Icodextrin-based peritoneal dialysis (PD) has many advantages over glucose-based PD. The present study aimed to investigate when icodextrin should be started for better management of cardiovascular status (as defined by echocardiography findings) and residual renal function (RRF).

We retrospectively analyzed 40 patients treated with continuous ambulatory PD or automated PD. The patients were divided into these groups:

- Group A: started icodextrin within 2 weeks after PD onset
- Group B: started icodextrin 1 year after PD onset
- Group C: started icodextrin 2 years after PD onset
- Group D: never used icodextrin during the study period

At the start of PD, we observed no significant difference in left ventricular mass index (LVMI) or urine volume (UV) between the groups. At 4 years, LVMI and UV were both significantly improved in group A compared with group D. The amelioration in LVMI was negatively associated with phosphate elimination.

Our study showed that icodextrin preserved RRF and ameliorated left ventricular hypertrophy. Moreover, the timing of icodextrin introduction in PD patients influenced the clinical effects, including progression of cardiac hypertrophy and RRF.

**Key words**
Icodextrin, phosphate, left ventricular mass index, residual renal function

**Introduction**
Comorbidity is one of the most important factors determining the outcome of patients with end-stage renal disease (ESRD). Of the various comorbidities seen in ESRD patients, cardiovascular disease is very common; it is therefore recognized as the most important factor affecting clinical outcomes such as survival and morbidity. Patients with ESRD are reported to be frequently affected by cardiac hypertrophy and valvular calcification because of conditions such as anemia, hypertension, acidosis, hyperphosphatemia, and hypoalbuminemia caused by uremia (1–4).

With regard to treatment for uremic disease, PD has become a major modality choice for chronic renal replacement therapy, providing continuous maintenance of body-fluid and hemodynamic stability that prevents disequilibrium syndrome. However, fluid overload may still cause cardiovascular complications and subsequent withdrawal from PD (5,6). Residual renal function (RRF) has been reported to be associated with left ventricular hypertrophy, and cardiac hypertrophy and hypoalbuminemia may be associated with poor survival. Disturbed mineral metabolism, including hyperphosphatemia, has been suggested to play a major role in vascular and valvular calcification (7), and therefore current therapeutic strategies for vascular and valvular calcification in ESRD patients are directed toward control of hyperphosphatemia.

Glucose is currently the main osmotic agent used in PD fluids, but undesirable effects such as loss of ultrafiltration, metabolic disorders, and obesity have been shown to occur in patients who receive long-term PD with glucose-based solution. To ameliorate those effects, icodextrin—another osmotic agent composed of high molecular weight polyglucose that sustains ultrafiltration and has little effect on lipid metabolism—has been developed and used in PD patients whose body fluid is inadequately controlled by glucose-based dialysate (8). In addition, RRF is expected to be preserved in patients who receive icodextrin-based PD solution (9–12). However, the most suitable time at which to introduce icodextrin
for better cardiovascular disease control is not clear. We therefore investigated the effect of icodextrin on cardiovascular and RRF management according to the time of its introduction in PD patients.

**Methods**
Our study enrolled 40 incident patients [24 with diabetes; mean age: 61.9 ± 9.9 years (range: 41 – 83 years); Table I]. The patients were allocated to these groups:

- Group A: started icodextrin within 2 weeks after PD onset
- Group B: started icodextrin 1 year after PD onset
- Group C: started icodextrin 2 years after PD onset
- Group D: never used icodextrin during the study period

Icodextrin was introduced to patients with overt edema or poor ultrafiltration volume (<500 mL daily). Laboratory data and cardiovascular ultrasonography examination results were retrieved every 6 months for 4 years from PD start. We compared clinical parameters for the groups according to when they started using icodextrin.

**Results**
At baseline, there was no significant difference in left ventricular mass index (LVMI) between the groups; however, at 4 years from study initiation, LVMI was significantly lower in group A than in groups B, C, and D. Compared with baseline, LVMI in groups C and D had increased [Figure 1(A), Table II].

**FIGURE 1** Change in (A) cardiac hypertrophy and (B) daily urine volume according to the timing of icodextrin use. LVMI = left ventricular mass index; A = icodextrin started within 2 weeks after PD onset; B = icodextrin started 1 year after PD onset; C = icodextrin started 2 years after PD onset; D = icodextrin never used during the study period. *p < 0.05 and **p < 0.01 vs. group A.

**TABLE I** Baseline characteristics of the patients by study group

<table>
<thead>
<tr>
<th>Patient group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.6±10.9</td>
<td>62.5±13.6</td>
<td>61.9±10.7</td>
<td>61.4±4.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.7±3.4</td>
<td>21.2±2.4</td>
<td>23.8±4.5</td>
<td>23.4±2.8</td>
</tr>
<tr>
<td>Sex (men/women)</td>
<td>6/4</td>
<td>5/5</td>
<td>5/5</td>
<td>5/5</td>
</tr>
<tr>
<td>Diabetes (yes/no)</td>
<td>6/4</td>
<td>6/4</td>
<td>6/4</td>
<td>6/4</td>
</tr>
<tr>
<td>D/P creatinine</td>
<td>0.766±0.065</td>
<td>0.595±1.117&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.537±0.087&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.526±0.070&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Modality (APD/CAPD)</td>
<td>7/3</td>
<td>7/3</td>
<td>7/3</td>
<td>7/3</td>
</tr>
<tr>
<td>Icodextrin start time (after PD start)</td>
<td>7–14 Days</td>
<td>1 Year</td>
<td>2 Years</td>
<td>Never used</td>
</tr>
</tbody>
</table>

<sup>a</sup> p < 0.01 vs. group A.

<sup>b</sup> p < 0.001 vs. group A.

BMI = body mass index; D/P = dialysate-to-plasma ratio; APD = automated peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis.
As with LVMI, we observed no significant difference in urine volume (UV) between the groups at baseline; however, at 4 years, UV was significantly less in groups B, C, and D than in group A [Figure 1(B)]. Brain natriuretic peptide was substantially lower in group A throughout the study period, and a constant increase was seen in group D [Figure 2(A)]. In groups A and B, phosphate elimination gradually increased to 3 years and 2 years respectively, but declined at 4 years [Figure 3(A)]. On the other hand, phosphate elimination constantly declined in groups C and D, reaching statistical significance in group D compared with group A [Figure 3(A)]. In a correlation analysis of phosphate elimination and LVMI amelioration, a negative association was revealed [Figure 3(B)].

**Discussion**

The results of the present study demonstrate that early introduction of icodextrin to PD patients is associated with better cardiac and RRF parameters and that phosphate elimination and LVMI improvement are significantly correlated. The improvement in LVMI might be attributable to better fluid control with the use of icodextrin. Our findings may reinforce a previous report of better fluid management of icodextrin (13).

In the present study, UV was higher with the use of icodextrin than with glucose. That finding is consistent with a previous report that icodextrin preserves 24-hour UV (12). However, Takatori et al. showed that UV in incident diabetic patients 2 years after PD start was not significantly different between groups using icodextrin and glucose (14). This controversial

**FIGURE 2** Change in (A) brain natriuretic peptide (BNP) and (B) atrial natriuretic peptide (ANP) according to the timing of icodextrin use. A = icodextrin started within 2 weeks after PD onset; B = icodextrin started 1 year after PD onset; C = icodextrin started 2 years after PD onset; D = icodextrin never used during the study period. **p < 0.02 vs. group A.

**FIGURE 3** (A) Change in the phosphate elimination into effluent according to the timing of icodextrin use. (B) Correlation between average daily phosphate elimination and ratio of left ventricular mass index (LVMI) at 4 years to the index at baseline (LVMI/LVMI0). A = icodextrin started within 2 weeks after PD onset; B = icodextrin started 1 year after PD onset; C = icodextrin started 2 years after PD onset; D = icodextrin never used during the study period. *p < 0.02 and **p < 0.01 vs. group A.
<table>
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<td>A</td>
<td>Baseline</td>
<td>At 4 years</td>
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<td>At 4 years</td>
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<tr>
<td>Creatinine (mg/dL)</td>
<td>6.34±1.62</td>
<td>8.85±2.73</td>
<td>7.29±2.43</td>
<td>9.74±2.48</td>
<td>6.62±1.05</td>
<td>10.34±1.73</td>
<td>7.01±1.27</td>
<td>10.46±1.90</td>
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<td>β₂-Microglobulin (mg/dL)</td>
<td>18.2±3.7</td>
<td>30.5±7.1</td>
<td>20.1±8.1</td>
<td>33.7±10.1</td>
<td>19.0±7.2</td>
<td>31.1±9.2</td>
<td>18.8±7.4</td>
<td>31.0±6.9</td>
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<tr>
<td>CRP (mg/dL)</td>
<td>0.22±0.19</td>
<td>0.19±0.56</td>
<td>0.23±0.28</td>
<td>0.20±0.15</td>
<td>0.23±0.26</td>
<td>0.24±0.19</td>
<td>0.25±0.28</td>
<td>0.23±0.24</td>
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<td>Daily UV (mL)</td>
<td>828.6±275.2</td>
<td>393.4±258.2</td>
<td>842.9±442.0</td>
<td>207.1±207.1</td>
<td>914.3±302.4</td>
<td>207.1±226.3</td>
<td>885.7±539.8</td>
<td>78.6±115.0</td>
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<tr>
<td>Daily UF (mL)</td>
<td>420.5±389.5</td>
<td>1009.1±364.6</td>
<td>431.8±588.3</td>
<td>1132.9±201.9</td>
<td>522.7±524.8</td>
<td>1020.0±414.2</td>
<td>249.1±390.0</td>
<td>1131.4±361.7</td>
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<tr>
<td>BNP (pg/mL)</td>
<td>482.0±311.2</td>
<td>186.9±129.8</td>
<td>460.8±422.6</td>
<td>526.3±833.1</td>
<td>358.7±242.6</td>
<td>317.5±211.3</td>
<td>141.7±81.6</td>
<td>513.0±420.9</td>
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<td>ANP (pg/mL)</td>
<td>147.8±122.2</td>
<td>104.0±53.9</td>
<td>146.4±82.6</td>
<td>124.5±55.0</td>
<td>194.8±132.3</td>
<td>118.1±82.1</td>
<td>106.2±80.0</td>
<td>171.5±154.9</td>
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<tr>
<td>Daily phosphate elimination (mg)</td>
<td>384.6±59.3</td>
<td>350.1±58.6</td>
<td>363.3±37.1</td>
<td>340.1±33.7</td>
<td>386.1±91.1</td>
<td>329.4±41.5</td>
<td>421.4±67.1</td>
<td>276.0±42.4</td>
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<td>Daily Glu absorption (g)</td>
<td>45.3±7.0</td>
<td>43.6±8.7</td>
<td>42.8±6.8</td>
<td>45.5±3.5</td>
<td>50.6±10.0</td>
<td>50.1±6.7</td>
<td>48.5±6.0</td>
<td>51.4±8.2</td>
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<tr>
<td>D/P creatinine</td>
<td>0.76±0.065</td>
<td>0.654±0.085</td>
<td>0.595±0.11</td>
<td>0.629±0.068</td>
<td>0.537±0.087</td>
<td>0.671±0.096</td>
<td>0.526±0.070</td>
<td>0.654±0.074</td>
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<tr>
<td>LVMI (g/m²)</td>
<td>151.4±49.4</td>
<td>116.8±38.4</td>
<td>164.5±47.3</td>
<td>162.0±21.5</td>
<td>153.9±41.1</td>
<td>165.5±26.2</td>
<td>174.5±58.4</td>
<td>207.2±44.8</td>
<td></td>
</tr>
</tbody>
</table>

a  p < 0.05 vs. group A.
b  p < 0.01 vs. group A.
c  p < 0.02 vs. group A.
d  p < 0.001 vs. group A.

CRP = C-reactive protein; UV = urine volume; UF = ultrafiltration; BNP = brain natriuretic peptide; ANP = atrial natriuretic peptide; Glu = glucose; D/P = dialysate-to-plasma ratio; LVMI = left ventricular mass index.
finding may be partly explained by the fact that, in the latter report, more than half the patients in the glucose group discontinued PD because of volume overload, indicating that the data being analyzed were those from patients who showed better volume control. A UV more similar to our results might have been obtained if data from all the patients had been included. Overall, we suggest that better volume control with the use of icodextrin leads to amelioration of LVMI (and better levels of brain natriuretic peptide, atrial natriuretic peptide, and UV) than are seen in patients using glucose.

Our study has some limitations. It was not randomized, but was conducted at a single center, with a small sample size. Also, patients were allocated to icodextrin when they showed overtly insufficient ultrafiltration. It is possible that those factors led to selection bias. Further studies are required to clarify our observations.

Conclusions
The early use of icodextrin in PD patients may yield beneficial effects with respect to atherosclerosis, RRF, and clinical status.

Disclosures
The authors declare no financial conflicts of interest relevant to the present study.

References

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