Increasing Body Fat Mass in the First Year of Hemodialysis

EIJI ISHIMURA,* SENJI OKUNO,† MASAO KIM,‡ TADASHI YAMAMOTO,‡
TSUYOSHI IZUMOTANI,‡ TATSUYUKI OTOSHI,‡ TETSUO SHOJI,*
MASAAKI INABA,* and YOSHIKI NISHIZAWA*
*Second Department of Internal Medicine, Osaka City University Medical School, and †Shirasagi Hospital Kidney Center, Osaka, Japan.

Abstract. Nutritional status affects well-being and survival in patients who are undergoing hemodialysis. It was examined how maintenance hemodialysis altered body fat mass. In 72 patients with chronic renal failure (age, 62 ± 12 yr; 42 men, 30 women), body fat was measured by dual x-ray absorptiometry 1 mo after initiation of maintenance hemodialysis and approximately 1 yr later (mean ± SD, 11 ± 2 mo). The second measurement showed significantly greater body fat mass than the first (11.38 ± 3.84 versus 10.09 ± 4.12 kg; P < 0.0001). After calculation of the change in body fat mass per month, no significant differences were evident in relation to gender or to presence of diabetes. Changes in body fat mass per month correlated negatively with baseline serum albumin concentration (r = −0.449, P < 0.0001) and baseline body fat mass (r = −0.423, P < 0.001). These factors independently influenced the change according to multiple regression analysis (R² = 0.323, P < 0.0001). In conclusion, body fat mass increases significantly in the first year of maintenance hemodialysis, especially in patients with poor nutritional status. More general, dual x-ray absorptiometry assessment of body fat mass was found to be useful for evaluating the nutritional status of hemodialysis patients.

Nutritional status is an important factor that affects morbidity and mortality in patients with end-stage renal disease (1–6). Several assessment methods have been reported to be of value in this population, such as subjective global assessment (7–9), as well as comparison of anthropometric (2,4,10–13) and serum parameters (e.g., albumin, insulin-like growth factor, transferrin) (2,3,6,9,14–17). Body composition measured by bioimpedance methods and dual x-ray absorptiometry (DXA) also has been examined in this context (6,10,11,18–24), although the clinical applicability of these methods has not been well established. DXA can separately measure bone mineral content, fat mass, and fat-free soft-tissue mass (lean body mass); the estimation of body fat mass is relatively precise and, importantly in dialysis patients, is unaffected by hydration status (11,21–23,25–27).

Generally, hemodialysis patients have been reported to be undernourished, although initiation of maintenance hemodialysis has been reported to improve not only quality of life but also nutritional status (2,12,14,28,29). However, few reports have clarified the extent to which nutritional status is enhanced by maintenance hemodialysis (14,28,29), and, to our knowledge, none have made use of serial DXA. We used this method to examine whether hemodialysis affects body fat mass. We also analyzed various factors that might influence fat mass in this population. Finally, we considered how well DXA changes reflected the nutritional status of patients who are undergoing hemodialysis.

Materials and Methods

Patients

Maintenance hemodialysis was initiated at Shirasagi Hospital, Osaka, in all patients between January 1995 and March 1996. During the period, a total of 124 patients with end-stage renal disease commenced hemodialysis at Shirasagi Hospital. Ten patients died, and 28 patients moved to other dialysis clinics within 2 mo. Eighty-six patients participated in the study protocol; however, six patients died during the study period, and eight patients could not complete the protocol because they moved to another dialysis clinic later (n = 6) or refused the second DXA measurement (n = 2). No patient received transplantation. The remaining 72 patients with end-stage renal failure (mean age ± SD, 62 ± 12 yr) were studied. At the start of hemodialysis, serum creatinine levels were 9.5 ± 1.2 mg/dl. They consisted of 42 men and 30 women (age, 62 ± 12 yr for both). Causes of end-stage chronic renal disease were diabetes mellitus in 36 patients (21 men and 15 women) and other conditions in 36 (21 men and 15 women), including chronic glomerulonephritis in 23 patients, hypertensive nephrosclerosis in 6, and unknown causes in 7. At the stage of preterminal renal failure, all patients were advised by dietitians to consume food that contain 30 to 35 kcal/kg ideal body weight and protein of 0.8 g/kg ideal body weight. After the start of hemodialysis, all of the patients were advised regularly to consume food containing 35 kcal/kg ideal body weight.

Patients underwent three 4-h sessions of hemodialysis per week that used cuprophane dialyzers and bicarbonate-buffered dialysate, which contains 100 mg/dl glucose and 30 mEq/L bicarbonate. All patients were free of significant acute illness at the onset of maintenance hemodialysis as well as through the second DXA measurement approximately 1 yr later. Blood was drawn for routine analysis before
a session of hemodialysis. Total protein, serum albumin, calcium, phosphate, and cholesterol were measured by an autoanalyzer.

**Measurements of Body Fat Mass**

Body fat mass was measured twice by DXA (QDR-1000W; Hologic Inc., Waltham, MA), with both measurements performed 21 to 24 h after completion of a dialysis session. The first measurement was carried out between 1 and 2 mo after initiation of hemodialysis, after stable hemodialysis conditions were achieved in each patient in terms of stable dry weight and cardiothoracic ratio (45 ± 5%). The second measurement was performed approximately 1 yr after the first (11 ± 2 mo). Body fat mass was expressed in kilograms. Changes in body fat mass were calculated as grams per month. Reproducibility of the fat mass measurement expressed by coefficient of variation was excellent and has been reported as <1% for body fat mass in adults (21,23,25,30). In our previous study, the reproducibility was <2% in patients who were undergoing hemodialysis (31).

**Statistical Analyses**

Statistical analyses were performed by use of the StatView V system (SAS Institute, Cary, NC) with a Macintosh computer. All data are expressed as mean ± SD unless otherwise stated. Differences in clinical data between the times of the first and second DXA measurements were compared by paired t tests. \( \chi^2 \) tests were performed for comparisons between two groups. Correlation and linear regression analyses were used to examine the relationship between clinical parameters. Multiple regression analysis with a forward elimination analyses were used to examine the relationship between clinical parameters. A positive correlation between monthly fat mass change and age levels and fat mass of the patients with an increased fat mass were significantly lower than those with a decreased fat mass \( (P < 0.05, \text{unpaired } t \text{ test}; \text{Table } 2) \). At the second DXA measurement, however, there were no significant differences between the patients with increased and decreased fat mass in serum parameters, including albumin and cholesterol. Fat mass at the second measurement was not significantly different between patients with increased and decreased fat mass \( (11.67 \pm 3.32 \text{ kg } \text{versus } 10.68 \pm 4.83 \text{ kg}, \text{respectively}; P = 0.312, \text{unpaired } t \text{ test}) \).

**Fat Mass Change per Month**

Because the interval between the first and second DXA measurements varied from 9 to 14 mo \( (11 \pm 2 \text{ mo}) \), changes in fat mass between the two measurements were assessed as grams per month. Fat mass increase was +118 ± 26 g/mo overall \( (\text{mean } \pm \text{SEM}) \).

**Factors Related to Fat Mass Change**

No significant difference in monthly fat mass change was evident between men and women \( (133 \pm 27 \text{ versus } 96 \pm 50 \text{ g/mo, mean } \pm \text{SEM}) \). Monthly fat mass change in patients with diabetes mellitus was not significantly different from change in patients without diabetes mellitus \( (117 \pm 31 \text{ versus } 118 \pm 42 \text{ g/mo, mean } \pm \text{SEM}) \).

By linear-regression analysis, significant negative correlations were noted between monthly fat mass change and baseline serum albumin \( (r = -0.449, P < 0.0001; \text{Figure } 2) \), as well as baseline fat mass \( (r = -0.423, P < 0.001; \text{Figure } 2) \) and baseline serum calcium \( (r = -0.391, P < 0.01) \). A positive correlation between monthly fat mass change and age

**Table 1.** Clinical parameters, lean body mass, and fat mass at the time of serial measurement by DXA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DXA Measurement</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>Body weight (dry weight) (kg)</td>
<td>51.2 ± 9.1</td>
<td>51.9 ± 9.2</td>
</tr>
<tr>
<td>Body mass index</td>
<td>20.6 ± 3.1</td>
<td>20.8 ± 3.0</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>78.8 ± 12.9</td>
<td>80.9 ± 10.2</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>8.3 ± 2.1</td>
<td>10.0 ± 2.4</td>
</tr>
<tr>
<td>Total protein (g/dl)</td>
<td>6.7 ± 0.6</td>
<td>6.8 ± 0.5</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>3.9 ± 0.3</td>
<td>4.1 ± 0.3</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)</td>
<td>8.9 ± 0.5</td>
<td>9.4 ± 0.5</td>
</tr>
<tr>
<td>Serum phosphate (mg/dl)</td>
<td>5.5 ± 0.9</td>
<td>5.8 ± 0.9</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>163 ± 34</td>
<td>155 ± 40</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.17 ± 0.22</td>
<td>1.19 ± 0.25</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>10.09 ± 4.12</td>
<td>11.38 ± 3.84</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>39.62 ± 6.50</td>
<td>38.91 ± 7.04</td>
</tr>
</tbody>
</table>

\( a \) All data are expressed as mean ± SD. DXA, dual x-ray absorptiometry; PTH, parathyroid hormone.  
\( b \) P < 0.05 \( (\text{paired } t \text{ test}) \).  
\( c \) P < 0.01 \( (\text{paired } t \text{ test}) \).  
\( d \) P < 0.0001 \( (\text{paired } t \text{ test}) \).
showed borderline significance \( r = 0.232, P = 0.051 \). Monthly fat mass change, however, had no significant correlation with body weight, body mass index, blood urea nitrogen, serum creatinine, phosphate, cholesterol, Kt/V, or lean body mass at the time of the first DXA measurement (baseline), although there tended to be a negative correlation between monthly fat mass change and serum cholesterol \( r = -0.271, P = 0.102 \). The monthly fat mass change was not significantly correlated with the changes in serum albumin, cholesterol, or creatinine levels between the two DXA measurements.

To analyze factors that affect fat mass changes, we performed multiple regression analysis that used a model in which serum albumin, fat mass, calcium, and age were included as independent variables. These independent variables were selected on the basis of the linear regression analysis. Baseline serum albumin and fat mass showed independent relationships to monthly fat mass change \( R^2 = 0.323, P < 0.0001 \; \text{(Table 3)} \).

**Discussion**

In the present study, body fat mass was demonstrated by DXA to increase significantly during the first year of maintenance hemodialysis. The baseline serum albumin and cholesterol levels and fat mass of the patients with increased fat mass were significantly lower than those with decreased fat mass. The fat mass increase was negatively related to serum albumin concentration and body fat mass at baseline. Hemodialysis, then, particularly increased body fat mass in patients with poorer initial nutritional status.

Various methods have been used to assess nutritional status of patients undergoing dialysis. Anthropometric parameters, such as weight, body mass index, skin-fold thickness, and midarm muscle circumference, frequently were used \( (2,4,10–13) \). Body composition changes indicated by bioimpedance measurement \( (6,10,18,19) \), computed tomographic determination of fat mass distribution \( (32) \), and DXA \( (11,18,20–22,24) \) also were examined as methods for assessment of nutritional status in dialysis patients. Although anthropometry is easy and inexpensive to perform, it is subject to artifacts from fluid accumulation in patients who are undergoing hemodialysis.
Bioimpedance also can be affected by hydration status (6,10,19,24). DXA measures the differential attenuation of two x-rays as they pass through the body, distinguishes bone mineral from soft-tissue mass, and subsequently divides soft-tissue mass into fat mass and fat-free soft-tissue mass (lean body mass). Reproducibility of the measurement is excellent; the reported CV is <1% for body fat mass in adults (21,23,25,30). Unlike estimates from anthropometry and bioimpedance, body fat mass measurements by DXA are affected little by hydration status, even though lean body mass by DXA is affected by hydration (11,21–23). Reproducibility of the fat mass measurement by DXA expressed by coefficient of variation also was excellent: 2% in patients who were undergoing hemodialysis recently reported by us (31). So far, to our knowledge, nothing has been reported about longitudinal change in body fat mass in patients who are undergoing hemodialysis. In the present study, body fat mass measured by DXA was significantly increased in the first year of maintenance hemodialysis, even though anthropometric parameters such as weight and body mass index did not change significantly. In the present study, lean body mass at the time of second measurement was significantly lower than that at the first measurement (−0.71 ± 2.39 kg; P < 0.05). However, the size and statistical significance of changes in lean body mass were smaller than the increase of body fat mass (P < 0.0001, ± 1.29 ± 2.20 kg). The decrease in lean body mass may reflect gradual fluid removal to achieve optimal dry weight during the year of hemodialysis. Lean body mass in patients who are undergoing hemodialysis is affected greatly by hydration status (11,21–23).

In our recent study (31), the fat mass of 104 patients who were undergoing hemodialysis with a hemodialysis duration of 7.5 ± 5.1 yr (age, 53.9 ± 9.1; 39 men and 64 women) was 12.55 ± 4.8 kg, which was significantly lower than 167 age- and gender-matched healthy control subjects (14.24 ± 3.70 kg fat mass; 52.9 ± 9.0 yr old; 53 men and 114 women; P < 0.05). The fat mass of the present study at both the first and second measurements was significantly lower than that of both the patients who were undergoing hemodialysis and the healthy control subjects in the previous study (P < 0.05, unpaired t test), although the patient age in the present study was significantly older. In a preliminary study the fat mass of 15 patients with a hemodialysis duration of 15.3 ± 2.7 yr (61 ± 8 yr old; 9 men and 6 women) was 9.23 ± 2.84 kg, which was significantly lower than the fat mass at the second measurement in the present study (P < 0.05, unpaired t test). Taken together, we suggest that the fat mass change

Table 3. Factors that affect monthly fat mass changea

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>F</th>
<th>R²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat mass change</td>
<td>Serum albumin</td>
<td>−0.386</td>
<td>14.673</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fat mass (kg)</td>
<td>−0.354</td>
<td>12.368</td>
<td>0.323</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.179</td>
<td>2.245</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcium</td>
<td>−0.141</td>
<td>0.829</td>
<td></td>
</tr>
</tbody>
</table>

a Multiple regression analysis with a forward elimination procedure was performed to assess the combined influence of variables on fat mass change. Serum albumin and fat mass are values at the time of initial fat mass measurement, β is a standard regression coefficient, and R² a multiple coefficient of determination.
may increase initially in the first year after hemodialysis initiation and continue to increase slowly thereafter for approximately 7 yr and then decrease thereafter until approximately 15 yr, although further examination that uses a longitudinal follow-up of a large number of patients is required to confirm this.

Several serum parameters have been advocated for assessment of nutritional status in patients who are undergoing hemodialysis in relation to morbidity and mortality. Among these, low serum concentrations of albumin have been reported to be the most significant and useful indicator of poor nutritional status (1–3,14,33,34). Low levels of serum creatinine also have been reported to indicate poor nutrition and predict decreased survival in patients who are undergoing hemodialysis (14,33–35). After initiation of maintenance hemodialysis, serum albumin and creatinine were reported to increase significantly in the first 6 mo (14,28,29). Poor nutritional status during the first year of dialysis, compared with that thereafter, also has been reported (12). In the present study, serum levels of albumin and creatinine were significantly increased ($P < 0.001$), which suggests that nutritional status improves in most patients during the first year of dialysis.

We found significantly lower concentrations of baseline serum albumin and cholesterol in patients with increased fat mass than in patients with decreased fat mass. Furthermore, we found a significant negative correlation between monthly fat mass change and baseline serum albumin. Considering that low serum albumin concentrations reflect poor nutritional status (1–3,14,33,34), the present study demonstrates that patients with poorer nutritional status accumulated more body fat during the first year of hemodialysis. We also found a significant negative correlation between monthly fat mass change and baseline body fat mass, which indicates more gain at 1 yr when initial fat mass was low. By multiple regression analysis, both of these effects were independent. Therefore, lower body fat mass at baseline represents poorer nutritional status in these patients. Because there was no significant correlation between baseline serum albumin and baseline body fat mass by linear regression analysis ($P = 0.1333$), we speculate that body fat mass measured by DXA may be a separate aspect of nutritional status clinically different from serum albumin. After initiation of hemodialysis, most patients generally experience increased well-being and improved appetite. Most symptoms associated with uremia, such as loss of appetite, nausea, and generalized fatigue, diminish or disappear. Proteinuria also decreases as residual renal function decreases, which leads to increased serum albumin concentrations (14). One result is improvement of nutritional status (2,12,14), which was related to the increase in body fat mass in the present study.

Malnutrition, reported to be common in maintenance dialysis patients, is associated with increased morbidity and mortality in this population (1–6). To assess malnutrition, various laboratory parameters have been advocated, including serum albumin, creatinine, cholesterol, prealbumin, insulin-like growth factor, interleukin-6, C-reactive protein, transferrin, and plasma free amino acids (2,3,6,9,13–17). Body fat mass seems to be a parameter distinct from serum albumin. Serum parameters such as albumin concentrations are affected easily by degree of proteinuria (14,28), particularly in the 6 mo of maintenance hemodialysis, by inflammatory conditions as reflected by C-reactive protein (1,3,6), and also by hydration status (3,14,19,29). Given these limitations of serum parameters, DXA should provide a very useful nutritional marker in these patients.

In conclusion, body fat mass increased significantly during the first year of maintenance hemodialysis. Degree of change per month was influenced by baseline serum albumin and baseline body fat mass in an independent manner. Complementing subjective global assessment, anthropometric methods, and serum parameters, DXA assessment of fat mass change should be a particularly reliable way to evaluate nutritional status in patients who are undergoing hemodialysis.

References


