PART FOUR

Metabolism and Nutrition
Protein nitrogen appearance (PNA) estimated from urea nitrogen appearance (UNA) reflects dietary protein intake and is an important index of nutrition in peritoneal dialysis (PD). Normalization of PNA by several body size indicators has resulted in discrepancies between normalized PNA (nPNA) values and other nutrition indices in PD patients with varying weight status. To test whether a particular size indicator produces nPNA values that eliminate the discrepancies, we normalized PNA values obtained at the first clearance study in 925 PD patients by weight (W), by fat-free mass (FFM) obtained from body water, by lean body mass (LBM) derived from creatinine kinetics, by desirable weight (DW), by standard weight (SW), and by adjusted edema-free body weight (aBW). We classified patients into three groups according to W/DW: an underweight group [group I: W/DW < 0.9, n = 147 (15.9%)], a normal-weight group [group II: 0.9 ≤ W/DW < 1.2, n = 506 (54.7%)], and an obese group [group III: W/DW ≥ 1.2, n = 272 (29.4%)]. The UNA and PNA increased progressively from group I to group III. The W, FFM, LBM, SW, and aBW also increased progressively, and the corresponding nPNA values decreased progressively from group I to group III—all at p < 0.001. The DW did not differ significantly between the three groups. The PNA values normalized by DW were 0.91 ± 0.21 (group I), 0.96 ± 0.24 (group II), and 1.07 ± 0.25 (group III), p < 0.001. Of the six size indicators tested, only DW produced values of nPNA consistent with the nutrition status of PD patients with varying weight status. Our findings indicate that DW is the proper size indicator for normalizing PNA in PD patients.

Key words
Protein nitrogen appearance, actual body weight, fat-free mass, lean body mass, desirable weight, standard weight, adjusted edema-free body weight

Introduction
Nutrition affects the outcome of peritoneal dialysis (PD). Consequently, monitoring the nutrition status of PD patients is recommended (1,2). Protein nitrogen appearance (PNA), estimated from urea nitrogen excretion in urine plus dialysate, is a useful index of nutrition in PD (1,2). The PNA is routinely normalized (nPNA) by a size indicator to allow for comparisons between subjects of varying body size. However, discrepancies have been reported between nPNA values and other indices of nutrition in PD patients with varying weight status. Normalization of PNA by actual weight (W) or standard weight (SW: V/0.58, where V is body water) produces relatively low nPNA values in obese PD patients, who tend to have good nutrition indices, and relatively high values in underweight PD patients, who routinely have poor nutrition indices (3–5).

The question about normalization of PNA that remains unanswered to date is whether a particular size indicator produces nPNA values that reflect, without systematic errors, the nutrition status of PD patients with varying weight status. Several studies have simultaneously used multiple size indicators for such a purpose (4–6). Furthermore, current guidelines offer conflicting instructions about the size indicator that should properly be used to normalize PNA. The guide-
lines on adequacy of nutrition in renal failure patients (1) recommend use of adjusted-edema free body weight (aBW), but the guidelines for adequacy of PD (2) suggest the use of both standard weight (SW) and lean body mass (LBM) estimates derived from creatinine kinetics.

The present study tested whether any particular size indicator might produce nPNA values consistent with the prevailing nutritional characteristics of obese, normal-weight, and underweight PD patients. To properly describe the differences, the nPNA values should increase progressively from the underweight patients to the patients in the obese group.

**Patients and methods**

We analyzed PNA values for 925 North American patients at the time of their first clearance study, which was performed 7.1 ± 6.5 months after initiation of PD. The dialysis units following the patients, the characteristics of the patients and their PD schedules, and the details of the clearance methods have been described elsewhere (4,5,7–10).

In calculating clearances and nutrition indices derived from urea nitrogen appearance, we made these modifications:

- **Body water** ($V$) was estimated using the Sahlgrenska formulas (11). We elected to use those formulas because they are the only ones that were derived in PD patients. Estimates of $V$ by the Sahlgrenska formulas and the Watson formulas agree closely (11,12).

- The PNA was computed by the Bergström formula (13), because that formula was derived in PD patients and is recommended by current guidelines (2). The Bergström formula is

$$\text{PNA} = 20.1 + 7.50 \times \text{UNA}, \quad [1]$$

where UNA (urea nitrogen appearance in urine plus dialysate) and PNA are expressed as grams in a 24-hour period.

The PNA was then normalized to these size indicators: actual body weight (nPNA$_W$), fat-free mass (nPNA$_{FFM}$), lean body mass (nPNA$_{LBM}$), desirable weight (nPNA$_{DW}$), standard weight (nPNA$_{SW}$), and adjusted edema-free body weight (nPNA$_{aBW}$). The FFM was calculated as $V/0.73$ (12). The LBM was obtained from creatinine kinetics (14,15). The DW was obtained from the Metropolitan Life Insurance tables (16), assuming medium skeletal frame. The SW was calculated as $V/0.58$ (7), and the aBW was obtained by using this formula (17):

$$\text{aBW} = \text{BW}_{ef} + [ (\text{NW} – \text{BW}_{ef}) \times 0.25 ], \quad [2]$$

where BW$_{ef}$ is a clinical estimate of edema-free body weight, and NW is the “normal” body weight (2,17).

In a previous study, we estimated that edema represents, on average, 3% of actual body weight in PD patients (18). The BW$_{ef}$ was therefore estimated as $0.97 \times W$. Calculation of NW requires elbow-breadth measurement (17), which was unavailable in the present study. We therefore estimated NW according to this formula (17,19):

$$\text{NW} = 1.09 \times \text{DW}. \quad [3]$$

Patients were classified into one of three weight categories based on the ratio of their actual weight ($W$) to their desirable weight ($DW$). Patients whose $W/DW < 0.9$ were classified as underweight; those with $0.9 < W/DW \leq 1.2$ were classified as normal-weight; and those with $W/DW > 1.2$ were classified as obese (20).

Continuous variables were first compared between underweight, normal-weight, and obese patients by one-way analysis of variance (one-way ANOVA), which requires equal variances for all the groups tested. However, for some parameters, the Bartlett test showed lack of homogeneity of group variances. Therefore, the comparisons of continuous variables were repeated using a nonparametric statistical method—namely, the Kruskal–Wallis one-way ANOVA. Differences between the one-way ANOVA and the Kruskal–Wallis statistic are noted in the text. Categorical variables were compared by chi-square test.

**Results**

Table I summarizes the characteristics of the PD patients by their classifications as underweight, normal-weight, and obese. The normal-weight group contained relatively fewer women than either the underweight or the obese group. The percentage of patients with diabetes mellitus increased progressively from the underweight group to the obese group. The
underweight group was younger and had higher normalized urea clearances than either the normal-weight group or the obese group.

Table II shows the PNA and nPNA values and their determinants. The UNA, PNA, W, FFM based on the Sahlgrenska formula, LBM derived from creatinine kinetics, SW, and aBW all increased progressively from the underweight group to the obese group. The DW did not differ between the three weight groups. Despite the increase in PNA values from the underweight group to the obese group, the corresponding values of PNA normalized by W, FFM, LBM, SW, and aBW all increased progressively from the underweight group to the obese group.

**Other relevant values**

Blood urea nitrogen (BUN) was 51.1 ± 16.2 mg/dL in the underweight group, 55.6 ± 14.5 mg/dL in the normal-weight group, and 55.1 ± 18.0 mg/dL in the obese group (one-way ANOVA: p = 0.036; Kruskal–Wallis statistic: p = 0.083). Serum creatinine was 8.6 ± 3.0 mg/dL in the underweight group, 9.9 ± 3.7 mg/dL in the normal-weight group, and 9.9 ± 3.4 mg/dL in the obese group (one-way ANOVA and Kruskal–Wallis statistic: p < 0.001). Creatinine excretion was 784 ± 270 mg in 24 hours in the underweight group, 1002 ± 389 mg in 24 hours in the normal-weight group, and 1117 ± 405 mg in 24 hours in the obese group (one-way ANOVA and Kruskal-Wallis statistic: p < 0.001).

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**Table I** Summary of the characteristics of the three weight groups of peritoneal dialysis (PD) patients

<table>
<thead>
<tr>
<th></th>
<th>Group I Underweight</th>
<th>Group II Normal-weight</th>
<th>Group III Obese</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients [n (%)]</td>
<td>147 (15.9%)</td>
<td>506 (54.7%)</td>
<td>272 (29.4%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>75 (51.0%)</td>
<td>336 (66.4%)</td>
<td>141 (51.8%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>72 (49.0%)</td>
<td>170 (33.6%)</td>
<td>131 (48.2%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>49 (33.3%)</td>
<td>206 (40.7%)</td>
<td>143 (52.6%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>98 (66.7%)</td>
<td>300 (59.3%)</td>
<td>129 (47.4%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.7 ± 4.2</td>
<td>7.1 ± 3.1</td>
<td>24.3 ± 2.0</td>
<td>31.8 ± 3.9</td>
</tr>
<tr>
<td>PD duration (months)</td>
<td>18.8 ± 1.6</td>
<td>2.22 ± 0.56</td>
<td>72.2 ± 27.9</td>
<td>68.9 ± 26.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>18.8 ± 0.07</td>
<td>0.81 ± 0.07</td>
<td>6.5 ± 6.0</td>
<td>6.0 ± 6.0</td>
</tr>
<tr>
<td>W/DW</td>
<td>24.3 ± 2.0</td>
<td>0.57 ± 0.08</td>
<td>12.7 ± 3.9</td>
<td>11.8 ± 3.9</td>
</tr>
<tr>
<td>Kt/V urea</td>
<td>0.55 ± 0.08</td>
<td>1.05 ± 0.08</td>
<td>3.5 ± 1.13</td>
<td>3.9 ± 1.38</td>
</tr>
<tr>
<td>CCr a (L/1.73 m²)</td>
<td>0.17 &lt;0.001</td>
<td>0.25 &lt;0.001</td>
<td>0.28 &lt;0.001</td>
<td>0.21 &lt;0.001</td>
</tr>
</tbody>
</table>

a The p values in the comparisons of continuous variables in this table were obtained by one-way ANOVA. The Kruskal–Wallis statistic produced the same p values for all comparisons except Kt/V urea (Kruskal–Wallis statistic: p < 0.001).

b Weekly values.

NS = nonsignificant; BMI = body mass index; W = actual weight; DW = desirable weight; CCr = creatinine clearance.

**Table II** Comparisons of values for urea nitrogen appearance (UNA) and protein nitrogen appearance (PNA), normalizing size indicators, and nPNA values between the three weight groups of peritoneal dialysis (PD) patients

<table>
<thead>
<tr>
<th></th>
<th>Group I Underweight</th>
<th>Group II Normal-weight</th>
<th>Group III Obese</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNA (g/24 h)</td>
<td>4.7 ± 1.7</td>
<td>5.6 ± 2.1</td>
<td>6.3 ± 2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PNA (g/24 h)</td>
<td>55.3 ± 13.0</td>
<td>62.4 ± 15.9</td>
<td>67.6 ± 17.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>W (kg)</td>
<td>49.7 ± 7.0</td>
<td>68.1 ± 8.7</td>
<td>87.6 ± 14.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>41.1 ± 7.0</td>
<td>50.2 ± 8.8</td>
<td>55.9 ± 11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>34.8 ± 8.6</td>
<td>43.9 ± 13.0</td>
<td>49.5 ± 14.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SW (kg)</td>
<td>61.1 ± 6.0</td>
<td>64.9 ± 6.7</td>
<td>63.5 ± 7.7</td>
<td>NS</td>
</tr>
<tr>
<td>aBW (kg)</td>
<td>51.7 ± 8.8</td>
<td>63.2 ± 10.5</td>
<td>70.4 ± 14.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA w a</td>
<td>1.13 ± 0.27</td>
<td>0.92 ± 0.22</td>
<td>0.78 ± 0.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA f a b</td>
<td>1.38 ± 0.35</td>
<td>1.26 ± 0.33</td>
<td>1.24 ± 0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA LBM a b</td>
<td>1.65 ± 0.40</td>
<td>1.48 ± 0.38</td>
<td>1.42 ± 0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA SW a b</td>
<td>0.91 ± 0.21</td>
<td>0.96 ± 0.24</td>
<td>1.07 ± 0.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA a b</td>
<td>1.09 ± 0.28</td>
<td>1.00 ± 0.26</td>
<td>0.98 ± 0.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>nPNA a b</td>
<td>1.06 ± 0.25</td>
<td>0.93 ± 0.23</td>
<td>0.84 ± 0.19</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

a The p values in this table were the same for both the one-way ANOVA and the Kruskal–Wallis statistic.

b g/kg in 24 hours.

W = actual weight; FFM = fat-free mass; LBM = lean body mass; DW = desirable weight; NS = nonsignificant; SW = standard weight; aBW = adjusted edema-free body weight; nPNA = normalized protein nitrogen appearance.
Discussion
The present study aimed to provide a clear answer to the question “What is the proper size indicator for normalizing PNA in PD patients?” Ideally, the proper size indicator should avoid introducing systematic bias when applied to patients with varying weight status. Consequently, nPNA should reflect the observation that obese PD patients have, in general, better nutrition indices than patients of normal body weight (6), and that underweight PD patients have worse nutrition indices than patients of normal body weight (5).

Our study revealed that urea nitrogen excretion [an index of protein intake (21)] and creatinine excretion [an index of somatic nutrition (22)] are highest in obese PD patients and lowest in underweight PD patients. Concomitantly, five of the six size indicators tested also increased progressively from the underweight group to the obese group (Table II). The aBW values that were used in the present study are approximations based on DW, which underestimates normal weight by 8%–10% (17,19). However, aBW in PD patients always represents an approximation, because it requires a clinical estimate of dry weight (7,17).

The DW was the only size indicator that did not vary between the three weight groups. Consequently, only PNA normalized by DW increased progressively from the underweight group to the obese group. All other nPNA values decreased (Table II).

Conclusion
Only PNA normalized by DW reflects the differences in nutrition between PD patients with varying weight status, and thereby eliminates the systematic errors introduced by the other size indicators tested. We propose that nPNA_{DW} is the appropriate way of expressing normalized PNA in PD patients.

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References


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