We set out to assess the effect of continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) on residual renal function (RRF) in children with end-stage renal disease (ESRD).

In 101 children (age: 8.84 ± 5.25 years; 44 on CAPD, 57 on APD) over 36 months, we evaluated RRF [as daily diuresis (DD) in mL/kg/24 h and mL/m²/24 h], glomerular filtration rate [GFR (in mL/min/1.73 m²)], ESRD cause, presence of arterial hypertension (HTN), biochemical parameters, peritoneal equilibration test (PET), adequacy [as total weekly Kt/V (twKt/V) and creatinine clearance (twCCr)], and infectious complications of PD.

Initially, the CAPD and APD groups did not differ significantly in DD, but mean GFR was significantly higher in the APD group ($p < 0.05$). In the CAPD group, the volume of high osmolarity PD fluid was significantly lower ($p < 0.05$), and the rates of peritonitis and exit-site infection and of aminoglycoside use were higher ($p < 0.001$, $p < 0.05$, and $p < 0.005$ respectively). Over 36 months, the mean twKt/V and twCCr were within norms in both groups, but were higher in APD, significantly so ($p < 0.05$) for twKt/V at 24 and 36 months and for twCCr initially. In both groups, RRF decreased systematically, with a significantly lower ($p < 0.05$) rate of DD (mL/m²/24 h) and GFR decline in the first year in CAPD, but without a difference in the next 2 years. The longest RRF preservation was in children with tubulointerstitial nephropathies, particularly hypoplasia and dysplasia ($p < 0.05$). Children with hemolytic uremic syndrome (HUS) and hereditary nephropathy were at the highest anuria risk. Compared with the 22 children (7 CAPD, 15 APD) who became anuric, the 20 children (10 CAPD, 10 APD) with RRF preserved for 36 months had a higher DD and GFR before dialysis onset; higher hemoglobin and albumin; and lower HTN prevalence, cholesterol, triglycerides, and proteinuria ($p < 0.05$). Risk of anuria during 36 months did not differ significantly between the CAPD and APD groups.

In children on CAPD or APD, risk factors for RRF loss include HUS, hereditary nephropathy, low diuresis and GFR before dialysis onset, HTN, anemia, hypoalbuminemia, hyperlipidemia, and proteinuria. Compared with children on APD, those on CAPD show better preservation of RRF during year 1, although the risk of anuria seems to be the same for both methods. In children with risk factors for rapid diuresis loss, CAPD might be considered the preferred initial dialysis method.

Key words
Residual renal function, children, continuous ambulatory peritoneal dialysis, automated peritoneal dialysis

Introduction
Preservation of residual renal function (RRF) is important in patients with end-stage renal disease (ESRD)—particularly in those treated with chronic peritoneal dialysis (PD). Preserved RRF improves response to recombinant human growth hormone treatment for uremic growth failure (1), has a positive effect on parameters of calcium–phosphate metabolism (2) and on left ventricular mass index and diastolic function (3), and reduces serum levels of advanced glycation endproducts (4). A more rapid decline of RRF has been noted in children and adults treated with hemodialysis than in those treated with continuous ambulatory PD (CAPD) or automated PD (APD) (5–7), but the literature contains no data about the effect of PD method on the rate of RRF deterioration in children with ESRD.
Methods

We performed a retrospective evaluation of 101 children [mean age: 8.84 ± 5.25 years (range: 3 months – 18 years, 9 months)] with ESRD and preserved RRF treated with PD during 1992 – 2009 at 4 centers providing pediatric dialysis therapy in Poland. In these children, CAPD ($n = 44$) or APD ($n = 57$) was the initial method of renal replacement therapy (RRT).

In the CAPD group, 4 – 5 dialysis fluid exchanges were routinely performed daily, using 30 – 50 mL/kg fluid containing 1.36% glucose for daytime exchanges and 2.27% or 3.86% glucose for nighttime exchanges [Baxter International, Deerfield, IL, U.S.A., 32 patients (72.7%); Bieffe Medital, Lugano, Switzerland, 7 patients (15.9%); Fresenius SE, Bad Homburg, Germany, 5 patients (11.4%)].

In the APD group, dialysis was performed using Baxter HomeChoice cyclers (Baxter International) and 5 – 8 exchanges per night of fluid containing 1.36% or 2.27% glucose. In some cases, long exchanges of fluid containing 3.86% glucose or glucose polymer [icodextrin (Extraneal: Baxter International)] were used during the day. The percentage of APD patients requiring a daytime dwell increased from 33.3% initially (19 of 57) to 50.9% after 12 months (27 of 53), to 57.7% after 24 months (15 of 26), and to 70.0% after 36 months (7 of 10).

Glucose content and fluid volumes were individually adjusted in all children to provide RRT adequacy. Cephazolin or cephalothin with aminoglycoside were used for the treatment of PD-related peritonitis until 2000; ceftazidime was used thereafter.

Based on the available medical records, RRF [expressed as daily diuresis (mL/kg/24 h and mL/m²/24 h)] and glomerular filtration rate [GFR (mL/min/1.73 m²)] were evaluated using the averaged urea and creatinine clearances in 24-hour urine collections before RRT initiation and every 12 months thereafter. Loss of RRF was defined as anuria lasting for at least 3 months. In the initial period of PD (3 months after PD initiation) and every 12 months thereafter, an evaluation was also performed of the volume of dialysis fluid containing 1.36%, 2.27%, and 3.86% glucose, or icodextrin (mL/kg/24 h); ultrafiltration (mL/kg/24 h); and RRT adequacy based on total weekly urea clearance (twKt/V) and total weekly creatinine clearance [twCCr (L/1.73 m²)], which were compared with the European recommendations for adequacy in children (8). In addition, we analyzed factors that might have affected the rate of RRF deterioration, including the cause of ESRD according to the pediatric European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) registry (9), peritoneal permeability as evaluated by peritoneal equilibration test [4-hour dialysate-to-plasma creatinine ($D/P_{Cr4h}$) and end-to-initial dialysate glucose ($D/D_0 \text{Glu}_{4h}$)] performed according to the protocol devised by the European Pediatric Peritoneal Working Group (8). Infectious complications of PD were also analyzed: PD-related peritonitis, exit-site infections, presence of arterial hypertension (HTN), antihypertensive drugs used, aminoglycoside antibiotics used, and biochemical parameters including hemoglobin, total protein, cholesterol, triglycerides, calcium, phosphorus, parathormone (PTH), and proteinuria. Total duration of follow-up was 36 months. Factors potentially affecting RRF were analyzed in two groups: group A included children with diuresis preserved throughout 36 months; group B included children who developed anuria during follow-up.

The statistical analysis was performed using the Statistica software application (version 9.0: StatSoft, Tulsa, OK, U.S.A.). Normal distribution of variables was evaluated using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Depending on distribution, data are presented as mean ± standard deviation or as medians and ranges. Statistical tools used included the Student t-test, Mann–Whitney U-test, Wilcoxon test, Pearson chi-square test, simple linear regression, logistic regression, Kaplan–Meier analysis, and the log-rank test. A value of $p < 0.05$ was considered to indicate statistical significance.

Results

The CAPD group included 44 children 3 months to 14 years of age (mean: 5.87 ± 4.49 years), and the APD group included 57 children 3 months to 18 years, 9 months of age (mean: 9.58 ± 5.20 years). The difference in age was statistically insignificant.

Table I shows clinical data and biochemical parameters for children treated with CAPD and APD. Before RRT initiation, mean daily diuresis and GFR were lower in the CAPD group than in the APD group, the difference being significant only for GFR ($p < 0.01$). The groups did not differ with respect to causes of ESRD according to ERA-EDTA; to HTN...
prevalence or antihypertensive drugs used; to mean hemoglobin, total protein, albumin, cholesterol, triglycerides, calcium, phosphorus, and PTH level; or to the rate and severity of proteinuria.

Among the 101 children studied, 93 (40 CAPD, 53 APD) were observed for 12 months; 47 (21 CAPD, 26 APD), for 24 months; and 20 (10 CAPD, 10 APD), for 36 months. The most common causes of follow-up termination were kidney transplantation \([n = 32 (31.7\%)]\), RRF loss \([n = 22 (21.8\%)]\), and change of RRT method \([n = 17 (16.8\%)]\).

Figure 1 shows median values for the volumes of high-osmolarity dialysis fluids used (containing 2.27% or 3.86% glucose, or icodextrin) and mean values for RRT adequacy parameters (twKt/V, tw-CCr) and ultrafiltration in the CAPD and APD groups. Compared with the APD group, the CAPD group used a significantly lower volume of high-osmolarity
dialysis fluid (in mL/kg/24 h) in the initial period and after 12 and 24 months (p < 0.001, p < 0.00001, and p < 0.01 respectively). They also used fewer dialysis fluid exchanges per day on average (4.28 ± 0.56 vs. 6.34 ± 2.12, p < 0.001). Individual adjustment of PD treatment parameters had no effect on mean ultrafiltration, which did not differ significantly between the groups. Also, among children with preserved RRF who underwent CAPD and APD, mean values of twKt/V and twCCr remained within the recommended ranges (8) throughout the 36-month follow-up, but were higher in the APD group, with significant differences (p < 0.05) in twKt/V after 24 and 36 months and in twCCr in the initial treatment period.

Results of peritoneal equilibration tests were analyzed in 17 patients in the CAPD group (38.6%) and in 35 patients in the APD group (61.4%). We found no significant differences between the groups in mean D/P_Cr 4h (0.70 ± 0.16 vs. 0.62 ± 0.14) and D/D_0_Glu 4h (0.34 ± 0.12 vs. 0.38 ± 0.13). A positive correlation was found between D/P_Cr 4h and change in GFR (r = 0.41, p < 0.05) in the APD group.

Infectious complications of PD were significantly more common in the CAPD group than in the APD group (PD-related peritonitis: 1 episode in 15.82 vs. 30.68 patient–months, p < 0.001; exit-site infection: 1 episode in 13.08 vs. 19.48 patient–months, p < 0.05). In addition, aminoglycosides were significantly more commonly used to treat PD-related peritonitis in the CAPD group [38 episodes (61.3%) vs. 7 episodes (17.5%), p < 0.0005]. In both groups, we found no effect of infectious complications and aminoglycoside use on the rate of daily diuresis and GFR loss.

Figure 2 shows the rate of RRF loss expressed as change in daily diuresis and in GFR in the CAPD
Effect of PD Method on RRF in Children

During the 36 months of follow-up, a systematic decline in daily diuresis and GFR was noted in both groups. In the first year of follow-up, the rates of deterioration in daily diuresis (mL/m²/24 h) and GFR were significantly lower ($p < 0.05$) in the CAPD group than in the APD group, but no difference was noted in the subsequent years of follow-up. Also, no significant differences in the rate of RRF decline were found between children on nightly intermittent and continuous cycling PD.

Throughout 36 months of PD treatment, RRF was preserved in 20 children (19.8%; 10 on CAPD, 10 on APD; group A) and lost in 22 (21.8%; 7 on CAPD, 15 on APD; group B). In group A, significant reductions ($p < 0.05$) in mean daily diuresis (mL/m²/24 h) and GFR were noted in the 10 patients treated with CAPD, and significant reductions in mean daily diuresis [mL/kg/24 h ($p < 0.001$), mL/m²/24 h ($p < 0.01$)] and GFR ($p < 0.05$) were similarly noted in the 10 patients treated with APD. In contrast, no significant differences in the rate of RRF loss were found in group A between the patients treated with CAPD and those treated with APD. The mean time to RRF loss in group B was $15.2 \pm 8.4$ months (range: 3 – 29 months), which did not differ significantly between patients treated with CAPD and APD ($11.29 \pm 7.32$ months vs. $17.00 \pm 8.53$ months). Cumulative risk of RRF loss estimated using the Kaplan–Meier method did not differ significantly between the CAPD and APD groups (Figure 3).

Table II shows clinical data, RRF before PD initiation, and selected biochemical parameters in groups A and B. Mean patient age did not differ between the groups. Mean daily diuresis (mL/kg/24 h and mL/m²/24 h) and GFR before PD initiation were significantly higher ($p < 0.05$) in group A than in group B. Patients in group A required significantly lower volumes of dialysis fluid ($p < 0.01$) to obtain RRT adequacy. During anuria in group B patients, mean twKt/V remained within the recommended range regardless of the PD method used ($2.17 \pm 0.25$ for CAPD, $2.46 \pm 0.60$ for APD). In contrast, RRF loss contributed to a significant reduction ($p < 0.05$) in mean twCCr below the recommended European norm ($52.55 \pm 18.16$ L/week/1.73 m² in CAPD, $53.27 \pm 14.03$ L/week/1.73 m² in APD). In children in whom diuresis was maintained, a trend ($p = 0.06$) toward higher mean serum albumin was noted, and mean cholesterol and triglycerides were significantly lower ($p < 0.0001$ and $p < 0.05$ respectively). No significant differences in mean hemoglobin, calcium, or phosphorus and median PTH were found. When hemoglobin was analyzed separately in children treated with CAPD and APD, mean values were higher in children with preserved RRF than in children with anuria, the difference being significant in the APD group ($11.48 \pm 0.59$ g/dL vs. $10.34 \pm 0.72$ g/dL, $p < 0.0005$) and trending toward significance in the CAPD group ($10.49 \pm 1.80$ g/dL vs. $9.32 \pm 1.30$ g/dL,
In addition, proteinuria was significantly lower ($p < 0.005$) in group A than in group B. Throughout follow-up, the prevalence of HTN was significantly lower ($p < 0.005$) in group A. The number and types of antihypertensive drugs did not differ between the groups.

Analysis of the effect of primary renal disease on RRF showed that, during the 36 months of follow-up, diuresis was maintained for the longest time in patients with renal hypoplasia or dysplasia [8 of 14 patients (57.1%)], significantly longer ($p < 0.05$) than in children with other causes of ESRD according to the ERA-EDTA. Anuria was most commonly noted in children with hemolytic uremic syndrome [3 of 5 patients (60.0%)], significantly more frequently ($p < 0.05$) than in patients with pyelonephritis [2 of 23 patients (8.7%)], cystic kidney disease [1 of 13 patients (7.7%)], and renal hypoplasia or dysplasia [0 of 14 patients (0%)]. Anuria was also more common in patients with hereditary nephropathy [4 of 9 patients (44.4%)], but that difference did not reach statistical significance. Among patients with hereditary nephropathy, 4 patients had congenital nephrotic syndrome, 2 had nail–patella syndrome, and 1 patient each had Alport syndrome, cystinosis, and diffuse mesangial sclerosis.

The rate of infectious PD complications did not differ significantly between groups A and B.

### Table II

Clinical parameters, residual renal function, and selected biochemical parameters in groups A (residual renal function maintained at end of follow-up) and B (anuric at the end of follow-up)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A</th>
<th>Group B</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients ($n$)</td>
<td>20</td>
<td>22</td>
<td>NS</td>
</tr>
<tr>
<td>Age of peritoneal dialysis (PD) onset (years)</td>
<td>8.30±5.80</td>
<td>8.89±5.05</td>
<td>NS</td>
</tr>
<tr>
<td>Residual renal function before PD onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily diuresis (mL/kg/24 h)</td>
<td>53.00±27.41</td>
<td>32.26±21.18</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>(mL/m²/24 h)</td>
<td>1366.40±657.46</td>
<td>866.54±565.17</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>GFR (mL/min/1.73 m²)</td>
<td>7.73±4.01</td>
<td>5.40±3.09</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Dialysis fluids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total volume (mL/kg/24 h)</td>
<td>172.61±83.63</td>
<td>239.28±72.14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Biochemical parameters&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>6.17±1.14</td>
<td>6.17±1.25</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.50±0.54</td>
<td>3.20±0.65</td>
<td>0.06</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>185.73±47.03</td>
<td>253.91±59.32</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>195.62±82.83</td>
<td>249.16±106.67</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.46±1.79</td>
<td>10.0±1.52</td>
<td>NS</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.00±1.21</td>
<td>8.94±1.26</td>
<td>NS</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>6.04±1.32</td>
<td>5.84±1.61</td>
<td>NS</td>
</tr>
<tr>
<td>Parathyroid hormone (pg/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>208</td>
<td>60.5</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>38–800</td>
<td>2–1490</td>
<td></td>
</tr>
<tr>
<td>Proteinuria [&lt;i&gt;n&lt;/i&gt; (%)]</td>
<td>14 (55.0)</td>
<td>21 (95.5)</td>
<td></td>
</tr>
<tr>
<td>Median (mg/kg/24 h)</td>
<td>8.90</td>
<td>80.32</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Range (mg/kg/24 h)</td>
<td>0.0–254.7</td>
<td>0.0–436.36</td>
<td></td>
</tr>
<tr>
<td>Arterial hypertension [&lt;i&gt;n&lt;/i&gt; (%)]</td>
<td>8 (40.0)</td>
<td>20 (90.9)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Antihypertensive medications [&lt;i&gt;n&lt;/i&gt; (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel antagonists</td>
<td>6 (75.0)</td>
<td>15 (75.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Angiotensin converting-enzyme inhibitors</td>
<td>4 (50.0)</td>
<td>8 (40.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Furosemide</td>
<td>4 (50.0)</td>
<td>14 (70.0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<sup>a</sup> Group A: mean value during 36 months of peritoneal dialysis therapy; group B: mean value for peritoneal dialysis therapy, from initiation to anuria.

NS = nonsignificant; GFR = glomerular filtration rate.
Effect of PD Method on RRF in Children

(PD-related peritonitis: 1 episode in 23.8 vs. 27.0 patient–months; exit-site infection: 1 episode in 21.0 vs. 20.4 patient–months). The rate of aminoglycoside use for the treatment of PD-related peritonitis also did not differ significantly [7 of 31 patients (22.6%) vs. 6 of 14 patients (42.9%)].

Discussion
Peritoneal dialysis has been an alternative method of ESRD treatment in children for more than 30 years. In CAPD, dialysis fluid exchanges are performed manually, with longer dwells. In APD, the exchanges are automatic and more frequent, resulting in shorter dwells. Benefits of APD over CAPD have been reported in many studies, including higher clearances of small molecules, lower rates of infectious complications and hernias, and better quality of life in patients on APD (10). The effect of PD method on the rate of RRF loss has not been clearly established (5,10), although loss of diuresis was found to be more rapid in patients treated with APD than in patients treated with CAPD (11–14).

In the present study, we compared the effect of PD method on RRF in children and found significantly higher ($p < 0.05$) rates of daily diuresis loss (in mL/m$^2$/24 h) and GFR reduction (mL/min/1.73 m$^2$) during the first 12 months of RRT among patients treated with APD than among those treated with CAPD, although the overall risk of anuria developing during the 3-year follow-up was the same for both dialysis methods as estimated using the Kaplan–Meier method. We also found no difference in the rate of RRF loss between APD patients with an additional long daytime dwell and those with an empty abdominal cavity during the day.

The higher rate of RRF loss with APD may be explained by individual adjustments of RRT parameters to maintain appropriate ultrafiltration and treatment adequacy. In this analyzed group of pediatric patients, dialysis fluid exchanges were significantly more frequent ($p < 0.005$) and the volume of hypertonic dialysis fluids was higher ($p < 0.05$) in patients treated with APD than in patients treated with CAPD. According to some authors, a rapid rate of diuresis loss with APD may be reduced by using continuous cyclic PD with icodextrin (11,15).

Analysis of clinical and biochemical data in 20 children who maintained RRF throughout the 36 months of follow-up and 22 children who developed anuria during that period identified risk factors for diuresis loss in pediatric patients treated with CAPD or APD. Those factors include low diuresis and GFR before RRT initiation, specific causes of ESRD (hemolytic uremic syndrome and hereditary nephropathy), HTN, anemia, hypoalbuminemia, hyperlipidemia, and proteinuria.

In our study population, RRF was preserved for the longest time in patients with tubulointerstitial nephropathies, particularly renal hypoplasia or dysplasia. The highest risk of anuria was noted in patients with hemolytic uremic syndrome and hereditary nephropathy. Those findings contrast with results from a study by Feber et al. (6) who found that the risk of anuria in children treated with CAPD or hemodialysis was increased by a factor of 6 in acquired compared with congenital kidney disease ($p < 0.05$). However, our results are consistent with observations in adults in whom long-term preservation of RRF was seen in patients with tubulointerstitial nephropathies (16) and adult polycystic kidney disease (17).

The presence of HTN was a significant ($p < 0.005$) risk factor for RRF loss in children in our study. Some authors looking at adult patients treated with PD were unable to identify an effect of HTN on the rate of RRF loss (18); others noted that both HTN (11) and hypotension (19) had an adverse effect on diuresis preservation.

In our study population, risk factors predisposing to rapid RRF loss included low hemoglobin (that is, anemia), proteinuria, and severe protein and lipid abnormalities (hypoalbuminemia, hypercholesterolemia, hypertriglyceridemia). Albumins constitute a protein class that plays a major role in maintaining plasma oncotic pressure, intravascular volume, and normal renal perfusion. In a pediatric population receiving RRT with PD, positive correlations were found between daily diuresis and serum albumin (20) and high-density lipoprotein cholesterol (3). Negative effects of proteinuria (21) and hypoalbuminemia (22) on the rate of RRF loss were also found in adult patients. Finally, a significant association was found between RRF and hemoglobin (3,20).

Conclusions
Our findings indicate that, in children with risk factors for rapid diuresis loss in whom PD is to be initiated, CAPD might be considered to be the preferred initial RRT method.

Disclosures
The authors have no financial conflicts of interest to declare.
References

Corresponding author:
Piotr Skrzypczyk, MD, Department of Pediatrics and Nephrology, Medical University of Warsaw, 24 Marszałkowska Street, Warsaw 00-576 Poland.
E-mail:
pskrzyp@gmail.com