Encapsulating peritoneal sclerosis (EPS) is a serious complication of long-term peritoneal dialysis (PD). The mortality rate for EPS has been high, primarily because of complications related to bowel obstruction. However, recent advances in clinical research have established the pathogenesis and course of the condition and a treatment strategy. The final therapeutic option for EPS is surgical enterolysis, and we have performed 239 surgical procedures in 181 patients and observed favorable outcomes.

Of 181 patients opting for surgery, 64 (35.4%) died. Death was related to EPS in 33 patients (18.2%), including 14 who died postoperatively. The overall survival rate at 1, 2, 3, 5, and 8 years after diagnosis was 93%, 83%, 78%, 71%, and 60% respectively. The survival rate for EPS-related death at 1, 2, 3, 5, and 8 years after diagnosis was 95%, 90%, 87%, 81%, and 74% respectively. Median survival after diagnosis, considering death from any cause and death from EPS, was 43.9 months and 35.7 months respectively.

In conclusion, we present favorable outcomes with EPS surgery in 181 patients encountered over a period of 17 years. These data reconfirm that surgical treatment is essential for EPS patients. Encapsulating peritoneal sclerosis may no longer be a fatal complication and can be improved with accurate diagnosis and treatment.

**Key words**

Encapsulating peritoneal sclerosis, EPS, surgical option, outcomes

**Introduction**

In encapsulating peritoneal sclerosis (EPS), intraperitoneal inflammation leads to adhesive and inflammatory encapsulation of the intestinal tract, which then manifests as bowel obstruction syndrome. With the widespread use of peritoneal dialysis (PD), the number of patients developing EPS, a potentially fatal PD-related complication, has increased (1,2). As a consequence, there is much debate about whether there should be an arbitrary expiry date for PD because of the risk of EPS. However, recent clinical studies have clarified the pathogenesis of EPS and have proposed therapeutic strategies (3).

In particular, the surgical option was previously contraindicated in patients with EPS (1); however, the final option for patients in whom bowel obstruction symptoms fail to improve is surgical enterolysis, and we have actively performed this procedure since 1993. In EPS, the intestine is degenerated and vulnerable, and so the risk of intestinal perforation is high because of persistent obstruction. Such occurrences are fatal. We therefore consider that surgery is indicated for all EPS patients with severe symptoms of bowel obstruction (4–7).

In the present study, we investigated changes in surgical technique and in long-term outcomes in 181 EPS patients who underwent surgical treatment at our facility between 1993 and the end of 2010.

**Methods**

**Patients**

Our first encounter with a patient with EPS who underwent surgical enterolysis occurred in 1993; that patient was completely cured. From then until the end of 2010, we performed 239 enterolysis procedures in 181 patients. Of those 181 patients, 14 died after surgery; all of the others showed improvement.

The 181 EPS patients who underwent surgery were withdrawn from PD at a mean age of 50.6 years (range: 10.9 – 77 years) after receiving PD for a mean period of 126 months (range: 22.1 – 235 months). Among those patients, 172 (95.0%) developed EPS at a mean of 20.2 months after withdrawal from PD.
(range: 0.3 – 117 months). The mean time from development of EPS to surgery was 14.4 months (range: 1 – 127 months). Steroids were administered to 129 of the patients (71.3%) after the development of EPS.

**Surgical procedure**

Considering the mechanism of EPS development, the surgical technique is simple, involving only the division of peritoneal adhesions by repeated lysis of fibrin membranes with a sharp instrument. Recently, to identify the site of stenosis, we have, after enterolysis, been inserting a Miller–Abbott ileus tube with an inflated balloon to the end of the ileum.

Surgery can reverse the bowel obstruction, but it does not improve the peritoneal deterioration. As a result, the capsules can re-form, and EPS can recur in some patients 6 – 12 months later. In addition, adhesions also occur as a result of surgical injury to the intestinal wall and mesenteric serosa. To prevent recurrences, we have, since April 2007, been performing the Noble plication procedure (8,9), in which intestine is sutured to intestine to prevent re-obstruction of the bowel (7). This technique prevents not only passage disturbances resulting from kinking and adhesion of the small intestine, but also escape into and adhesions in the pelvic cavity. In patients experiencing recurrence or presenting difficulties in complete adhesiolysis because of intestinal wall calcification bypass between the oral site jejunum and the ileum or large intestine is required.

**Statistics**

Categorical data are expressed as numbers and percentages. Survival and recurrence rates during follow-up are estimated using the Kaplan–Meier method. A difference was considered significant when the \( p \) value was less than 0.05.

**Results**

**Surgical results**

Most of the 14 patients (7.7%) who died postoperatively died of sepsis resulting from intestinal perforation and infection; 1 died from hepatic failure. Enterolysis was performed in 169 first surgeries; the Noble plication was added in 57 recent cases. Bypass between the oral site jejunum and the ileum or large intestine was performed in 9 patients in whom enterolysis could not be performed. In 3 patients with localized adhesions and mild degeneration of the wall of the small intestine, the adhered small intestine was resected and anastomosed.

Surgery for recurrence was performed in 41 patients (22.7%). These re-surgeries were conducted an average of 14 months (range: 2 – 66 months) after the first surgery. Surgery was performed 3 times in 16 patients, 4 times in 6 patients, and 6 times in 1 patient, for a total of 58 re-surgeries. Figure 1 shows the re-surgeries.

Of 112 patients treated solely with enterolysis in the first surgery, 34 (30.4%) required re-surgery. In 57 patients, enterolysis with Noble plication was performed in the first surgery; 7 of those patients (12.3%) required re-surgery. We compared the course of re-surgery between patients who underwent the Noble plication procedure and those who underwent enterolysis alone for their initial surgery. Although a long-term comparison is difficult because the follow-up period for the Noble plication group is short, the 1- and 2-year rates of freedom from a re-surgery are higher in the group treated with Noble plication (0.91 vs. 0.76 and 0.81 vs. 0.70 respectively), suggesting that the Noble plication is effective in preventing recurrence (Figure 2).

Bypass between the oral site jejunum and the ileum or large intestine was necessary for some patients with recurrence and for those in whom a complete dissection was difficult because of severe intestinal calcification. We performed 16 bypass surgeries in 14 patients (9 in the first surgery and 7 in a...
re-surgery). Passage disorder improved in 9 patients, but 5 patients died from suture failure after surgery. We reflected on the importance of ascertaining the severity of intestinal degeneration. Moreover, passage disorder was not improved by any surgical procedure in some patients. As the final option, percutaneous endoscopic gastrostomy was performed in 2 patients to reduce intestinal pressure; those patients currently continue on home parenteral nutrition.

Outcomes
At the end of 2010, outcomes in 6 of the 181 patients were unknown. Excluding those 6 patients, the mean duration of postoperative follow-up was 46.4 months (range: 0.3 – 208 months). A total of 64 patients who opted for surgery (35.4%) died. Death was related to EPS in 33 patients (18.2%), including the 14 who died postoperatively (Table 1). The overall survival rate at 1, 2, 3, 5, and 8 years after diagnosis was 93%, 83%, 78%, 71%, and 60% respectively. The survival rate for EPS-related death at 1, 2, 3, 5, and 8 years after diagnosis was 95%, 90%, 87%, 81%, and 74% respectively. Median survival after diagnosis, considering death from any cause and death from EPS, was 43.9 months and 35.7 months respectively (Figure 3). However, some EPS-related symptoms remained in 14 (7.7%) of the 111 survivors.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Patients (n)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total deaths</td>
<td>64</td>
<td>35.4</td>
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<tr>
<td>Deaths from EPS</td>
<td>33</td>
<td>18.2</td>
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<tr>
<td>Postsurgical</td>
<td>14</td>
<td>7.7</td>
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<td>Longer-term</td>
<td>19</td>
<td>10.5</td>
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<td>Deaths from other causes</td>
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<td>Cardiovascular disease</td>
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<td>2.2</td>
</tr>
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<td>Malignancy</td>
<td>4</td>
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<td>Intestinal disease</td>
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<td>1.7</td>
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<tr>
<td>Hepatic failure</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Suicide</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Alive at the time of writing</td>
<td>111</td>
<td>61.3</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>6</td>
<td>3.3</td>
</tr>
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</table>

Discussion
Previously, the literature contained only case reports of the use of the surgical option for EPS (10–12). Surgery was previously contraindicated in patients with EPS, and most patients treated surgically died of peritonitis as a postoperative complication (1). These
deaths occurred because the pathogenesis of EPS was not well understood by surgeons, and in many cases, simple resection of adherent intestinal loops with enterostomalization was performed by surgeons who had never been involved with PD.

We developed a surgical technique of total intestinal enterolysis without enterectomy, and since then, we have treated patients in the belief that surgical therapy is the only curative treatment for established EPS (4–7). In the period between 1993 and the end of 2010, we performed 239 enterolysis procedures in 181 patients. Of those 181 patients, 14 died after surgery; all of the others showed improvement.

Using careful surgical techniques, the first surgery can be completed in many patients. However, although the bowel obstruction can be resolved, degenerative deterioration of the peritoneum is not improved, and capsules can re-form 6 – 12 months after surgery, with EPS recurring in some patients. Moreover, adhesions because of surgical injury to the intestinal wall and mesenteric serosa can occur. In some recurrent cases, detachment of the adhesions cannot be completed, and bowel obstruction cannot be resolved, which re-confirms the seriousness of EPS. The postoperative recurrence rate was previously reported to be 23.4%, for which countermeasures are necessary (6).

Starting in 2007, we developed a useful modification of the Noble plication to prevent recurrent bowel obstruction related to adhesions (7). Intestine-to-intestine suturing helps to prevent re-obstruction of the bowel, by preventing not only passage disturbance resulting from kinking and adhesion of the small intestine, but also escape of the bowel into the pelvic cavity and formation of further adhesions (8,9). Usually, the entire small intestine is fixed between the mesenteric and antimesenteric borders from the ileum end proximaly. Although the follow-up period has been relatively short, the incidence of recurrence is reduced in patients receiving the Noble plication.

The mortality rate from EPS has been reported to be 24% – 66%, but those findings lack clarity because of variations in the follow-up periods and treatment methods. The results of a relatively long-term follow-up have recently been reported. In the Pan-Thames study, in which EPS was observed in 111 patients, the overall mortality and 1-year overall survival rates were 53% and 56% respectively (13). In the Australia and New Zealand Dialysis and Transplant Registry, the overall mortality rate in 33 EPS patients was 55%, and the 1-, 2-, 3-, and 5-year survival rates were 69%, 62%, 58%, and 35% respectively (14). In a multicenter Dutch study, EPS was retrospectively analyzed in 64 patients, and the efficacy of tamoxifen was presented, but the overall mortality rate was 63.5%, and the 1-, 2-, and 3-year survival rates in the tamoxifen group (24 patients with an overall mortality rate of 45.8%) were 80%, 75%, and 60% respectively (15). Compared with those recent reports, outcomes in our study were markedly favorable: the overall mortality rate was 35.4% and the 1-, 2-, 3-, and 5-year survival rates were 93%, 83%, 78%, and 71% respectively (Table II).

Given that the observation period in our study was 17 years, the severity of EPS may have changed, and surgical techniques have been modified. Moreover, the therapeutic results were collected at a single facility and so cannot be directly compared with results collected at multiple facilities. However, the usefulness of surgical therapy for EPS has not been ruled out because all surgeries were performed by the same operator and surgical team under a set therapeutic policy.

In the 1990s, Japan experienced a large number of EPS cases, and PD therapy faced a crisis (1). There were many negative viewpoints on surgical treatment of EPS at the beginning, but surgery became accepted in the face of an increasing number of cases, and several other facilities introduced surgical therapy. This activity promoted the understanding of, and countermeasures against, EPS in Japan, and EPS is no longer recognized as a fatal complication (2). In addition, biocompatible PD fluid (fluid low in glucose degradation products) became available for all patients, which may have reduced the EPS risk. A multicenter study on the efficacy of this biocompatible PD fluid for the prevention of EPS is now underway (16).

Summary
We present favorable outcomes of EPS surgery in 181 patients encountered over 17 years. Surgical treatment has been reconfirmed as essential for EPS patients with severe bowel obstruction. To improve the surgical results, a surgical team with a thorough understanding of the pathology of EPS is essential, for which the establishment of a regional EPS treatment center
in each community and the training of surgeons are necessary. Encapsulating peritoneal sclerosis might no longer be a fatal complication, and it can be improved with accurate diagnosis and treatment.

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

References

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