Blood pool $SUV_{max}$ | | | | |
| Pearson's partial correlation | 0.466 | 0.051 | 0.049 | 0.048 |
| P value | 0.000 | 0.01 | 0.014 | 0.0016 |
| Blood pool $SUV_{mean}$ | | | | |
| Pearson's partial correlation | 0.393 | 0.07 | 0.046 | 0.05 |
| P value | 0.000 | 0.000 | 0.02 | 0.011 |
| Liver $SUV_{max}$ | | | | |
| Pearson's partial correlation | 0.347 | 0.105 | 0.048 | 0.017 |
| P value | 0.000 | 0.000 | 0.015 | 0.404 |
| Liver $SUV_{mean}$ | | | | |
| Pearson's partial correlation | 0.354 | 0.116 | 0.042 | 0.03 |
| P value | 0.000 | 0.000 | 0.035 | 0.136 |

$^{18}$F-FDG, fluorine-18-fluorodeoxyglucose; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value; N, number.

**Table 3** Impact of related factors on SUVs of blood pool and liver in multivariate regression analysis

| Variable | Adjusted unstandardized beta coefficient | Adjusted standardized beta coefficient | P value |
|---|---|---|---|
| Blood pool $SUV_{max}$ | | | |
| Age | 0.009 | 0.462 | 0.000 |
| $^{18}$F-FDG dose | 0.020 | 0.119 | 0.028 |
| Weight | 0.004 | 0.164 | 0.003 |
| Serum glucose level | 0.020 | 0.048 | 0.003 |
| Blood pool $SUV_{mean}$ | | | |
| Age | 0.006 | 0.385 | 0.000 |
| $^{18}$F-FDG dose | 0.017 | 0.125 | 0.024 |
| Weight | 0.004 | 0.220 | 0.000 |
| Serum glucose level | 0.021 | 0.063 | 0.000 |
| Liver $SUV_{max}$ | | | |
| Age | 0.008 | 0.325 | 0.000 |
| $^{18}$F-FDG dose | 0.030 | 0.134 | 0.013 |
| Weight | 0.010 | 0.314 | 0.000 |
| Serum glucose level | 0.008 | 0.015 | 0.375 |
| Liver $SUV_{mean}$ | | | |
| Age | 0.007 | 0.376 | 0.000 |
| $^{18}$F-FDG dose | 0.004 | 0.022 | 0.701 |
| Weight | 0.008 | 0.284 | 0.000 |
| Serum glucose level | 0.016 | 0.036 | 0.042 |

$^{18}$F-FDG, fluorine-18-fluorodeoxyglucose; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value.

**Table 4** Mean SUVs of blood pool and liver in different subject age groups

| Age [N] | Blood pool $SUV_{max}$ | | Blood pool $SUV_{mean}$ | | Liver $SUV_{max}$ | | Liver $SUV_{mean}$ | |
|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI |
| 1–5 [47] | 1.06±0.24 | 0.99–1.13 | 0.89±0.18 | 0.83–0.94 | 1.38±0.25 | 1.30–1.45 | 1.10±0.20 | 1.04–1.16 |
| 6–10 [53] | 1.29±0.33 | 1.20–1.39 | 1.05±0.27 | 0.97–1.13 | 1.80±0.40 | 1.69–1.91 | 1.44±0.30 | 1.36–1.52 |
| 11–15 [56] | 1.54±0.27 | 1.47–1.61 | 1.28±0.25 | 1.21–1.34 | 2.40±0.42 | 2.29–2.51 | 1.88±0.34 | 1.79–1.97 |
| 16–20 [96] | 1.62±0.24 | 1.57–1.67 | 1.35±0.24 | 1.31–1.40 | 2.60±0.36 | 2.53–2.68 | 2.08±0.28 | 2.02–2.13 |
| 21–25 [165] | 1.70±0.31 | 1.65–1.74 | 1.44±0.26 | 1.40–1.48 | 2.73±0.42 | 2.67–2.80 | 2.18±0.34 | 2.13–2.24 |
| 26–30 [139] | 1.67±0.28 | 1.63–1.72 | 1.44±0.23 | 1.39–1.47 | 2.72±0.35 | 2.66–2.78 | 2.19±0.27 | 2.14–2.24 |
| 31–40 [491] | 1.81±0.31 | 1.78–1.84 | 1.53±0.24 | 1.50–1.55 | 2.78±0.37 | 2.75–2.82 | 2.25±0.30 | 2.22–2.28 |
| 41–50 [638] | 1.99±0.30 | 1.97–2.01 | 1.62±0.24 | 1.60–1.64 | 2.94±0.37 | 2.91–2.96 | 2.35±0.30 | 2.33–2.38 |
| 51–60 [386] | 2.01±0.28 | 1.98–2.04 | 1.63±0.22 | 1.61–1.65 | 2.97±0.38 | 2.93–3.00 | 2.38±0.29 | 2.35–2.41 |
| 61–70 [205] | 2.06±0.28 | 2.03–2.11 | 1.67±0.22 | 1.64–1.70 | 2.95±0.38 | 2.89–3.00 | 2.37±0.29 | 2.33–2.41 |
| 71–80 [127] | 2.10±0.29 | 2.05–2.15 | 1.68±0.24 | 1.64–1.72 | 2.97±0.36 | 2.91–3.03 | 2.38±0.30 | 2.33–2.43 |
| 81–100 [123] | 2.17±0.29 | 2.11–2.22 | 1.74±0.27 | 1.69–1.79 | 3.01±0.36 | 2.95–3.07 | 2.44±0.32 | 2.38–2.50 |

SD, standard deviation; CI, confidence interval; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value; N, number.

Age is also related to renal blood flow, glomerular filtration rate (GFR), and urea clearance, and the detailed mechanisms involved in these relationships may also facilitate the relationship between age and SUVs (26). It has been demonstrated that an age-related decline in GFR occurs during the human life span. After 30 years of age, a linear decline trend can be observed in GFR in healthy individuals. Moreover, previous studies have found that effective renal plasma flow was significantly lower in aging populations compared with the younger population (27). Similar clearance methods were also reported in infancy and childhood (28). The above physiological mechanisms are reminiscent of a potential explanation for age-related FDG uptake in the liver and blood pool.

Receptor, cytokine, and protein quality have been suggested to decrease with age, especially during the aging stages (29,30), though it remains uncertain whether glucose transporter (GULT) numbers increase, decrease, or remain stable with age. To understand the mechanism of the relationship between SUVs and age, it is useful to first understand the effects of molecular substances on the age-related decline. $^{18}$F-FDG is an analog of glucose that conjugates to glucose transport proteins to form FDG-6-phosphate (FDG-6-P). This cannot be metabolized by glycolysis pathways and therefore accumulates in cells (31). Glucose transmembrane transportation in the blood and hepatic tissue primarily depends on GLUT-1 and GLUT-4, respectively. The former is ubiquitous with basal-level glucose uptake and is found in erythrocytes and blood-tissue barriers, while the latter is the major hepatocyte isoform and is responsive to fed and fasting states (32,33). Robust studies have shown that overexpression of GLUT-1 and GLUT-3 results in a markedly enhanced demand for glucose in various solid tumors (34). Another study found that GLUT-1 plays a role in age-related insulin resistance, which may produce an indirect relationship between GLUT-1 and age (35). Hotta *et al.* (36) reported a significant inverse correlation between age and mRNA levels of GLUT-4, which suggests that age is associated with GLUTs. As the most highly conserved and widely distributed glucose transporter in mammalian cells (37), GLUTs, which have been shown to change with age, may be a factor that can explain the association between age and SUVs.

Our study had some limitations, the first being that retrospective studies are inherently limited in nature. Secondly, due to incomplete height data collection, the influence of BMI on SUVs could not be analyzed. Thirdly, our study was based on a group of Chinese subjects with a specific scan vendor, incubation time, and reconstruction algorithm. It was also a single-center study. As such, our

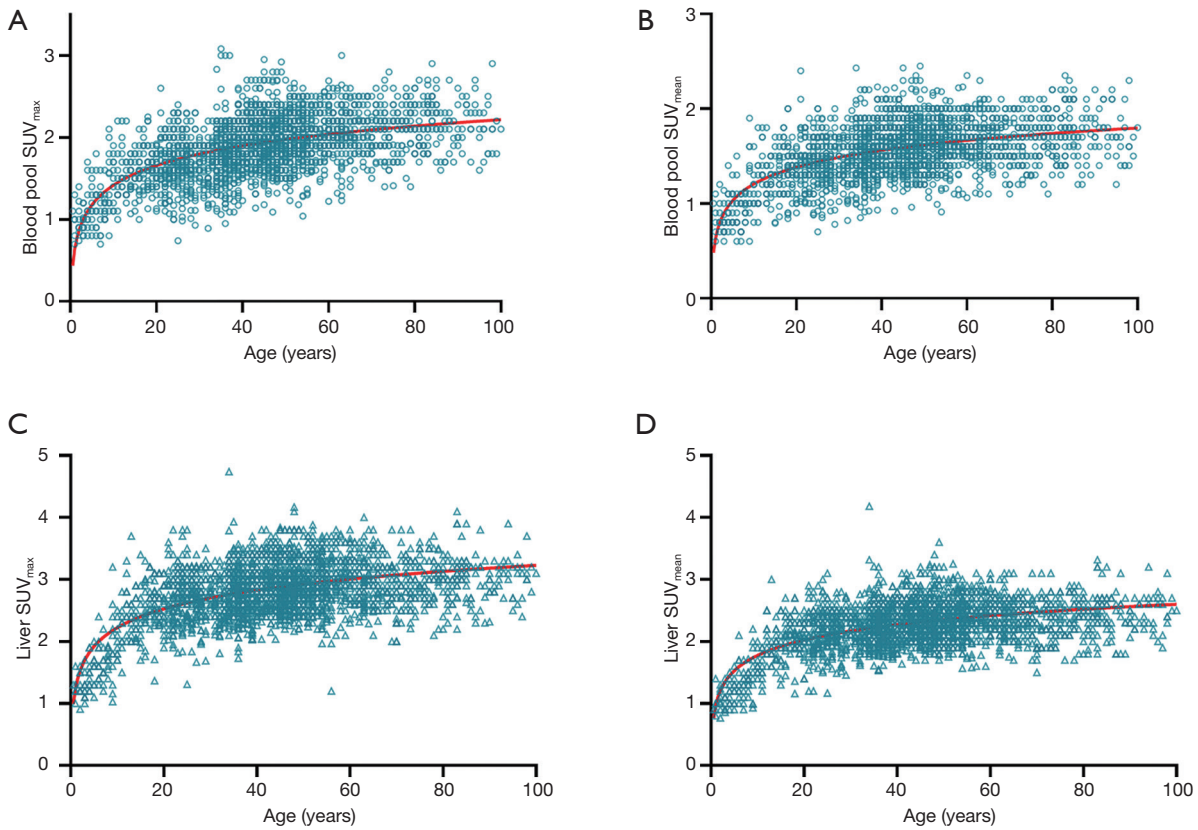


**Figure 4** A scatter diagram of associations between age and SUVs. The SUVs of the blood pool and liver increased until the age of 20. The growth trend slowed and continued to the age of 100. (A) Age variation in blood pool $SUV_{max}$ based on a large-scale population from 2009 to 2019. (B) Age variation in blood pool $SUV_{mean}$ based on a large-scale population from 2009 to 2019. (C) Age variation in liver $SUV_{max}$ based on a large-scale population from 2009 to 2019. (D) Age variation in liver $SUV_{mean}$ based on a large-scale population from 2009 to 2019. SUV, standardized uptake value.

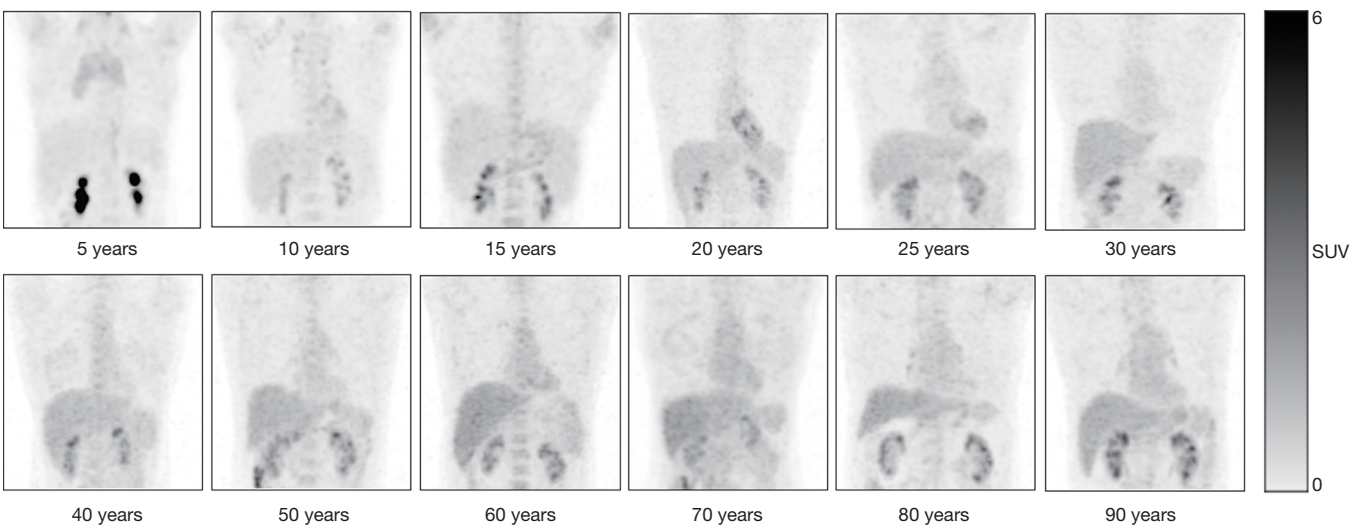


**Figure 5** MIP images illustrating $^{18}$F-FDG uptake in the liver and mediastinal blood pool across different ages (5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, and 90 years). MIP, maximum intensity projection; $^{18}$F-FDG, fluorine-18-fluorodeoxyglucose.

results must be verified in further studies that consider different populations to be deemed robust. Despite these limitations, the strength of our study cannot be ignored; its large sample size being evidence of its reliability and value. As this work was primarily focused on variations in SUVs with age, it lays the foundations for future studies to determine the clinical significance of age-related SUV changes. For example, if the liver or blood pool SUVs in a patient of a certain age were found to deviate from the normal range for that age as determined by PET/CT examination, the clinician should consider using blood pool and liver uptake as references for evaluating treatment response, especially when using Deauville scoring (5-PS) in the treatment of lymphoma or PET response criteria in solid tumor treatment.

## Conclusions

Of all factors that influence the blood pool and liver SUVs, age was found to have the greatest impact. Physiological FDG uptake in the blood pool and liver showed significant variations across age groups. Blood pool and liver background SUVs increased with age and should be determined to fall within the specific reference ranges before oncologic whole-body PET/CT images are interpreted.

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*Ethical Statement:* This study was approved by the ethics committee board of the West China Hospital of Sichuan University. This is a retrospective study, so no ethical approval or informed consent was obtained.



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## Supplementary

**Table S1** Correlations between SUVs with related factors (>18 years)

| Parameters (N=2,340) | Age | Weight | FDG dose | Serum glucose level |
|---|---|---|---|---|
| Blood pool $SUV_{max}$ | | | | |
| Pearson partial correlation | 0.412 | –0.068 | 0.005 | 0.248 |
| P value | 0.000 | 0.129 | 0.810 | 0.000 |
| Blood pool $SUV_{mean}$ | | | | |
| Pearson partial correlation | 0.317 | –0.072 | 0.011 | 0.261 |
| P value | 0.000 | 0.001 | 0.595 | 0.02 |
| Liver $SUV_{max}$ | | | | |
| Pearson partial correlation | 0.222 | –0.072 | 0.017 | 0.227 |
| P value | 0.000 | 0.001 | 0.417 | 0.001 |
| Liver $SUV_{mean}$ | | | | |
| Pearson partial correlation | 0.228 | –0.074 | 0.071 | 0.273 |
| P value | 0.000 | 0.258 | 0.399 | 0.01 |

$^{18}$F-FDG, fluorine-18-fluorodeoxyglucose; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value; N, number.

**Table S2** Impact of biological and procedural related factors on SUVs of blood pool and liver in multivariate regression analysis (>18 years)

| Variable | Adjusted unstandardized beta coefficient | Adjusted standardized beta coefficient | P value |
|---|---|---|---|
| Bood pool $SUV_{max}$ | | | |
| Age | 0.008 | 0.419 | 0.000 |
| $^{18}$F-FDG dose | 0.022 | 0.121 | 0.021 |
| Weight | –0.002 | –0.085 | 0.001 |
| Serum glucose level | 0.033 | 0.065 | 0.015 |
| Bood pool $SUV_{mean}$ | | | |
| Age | 0.005 | 0.332 | 0.000 |
| $^{18}$F-FDG dose | 0.016 | 0.111 | 0.042 |
| Weight | –0.003 | –0.133 | 0.015 |
| Serum glucose level | 0.03 | 0.073 | 0.010 |
| Liver $SUV_{max}$ | | | |
| Age | 0.587 | 0.626 | 0.000 |
| $^{18}$F-FDG dose | 0.003 | 0.111 | 0.012 |
| Weight | 0.022 | 0.044 | 0.006 |
| Serum glucose level | 0.006 | 0.035 | 0.433 |
| Liver $SUV_{max}$ | | | |
| Age | 0.004 | 0.238 | 0.000 |
| $^{18}$F-FDG dose | 0.021 | 0.118 | 0.031 |
| Weight | 0.005 | 0.179 | 0.001 |
| Serum glucose level | 0.043 | 0.008 | 0.000 |

$^{18}$F-FDG, fluorine-18-fluorodeoxyglucose; $SUV_{max}$, maximum standardized uptake value; $SUV_{mean}$, mean standardized uptake value; N, number.


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