Aging Is an Important Risk Factor for Peritoneal Dialysis–Associated Peritonitis

Peritonitis remains a leading complication of peritoneal dialysis (PD). The aim of this observational retrospective cohort study, conducted at our single center, was to determine the risk factors for peritonitis.

A Cox proportional hazards model was used for the multivariate analysis. The event investigated was peritonitis, and the variables studied were sex, age, diabetes mellitus, use of statins, and several laboratory values including albumin and total cholesterol. All PD patients who visited our clinic from January 2005 to September 2011 and who had complete medical records for at least 3 years were included.

Among the 82 patients who met the criteria (mean period of observation: 1086 ± 752 days; mean age: 62.0 ± 12.3 years), 47 had experienced at least 1 episode of peritonitis. Aging was a significant risk factor for peritonitis, with a relative risk of 1.04 per year ($p = 0.014$).

In our study, aging—rather than diabetes mellitus, efficiency of PD, or nutrition status—was an important risk factor for PD-associated peritonitis. Poor PD technique because of advanced age might be one of the reasons for this result.

Key words
Peritonitis, end-stage renal disease, geriatric

Introduction
A need for catheter removal is one of the major factors of technique failure in peritoneal dialysis (PD), even when the dialysis itself is adequate. Previously, our group reported that the main cause of PD catheter removal was PD peritonitis (1). Thus, peritonitis was the principal reason for cessation of PD and a switch to hemodialysis (HD).

Previously, many factors have been reported to be risks for PD-related peritonitis, including reduced residual renal function (2), increasing age (3,4), diabetes (5,6), nutrition status (5,7), obesity (8), PD modality (6,9,10), and noncompliance to continuous ambulatory PD (CAPD) procedure (11). Peritonitis rates can also be influenced by other factors such as education level, geographic region, distance from the PD center, or socio-economic status (12–14). Recently, a large nationwide multicenter study analyzing peritonitis risk factors was reported from Brazil (15). According to the report, education level was a strong risk predictor in addition to non-white race, PD center size, and geographic factors such as the region in which patients live and distance from the dialysis center. In contrast to other studies, socio-economic status, sex, age, diabetes, and PD modality did not have an effect on peritonitis risk.

Taken together, the above reports imply that risk factors for PD-related peritonitis are situational and should be evaluated for each PD center in each country. The aim of the present study was therefore to determine the risk factors for PD-related peritonitis in our kidney disease center in Japan. In the study, we concentrated on the clinical features considered to be risk factors for PD-associated peritonitis, because in Japan, compared with other countries, many nonmedical conditions are relatively uniform—for example, race, distance to the dialysis center, and education level.

Methods
This observational retrospective cohort study was conducted at our single center in Japan.

Subjects
All patients receiving CAPD therapy who visited our outpatient clinic at least once monthly from January 2005 to September 2011 and for whom we had complete medical records for at least 3 years were enrolled.
At our kidney center, we adhere to an average weekly creatinine clearance (CCr) of about 40 L, because that level maintains the most consistent conditions with regard to the patient’s quality of life. The PD dose (fluid quantity and frequency of bag exchanges) was adjusted to maintain the weekly CCr. If the CCr fell below 45 L despite a full dose of PD, once-weekly hemodialysis was introduced (16). Patients who received combination therapy with PD and HD (2 or more times per week) were excluded from the present study. Daily dietary protein intake was approximately 1 g per kilogram of body weight, and daily energy intake was more than 30 – 35 kcal per kilogram of body weight. Daily salt intake was restricted to between 7 g and 9 g (16).

First PD-related peritonitis in the observational period was recorded.

Predictors
Data on sex, age, diabetes mellitus, use of statins, and values of various laboratory measurements (albumin, total cholesterol, blood urea nitrogen), and calculated weekly CCr were collected.

Analytical methods
A Cox proportional hazards model was used for the multivariate analysis. The non-paired t-test and chi-square test were used to compare patient groups (those with and without peritonitis). Differences in the incidence rate of PD-related peritonitis between subgroups of patients (65 years of age or more and less than 65 years of age) were compared using the Peto log-rank test.

Results
Of the 82 patients who met the enrollment criteria [48 men (58.5%), 34 women (41.5%); mean period of observation: 1086 ± 752 days; mean age: 60.5 ± 12.4 years], 45 (54.9%) had experienced at least 1 episode of peritonitis during the study period.

Table I shows the clinical characteristics of the patients and compares the groups with and without PD-related peritonitis. The overall mean age was 62.0 years, and there was a significant difference in mean age between the groups. Moreover, compared with the non-peritonitis group, the peritonitis group included more geriatric subjects (that is, those 65 years of age and older). On the other hand, we observed no differences in the prevalence of diabetes or in any laboratory value (weekly CCr, total of CAPD and urine, rate of statin users) between the groups.

The results of the Cox proportional hazards model and the relative risks for each factor after adjustment for each other factor showed that aging was a significant risk factor for peritonitis, with a relative risk of 1.041 per year (p = 0.014, Table II). None of the other factors was shown to pose a significant risk for PD-related peritonitis. Figure 1 shows the time-dependent incidence rate of peritonitis for each group. We observed 1 patient who developed PD-related peritonitis just after starting PD, and the peritonitis incidence rate increased roughly in proportion to the duration of PD during the observation period. Further, we observed a significant difference between the groups in incidence rate (log-rank p = 0.033)

Discussion
In the present study, aging was revealed to be the most important risk factor for PD-related peritonitis at our kidney disease center.

The number of elderly patients (>80 years of age) receiving treatment for end-stage renal disease has risen by more than 50% since the year 2000. The age of new dialysis patients is rapidly increasing, with one third of those patients in Japan now being 75 years of age or older. As a continuous home-based therapy, PD offers several potential advantages for older people, and it remains an important modality of renal replacement therapy. Yet even when PD is going well, PD-associated peritonitis continues to be the major cause of PD cessation. It also affects patient morbidity and mortality, despite reductions in the incidence rates since 2000. The present study suggests that, to solve the PD-related peritonitis problem, an evaluation of the risk factors associated with aging is needed.

Among patient-related medical factors, advanced age (3,4) and race have been the most frequently reported risk factors for PD-related peritonitis. However, other studies have found similar peritonitis rates in older and younger PD patients (17,18). In looking at that contradiction, recently published data from Canada provide important information.

The Canadian study, which used the nationwide Baxter POET (peritonitis, organisms, exit sites, tunnel infections) database, included 4247 Canadian PD patients, of whom 1265 were more than 70 years of age (4). The study identified an
important association between age and PD-related infectious complications, as well as an effect of the PD initiation era. Although older age was associated with a higher overall peritonitis rate (1996 – 2005), that association was not present in the subgroup of patients who initiated dialysis in more recent years (2001 – 2005) (4). Moreover, peritonitis-related mortality was more common with older age among those initiating PD during 1996 – 2000, but not in those initiating PD during 2001 – 2005 (4).

The study discussed several factors that may explain that variability, especially the importance of recent advances in PD connection methods and exit-site care [reviewed in the same study (4)]. The lack of association between increasing age and peritonitis may reflect the fact that the “flush before

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**TABLE I**  Clinical characteristics of patients and intergroup comparisons

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Yes</th>
<th>No</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients [n (%)]</td>
<td>82 (100)</td>
<td>47 (57.3)</td>
<td>35 (42.7)</td>
<td>1.000a</td>
</tr>
<tr>
<td>Men [n (%)]</td>
<td>48 (58.5)</td>
<td>28 (59.6)</td>
<td>20 (57.1)</td>
<td>0.012b</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>62.0±12.3</td>
<td>65.0±10.9</td>
<td>58.1±13.2</td>
<td>0.024b</td>
</tr>
<tr>
<td>Geriatricc [n (%)]</td>
<td>36 (43.9)</td>
<td>26 (55.3)</td>
<td>10 (28.6)</td>
<td>0.474a</td>
</tr>
<tr>
<td>With diabetes [n (%)]</td>
<td>25 (30.5)</td>
<td>16 (34.0)</td>
<td>9 (25.7)</td>
<td>0.775</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>58.6±14.9</td>
<td>57.0±16.6</td>
<td>60.7±12.2</td>
<td>0.655</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>3.19±0.51</td>
<td>3.16±0.52</td>
<td>3.21±0.52</td>
<td>0.709</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>171.0±38.9</td>
<td>172.4±39.6</td>
<td>169.2±38.5</td>
<td>0.766</td>
</tr>
<tr>
<td>Weekly CCr (L)</td>
<td>40.7±16.4</td>
<td>41.2±17.2</td>
<td>40.1±15.7</td>
<td>0.542a</td>
</tr>
<tr>
<td>Using statin (%)</td>
<td>13 (15.9)</td>
<td>6 (12.8)</td>
<td>7 (20.0)</td>
<td>0.474a</td>
</tr>
</tbody>
</table>

* By chi-square test instead of t-test.
* Significant difference, p < 0.05.
* Sixty-five years of age and older.

**TABLE II**  Cox proportional hazards analysis and relative risks

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Lower</th>
<th>Upper</th>
<th>Relative risk</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>0.040</td>
<td>0.008</td>
<td>0.073</td>
<td>1.041</td>
<td>0.014b</td>
</tr>
<tr>
<td>Diabetes (with)</td>
<td>0.233</td>
<td>–0.149</td>
<td>0.591</td>
<td>1.593</td>
<td>0.224</td>
</tr>
<tr>
<td>BUN (per 1.0 mg/dL)</td>
<td>–0.014</td>
<td>–0.038</td>
<td>0.009</td>
<td>0.986</td>
<td>0.245</td>
</tr>
<tr>
<td>Serum albumin (per 1.0 g/dL)</td>
<td>0.690</td>
<td>–0.020</td>
<td>1.420</td>
<td>1.993</td>
<td>0.057</td>
</tr>
<tr>
<td>Total cholesterol (per 10.0 mg/dL)</td>
<td>0.050</td>
<td>–0.042</td>
<td>0.140</td>
<td>1.052</td>
<td>0.278</td>
</tr>
<tr>
<td>Weekly CCr (per 1.0 L)</td>
<td>0.014</td>
<td>–0.006</td>
<td>0.034</td>
<td>1.014</td>
<td>0.158</td>
</tr>
<tr>
<td>Statin (using)</td>
<td>–0.371</td>
<td>–0.920</td>
<td>0.073</td>
<td>0.477</td>
<td>0.107</td>
</tr>
</tbody>
</table>

* Relative risks for each factor are shown after adjustment for each other factor.
* Significant difference, p < 0.05.

CL = confidence limits; BUN = blood urea nitrogen; CCr = creatinine clearance.
fill” technique and the use of topical antibacterial agents in recent years have provided an added “safety net” against contamination of the system in elderly patients who may have impaired vision or dexterity. In fact, another study described a significant prevalence of improper bag exchange procedure in PD-related peritonitis. A significant association was observed between noncompliance to the bag exchange procedure and the frequency of peritonitis. In other words, adherence to aseptic procedure decreases the peritonitis rate and thus improves patient survival (11). Unfortunately, the relationship between inappropriate technique and increased age was not analyzed. However, it seems that improvement in equipment might help to prevent PD-related peritonitis in elderly PD patients and might result in a reduction of the mortality associated with infections.

**Conclusions**

Aging—rather than diabetes mellitus, nutrition status (based on albumin and total cholesterol), efficiency of dialysis (based on blood urea nitrogen and weekly CCr), or use of statins—was an important risk factor for PD-associated peritonitis in patients attending our kidney disease center in Japan. Poor PD technique because of advanced age may be a reason for that finding. Especially for elderly patients, PD remains an important modality of renal replacement therapy. Improvements in equipment and training programs aimed at elderly patients may help to limit the associated risk.

**Disclosures**

The authors have no financial conflicts of interest to declare.

**References**

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