Original Article

Comparison of FDG-PET/CT images between chronic renal failure patients on hemodialysis and controls

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Abstract: The whole-body 2-deoxy-2-[18F]fluoro-D-glucose (FDG) distribution in chronic renal failure (CRF) patients on hemodialysis would be different from that in subjects with normal renal function, because they lack urinary FDG excretion and remain in a constant volume overload. We evaluated the difference in the physiological uptake pattern of FDG between chronic renal failure patients on hemodialysis and control subjects. The subjects for this retrospective study consisted of 24 chronic renal failure patients on hemodialysis (HD group) and 24 age- and sex-matched control subjects (NC group). Standardized uptake values normalized by the body weight (SUVbw), ideal body weight (SUVibw), lean body mass (SUVlbm), and body surface area (SUVbsa) in the cerebellum, lungs, liver, gluteal muscles and subcutaneous fat, spleen, thoracolumbar spine, thoracic and abdominal aorta, and right atrium were calculated in positron emission tomography/computed tomography (PET/CT) images. SUVbw in the gluteal muscles, subcutaneous fat, spleen and right atrium was significantly higher in the HD group as compared to that in the NC group (p < 0.05; unpaired t test). In addition, SUVibm, SUVlbm, as well as SUVbsa in the abdominal aorta were significantly higher in the HD group as compared to those in the NC group (p < 0.05; unpaired t test). In conclusion, as compared to normal subjects, chronic renal failure patients on hemodialysis show significantly higher physiological FDG uptake in the soft tissues, spleen and blood pool.

Keywords: Chronic renal failure, hemodialysis, FDG-PET/CT, physiological uptake

Introduction

The number of chronic renal failure (CRF) patients on hemodialysis has been increasing yearly around the world [1]. These patients have a higher overall risk of developing cancer as compared to the general populations [2].

Positron emission tomography/computed tomography (PET/CT) with 2-deoxy-2-[18F]fluoro-D-glucose (FDG) is often used for the assessment of malignant tumors. Although about 10% of the injected FDG is excreted in the urine by 70 min post injection in patients with normal kidney function [3], CRF patients on hemodialysis lack urinary FDG excretion and remain in a constant volume overload. Therefore, the whole-body FDG distribution in CRF patients on hemodialysis would be different from that in subjects with normal renal function.

Although one previous study reported establishment of a model to estimate the tissue FDG uptake in patients with renal failure, the estimation was based on theoretical assessment and not in actual patients [4]. In some previous studies, whole-body FDG distribution [5], myocardial metabolism [6], and FDG uptake in atherosclerotic plaques [7] have been evaluated in renal failure patients. However, the subjects of these studies were not on maintenance hemodialysis and had relatively mild renal failure. To the best of our knowledge, there have been no reports of evaluation of the whole-body physiological FDG uptake pattern in CRF patients on hemodialysis. To understand whole-body FDG distribution in this patient is important for appropriate evaluation of FDG-PET/CT images in these patients.

Standardized uptake value (SUV) is a semi-quantitative index of FDG uptake that is gener-
FDG-PET/CT of patients on hemodialysis

Figure 1. Representative maximum intensity projection images of FDG-PET/CT of two subjects. Both cases are 67-year-old men. Chronic renal failure patients on hemodialysis (A) lack FDG uptake in the urinary tract (kidneys, ureters, and the bladder) compared to control subjects (B).

Material and methods

Our institutional review board has approved this retrospective study and the need for written informed consent was waived (approval number: 1513).

Subjects

We initially registered 37 CRF patients on hemodialysis who underwent whole-body FDG-PET/CT at our hospital between January 2006 and March 2013. Of these, 5 patients on peritoneal dialysis and 7 patients with hyperglycemia (> 120 mg/dl) were excluded from this study. We also excluded 1 patient with sepsis who showed extremely elevated FDG uptake in the bone marrow. Finally, 24 CRF patients were included in this study as the HD group. The mean period of hemodialysis was 13.7 (range; 1-37) years and the underlying kidney diseases were as follows: chronic glomerulonephritis (8 cases), nephrosclerosis (3 cases), membranous glomerulonephritis (1 case), diffuse mesangial proliferative glomerulonephritis (1 case), arteriopathic disease (1 case), drug-induced renal injury (1 case), and cause uncertain or missing (4 cases).

A total of 24 age- and sex-matched subjects who underwent FDG-PET/CT during the same period were included as the NC group. The inclusion criteria were as follows: (1) no previous history of malignancies, (2) no previous history of renal dysfunction and retained ability to evacuate the bladder before the PET/CT imaging, (3) normal blood sugar level (< 120 mg/dl), and (4) no symptoms suggestive of any inflammatory disorder at the time of the PET/CT imaging.

FDG-PET/CT protocol

After fasting for at least 4 h, the patients received an intravenous injection of 18F-FDG (3.7 MBq/kg). Then, 60 min after the FDG injection, whole-body PET/CT images were obtained using a PET/CT system (Aquiduo, Toshiba Medical Systems, Tokyo, Japan) consisting of a combination of a full-ring PET scanner with lute-
FDG-PET/CT of patients on hemodialysis

tium oxyorthosilicate crystals and a 16-row helical CT scanner. CT studies for attenuation correction were performed under expiratory breath-holding using the following parameters:

Figure 2. Globular regions of interest for measuring the standardized uptake value (same case as Figure 1A). Globular regions of interest were placed in the cerebellum (A), lungs (upper lobe) (B), liver (segment 8) (C), gluteal muscles (D), subcutaneous fat (E), spleen (F), thoracolumbar spine (Th11-L2) (G), thoracic aorta (H), abdominal aorta (I), and right atrium (J), as shown.
120 kV, 50-200 mAs, field of view 500 mm, pitch 15.0, and slice thickness 2.0 mm. PET emission data were obtained under free-breathing using the following parameters: 3D mode, 2 min per bed position (for 6-8 bed positions), matrix size 128 × 128, and Gaussian filter size 5 mm. All patients drank approximately 300 ml of water after the FDG injection for oral hydration and gastric dilatation. The subjects were instructed to evacuate their bladder just before the PET/CT imaging. No contrast media were used.

**Figure 1** shows maximum intensity projection images of representative cases from the HD and NC groups.

**Regions of interest for SUV measurements**

On the fused PET/CT images, one nuclear medicine physician and one radiologist placed, by consensus, globular regions of interest (ROI) in the cerebellum, lungs (upper lobe), liver (segment 8), gluteal muscles and subcutaneous fat, spleen, thoracolumbar spine (Th11-L2), thoracic and abdominal aorta, and right atrium. The diameters of the ROIs were 3 cm in both lungs, liver, and bilateral gluteal subcutaneous fat; 2 cm in bilateral cerebellar hemispheres, bilateral gluteus maximus muscles, spleen, Th11-L2 vertebral bodies, thoracic aorta (distal arch), and right atrium; 1 cm in the abdominal aorta (at the level of the renal arteries). If placing of ROI on the gluteal maximus muscles and subcutaneous fat was difficult because of muscular atrophy or a thin body, the diameter of the ROI was reduced to a minimum of 1 cm. **Figure 2** shows a representative illustrating the ROIs.

Although each ROI was carefully placed so as not to include any diseases or adjacent organs, placing of the ROI proved difficult in some organs in the HD group. Therefore, one right cerebellar hemisphere (old infarction), one right lung (pneumothorax), gluteal subcutaneous fat of either side in one patient (thin body), one spleen (previous splenectomy), one thoracolumbar spine (previous vertebroplasty), one thoracic aorta (aneurysm), two abdominal aortas (aneurysm and previous endovascular aneurysm repair), and two right atria (cardiac pacemaker insertion) were excluded from the analysis in the HD group. In the NC group, we were able to place the ROIs appropriately in all organs in all subjects.

In addition, we calculated the maximum SUV in the bladder urine, normalized by the body weight (SUV\text{bw}). However, 5 patients of the HD group in whom FDG uptake in the bladder could not be detected by visual interpretation were excluded.

**SUV measurements and normalization**

The mean SUV\text{bw} for each of the ROIs was calculated for all subjects. For the case of the thoracolumbar spine, the highest SUV\text{bw} among the Th11-L2 vertebral bodies was selected for the following evaluations. The obtained SUV\text{bw} was converted to SUVs normalized by the ideal body weight (SUV\text{ibw}), lean body mass (SUV\text{lbm}), and body surface area (SUV\text{bsa}) using the following equations [9-11]:

\[
\text{Ideal body weight [kg] for men} = 48.0 + 1.06 \times (\text{height [cm]} - 152.0) \\
\text{Ideal body weight [kg] for women} = 45.5 + 0.91 \times (\text{height [cm]} -152.0) \text{ (If the ideal body weight was greater than the weight, the ideal body weight was equal to the weight.)} \\
\text{Lean body mass [kg] for men} = 1.10 \times \text{weight [kg]} - 120 \times (\text{weight [kg]}/\text{height [cm]})^2 \\
\text{Lean body mass [kg] for women} = 1.07 \times \text{weight [kg]} - 148 \times (\text{weight [kg]}/\text{height [cm]})^2 \\
\text{Body surface area [m}^2] = (\text{weight [kg]})^{0.425} \times (\text{height [cm]})^{0.725} \times 0.007184 \\
\text{SUV\text{ibw} = SUV\text{bw} \times (ideal body weight [kg])/(body weight [kg])} \\
\text{SUV\text{lbm} = SUV\text{bw} \times (lean body mass [kg])/(body weight [kg])} \\
\text{SUV\text{bsa} = SUV\text{bw} \times (body surface area [m}^2]/\text{body weight [kg])} \\
\]

**Statistical analysis**

All numerical values are expressed as mean ± standard deviation. The differences in the clinical characteristics between the HD and NC groups were analyzed by student's t test. The mean SUV\text{bw}, SUV\text{ibw}, SUV\text{lbm}, and SUV\text{bsa} of each organs were compared between the HD and NC groups by an unpaired t-test. Differences with \( p < 0.05 \) were considered to be significant.
Results

The clinical characteristics of the HD and NC groups are shown in Table 1. The body weight in the HD group was significantly lower than that in the NC group (\( p = 0.003 \)). The height, injection-scan time, and blood sugar level were not significantly different between the two groups.

Table 2 shows mean SUV bw, SUV ibw, SUV lbm, and SUV bsa in each of the organs in the HD and NC groups. The SUV bw in the gluteus maximus muscle of both sides, gluteal subcutaneous fat of both sides, spleen, and right atrium was significantly higher in the HD group than those in the NC group. In addition, the SUV lbm, SUV ibw, and SUV bsa in the abdominal aorta were also higher in the HD group as compared to the NC group. For the case of the thoracic aorta, only the SUV bsa showed significant difference between the HD and NC groups. No significant differences in the values between the two groups were observed in the cerebellar hemisphere, lungs, liver and thoracolumbar spine.

The maximum SUV bw in the bladder urine was 2.69 ± 1.68 in the HD group and 25.3 ± 18.7 in the NC group. There was significant difference between the two groups (\( p < 0.001 \)).

Discussion

This was the first study conducted to evaluate the physiological FDG uptake pattern in CRF patients on hemodialysis. In these patients, the SUV bw in the gluteus maximus muscle, gluteal subcutaneous fat, and the right atrium were significantly higher as compared to the values in the control subjects. Given the insulin resistance in patients with kidney disease [12], the higher FDG uptake in the soft tissues may be an unexpected result. Although we cannot explain the mechanism from this study, these results indicate that the injected FDG, which should be excreted in the urine, accumulates in the soft tissues in CRF patients on hemodialysis. On the other hand, our finding of a higher SUV bw in the right atrium in the HD group as compared to that in the NC group was concordant with the previously published result by Derlin et al, who measured the SUV bw in the mid lumen of the upper and lower vena cava [7]. These findings suggest that the FDG accumulation in the central venous system may reliably reflect the degree of volume overload in CRF patients.

In our study, the splenic SUV bw also differed significantly between the HD and NC groups. In the HD group, two subjects had chronic hepatitis C and one was a silent hepatitis B carrier. However, we believe that hepatitis virus alone cannot explain our result, because of the small number of subjects with the virus. Patients on hemodialysis are known to have a high incidence of bacterial infections [13]. In these patients, the immune functions of the spleen may be activated by frequent exposure to potential infectious risk factors, such as repeated disruption of the skin barrier.

Because the reduced protein and energy intakes in CRF patients contribute to the decline in many of the nutritional measures [14], the body weight in the HD group was significantly lower than that in the NC group, as shown in Table 1. We expected that SUV normalization by the body size parameters had somewhat of an impact on the whole-body FDG uptake in the HD group. Consequently, the SUV bw, SUV ibw, and SUV bsa in the abdominal aorta differed significantly between the HD and NC groups. Furthermore, SUV bsa of the thoracic aorta in the HD group was significantly higher than that in the NC group. Although our findings of the absence of any significant difference in the SUV bw in the arterial blood pool (thoracic and abdominal aorta) between the HD and NC groups was discordant with the previous report by Minamimoto et al [5], FDG accumulation in the arterial blood pool should be elevated in CRF patients, based on our results of the analyses using the body size parameters.
Table 2. Standardized uptake values of each organs

<table>
<thead>
<tr>
<th>Group</th>
<th>HD</th>
<th>NC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right cerebellar hemisphere</td>
<td>(n = 23)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>6.65 ± 1.94</td>
<td>7.27 ± 1.14</td>
<td>0.194</td>
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<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>6.43 ± 1.97</td>
<td>6.70 ± 1.12</td>
<td>0.574</td>
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<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>5.48 ± 1.52</td>
<td>5.72 ± 0.95</td>
<td>0.531</td>
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<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.198 ± 0.053</td>
<td>0.196 ± 0.028</td>
<td>0.887</td>
</tr>
<tr>
<td>Left cerebellar hemisphere</td>
<td>(n = 24)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>6.68 ± 1.93</td>
<td>7.41 ± 1.23</td>
<td>0.123</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>6.46 ± 1.95</td>
<td>6.82 ± 1.16</td>
<td>0.444</td>
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<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>5.51 ± 1.52</td>
<td>5.82 ± 1.00</td>
<td>0.396</td>
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<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.198 ± 0.053</td>
<td>0.200 ± 0.030</td>
<td>0.890</td>
</tr>
<tr>
<td>Right lung</td>
<td>(n = 23)</td>
<td>(n = 24)</td>
<td></td>
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<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.31 ± 0.10</td>
<td>0.35 ± 0.07</td>
<td>0.156</td>
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<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.30 ± 0.09</td>
<td>0.32 ± 0.06</td>
<td>0.413</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.26 ± 0.08</td>
<td>0.27 ± 0.05</td>
<td>0.421</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.009 ± 0.002</td>
<td>0.009 ± 0.002</td>
<td>0.852</td>
</tr>
<tr>
<td>Left lung</td>
<td>(n = 24)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.35 ± 0.11</td>
<td>0.38 ± 0.10</td>
<td>0.292</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.34 ± 0.10</td>
<td>0.35 ± 0.08</td>
<td>0.665</td>
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<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.29 ± 0.09</td>
<td>0.30 ± 0.07</td>
<td>0.695</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.010 ± 0.002</td>
<td>0.010 ± 0.002</td>
<td>0.935</td>
</tr>
<tr>
<td>Liver</td>
<td>(n = 24)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>2.23 ± 0.39</td>
<td>2.39 ± 0.28</td>
<td>0.104</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>2.15 ± 0.42</td>
<td>2.20 ± 0.26</td>
<td>0.678</td>
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<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>1.85 ± 0.33</td>
<td>1.88 ± 0.23</td>
<td>0.700</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.066 ± 0.010</td>
<td>0.065 ± 0.005</td>
<td>0.415</td>
</tr>
<tr>
<td>Right gluteal muscle</td>
<td>(n = 24)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.67 ± 0.14</td>
<td>0.60 ± 0.10</td>
<td>0.048*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.65 ± 0.14</td>
<td>0.55 ± 0.08</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.56 ± 0.12</td>
<td>0.47 ± 0.08</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.020 ± 0.004</td>
<td>0.016 ± 0.002</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Left gluteal muscle</td>
<td>(n = 24)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.66 ± 0.14</td>
<td>0.59 ± 0.08</td>
<td>0.036*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.64 ± 0.15</td>
<td>0.54 ± 0.06</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.55 ± 0.12</td>
<td>0.46 ± 0.06</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.020 ± 0.003</td>
<td>0.016 ± 0.002</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Right subcutaneous fat</td>
<td>(n = 23)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.46 ± 0.25</td>
<td>0.29 ± 0.18</td>
<td>0.012*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.44 ± 0.24</td>
<td>0.27 ± 0.19</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.39 ± 0.22</td>
<td>0.23 ± 0.16</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.014 ± 0.007</td>
<td>0.008 ± 0.006</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Left subcutaneous fat</td>
<td>(n = 23)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>0.45 ± 0.26</td>
<td>0.29 ± 0.19</td>
<td>0.021*</td>
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<tr>
<td>SUV&lt;sub&gt;ibw&lt;/sub&gt;</td>
<td>0.44 ± 0.25</td>
<td>0.28 ± 0.19</td>
<td>0.016*</td>
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<tr>
<td>SUV&lt;sub&gt;lbm&lt;/sub&gt;</td>
<td>0.38 ± 0.22</td>
<td>0.24 ± 0.17</td>
<td>0.016*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bsa&lt;/sub&gt;</td>
<td>0.014 ± 0.008</td>
<td>0.008 ± 0.006</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Spleen</td>
<td>(n = 23)</td>
<td>(n = 24)</td>
<td></td>
</tr>
<tr>
<td>SUV&lt;sub&gt;bw&lt;/sub&gt;</td>
<td>2.08 ± 0.38</td>
<td>1.88 ± 0.25</td>
<td>0.039*</td>
</tr>
</tbody>
</table>

In other organs, the SUV<sub>ibw</sub>, SUV<sub>lbm</sub>, and SUV<sub>bsa</sub> showed similar trends to those of the SUV<sub>bw</sub>. The body weight was equal to the ideal body weight in 18/24 patients (75.0%) of the HD group, but in only 6/24 subjects (25.0%) of the NC group. Therefore, the SUV<sub>bw</sub> may be meaningless, particularly in CRF patients on hemodialysis. Recently, use of SUV<sub>lbm</sub> has been spreading for monitoring of the responses to anticancer therapy (PERCIST) [15]. The hepatic SUV<sub>lbm</sub>, which is the reference organ in PERCIST, did not differ significantly between the HD and NC groups. However, the effects of elevated FDG uptake in the background organs or blood pool may influence the judge of the therapeutic effect. Further studies will be needed to confirm the applicability of PERCIST in CRF patients on hemodialysis.

Our study has some limitations. First, because not all subjects in the NC group gave blood samples, there remains the possibility of inclusion of some patients with mild renal failure in the NC group as well. However, all the subjects in the NC group could evacuate their bladder prior to the PET/CT imaging and showed significantly higher FDG uptake in their bladder urine (maximum SUV<sub>bw</sub> was 25.3 ± 18.7). Therefore, we believe that these subjects were applicable for comparison with CRF patients on hemodialysis. Second, because most patients in the HD group had been undergoing hemodialysis at another hospital, the interval between the FDG-PET/CT and the last hemodialysis was not uniform, and information about the protocol of hemodialy-
FDG-PET/CT of patients on hemodialysis

sis and nutritional status was insufficient. The other limitations were the small sample size and retrospective design of the study.

In conclusion, CRF patients on hemodialysis show significantly higher physiological FDG uptake in the soft tissues, spleen, and the blood pool as compared to normal subjects.

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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