Encapsulating peritoneal sclerosis: a rare, serious but potentially curable complication of peritoneal dialysis—experience of a referral centre in Germany

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Keywords: encapsulating peritoneal sclerosis, histopathological findings, long-term outcome

ABSTRACT

Background. Chronic peritoneal dialysis (PD) can be complicated by encapsulating peritoneal sclerosis (EPS), the most severe complication associated with long-term PD. EPS is defined by the international Society for Peritoneal Dialysis (ISPD) with clinical signs of abdominal pain, bowel obstruction or weight loss in late stages [1]. During the course of the disease, the development of adhesions and symptoms of bowel obstruction

INTRODUCTION

Chronic peritoneal dialysis (PD) can be complicated by encapsulating peritoneal sclerosis (EPS), the most severe complication associated with long-term PD. EPS is defined by the international Society for Peritoneal Dialysis (ISPD) with clinical signs of abdominal pain, bowel obstruction or weight loss in late stages [1]. During the course of the disease, the development of adhesions and symptoms of bowel obstruction
often require major surgery. Earlier stages of the disease are difficult to detect, changes in transporter status or ultrafiltration failure can be first signs [2]. The incidence of EPS increases with increasing time of PD, younger age, glucose load and peritonitis rate [2–4]. The clinical features result from the underlying pathogenic process, particularly ileus, inflammation and/or peritoneal adhesions [5]. EPS may occur on PD, but most patients become symptomatic after cessation of PD [6–10]. The three diagnostic pillars of EPS are clinical symptoms, radiological findings and histological criteria [11].

There exists several non-evidence-based medical and surgical treatment options; although surgical treatment options, morbidity and mortality are still high (from 25 to 55%) especially in the first year after diagnosis [2, 3, 6, 7, 9]. Mostly, peritonectomy and enterolysis (PEEL) is the surgical treatment of choice. Fibrotic tissue and EPS membranes are peeled away from the parietal and visceral peritoneum. This seems to be the best option to restore bowel function by the surgical procedure in patients with late-stage disease [12, 13]. The value of medical therapy in EPS is still under discussion. Evidence for a specific medical treatment option is still lacking [14].

In this study, we retrospectively analysed the clinical, radiological and histological data and outcome of 49 EPS patients between March 1998 and the end of 2010.

**MATERIALS AND METHODS**

The present study included all EPS patients diagnosed between March 1998 and October 2011 in our department of nephrology. Data collection included demographic data, cause of primary renal disease, co-morbidities (diabetes, hypertension and smoking status), PD details and the start date of dialysis. Furthermore, body mass index (BMI), peritonitis rate, medications and time of onset of symptoms were recorded. Additionaly, peritoneal biopsies of the EPS patients were investigated.

**Diagnosis**

For the diagnosis of EPS, we used the clinical criteria outlined by Nakamoto [5], radiological criteria by Vlijm et al. [15] and histological criteria by Braun et al. [16] and Honda et al. [17].

Patients were divided into two clinical categories: severe and mild/moderate. Diagnostic criteria for the severe group were need for surgery due to extensive symptoms caused by bowel obstruction (vomiting, abdominal pain, weight loss). Mild to moderate EPS were all patients with EPS who did not fulfil the criteria for the severe group.

**Clinical outcome**

The onset of complaints related to EPS (abdominal pain, bowel obstruction, weight loss or anorexia) and the outcome of all EPS patients were reviewed by physicians, either in person or through telephone contact. The current complaints were prompted, and for comparison, a scale was performed (0, no complaints; 1, rarely complains; 2, frequently complains; 3, continuous complaint throughout the day). The first point of the contact was 1 December 2011.

Complications were categorized into minor complications, resolving without surgical or radiological intervention (e.g. wound infection, postoperative small bowel paralysis) and major complications, which required surgical intervention (e.g. small bowel fistulas, severe post-operative bleeding or complete wound rupture).

**Statistical analysis**

Continuous data are expressed as mean ± standard deviation (SD). Median with inter-quartile range is used where distribution is not normal.

Two observers blinded to the diagnosis performed the histopathological analysis. Variables were classified as either binary (present or absent) or ordinal. The ordinal variables were discriminated as absent, low, moderate and high grade. All data were processed using the software program GraphPad Prism (Version 5). Comparisons between different groups were made using the analysis of variances (ANOVA) and the Fisher test. The histological findings were described as from zero to three, or zero (absent) versus 1 (present).

The level of significance was defined as P < 0.05, with a high level of significance as P < 0.01. A highly significant level was defined by P < 0.001. Trend was defined between P = 0.05 and P = 0.10.

**Histopathological analysis**

Tissue samples from the peritoneum of 29 of 31 severe EPS patients and 9 of 11 mild/moderate EPS patients were performed during peritonectomy, laparoscopy or at PD catheter removal. One biopsy in the mild/moderate group was performed during herniotomy. All biopsies were formalin-fixed and paraffin-embedded following routine protocols [16]. All patients had given their informed consent concerning a scientific work-up of tissues taken during surgery. Variables were classified as either binary (present or absent) or ordinal. The ordinal variables were discriminated as absent, low, moderate and high grade. From each slide, we performed haematoxylin and eosin stains for morphological analysis.

Fibrosis: absent, 1–10%/LPF, 11–50%/LPF, >51%/LPF (0, 1, 2, 3); fibroblast-like cells (FLC): absent, 1/5 HPFs, 2–4/5 HPFs, >5/5 HPFs (0, 1, 2, 3); exudation: absent, 1 small area in 1 MPF, 1 area <5%/MPF, 1 area >5%/MPF (0, 1, 2, 3); cellularity was evaluated as 0 (1–2 nuclei/HPF), 1 (3–5 nuclei/HPF), 2 (6–20 nuclei/HPF) and 3 (>20 nuclei/HPF); vessel density: absent, 1–5/HPF, 6–10/HPF, >10/HPF in the submesothelial cell layer (0, 1, 2, 3); acute inflammation (neutrophils): absent, 1/HPF, 2–5/HPF, >5/HPF (0, 1, 2, 3); chronic inflammation (round cells): absent, 1–5/HPF, 6–20/HPF, >20/HPF (0, 1, 2, 3); haemorrhage: absent extravascular erythrocytes, 1 area <10%/5 LPF, 2 + 3 area/5 LPF or 1 area 11–30%/5 LPF, 4 + 5 area/5 LPF or 1 area >30%/5 LPF (0, 1, 2, 3); fibrin deposits: absent eosinophilic area, 1 area <5%/5 MPF, 1 area 6–20%/5 MPF, 1 area >20%/5 MPF (0, 1, 2, 3); presence of vasculopathy: thickening of vessel walls and/or inflammation of the vessel wall (0, 1); mesothelial denudation: no visible mesothelium (0, 1); presence of acellular areas...
(0, 1); FLC were defined as elongated cells, separated from vessel lumen with vesicular nucleus and one to three nucleoli. Acute inflammatory reaction was defined by the presence of neutrophilic granulocytes. Chronic inflammatory reaction was defined by the presence of round cells without taking into consideration further subclasses such as lymphocytes, plasma cells, monocytes and histiocytes. HPF = 0.26 mm², MPF = 0.91 mm², and LPF = 3.2 mm².

According to the small sample size, we reduced the initial four-step scale to a two-step scale. This approach compares only very severe histological changes with less severe changes and simplifies the way of histological analysis.

RESULTS

Between March 1998 and October 2011, 49 cases of EPS were identified in our nephrology department. During the work-up of these patients, sufficient data were given for 42 EPS patients.

Demographics

The mean age at diagnosis was 52.3 ± 11.5 years in the severe group and 55.5 ± 15.7 years in the mild/moderate group. Overall, there were nine females: three in the severe EPS group and six in the mild/moderate EPS group. The underlying disease leading to chronic renal failure revealed no predominant diagnosis. The cause of kidney disease was reported in the severe group as chronic glomerulonephritis in 16 patients, diabetic nephropathy in three patients, hypertension in five patients, polycystic kidney disease in two patients and other causes in five patients. In the mild/moderate group, five patients had a chronic glomerulonephritis, diabetic nephropathy was reported in one patient, hypertension in two patients and other causes in three patients.

Overall, 16 of 42 EPS patients were active smokers or were smokers in the past. Twenty-seven of 42 EPS patients had hypertension. There were no statistically significant differences between the severe and mild/moderate EPS group concerning the baseline characteristics, except the C-reactive protein (CRP) levels, which were significantly elevated in the severe group compared with the mild/moderate group (P = 0.02), and the higher peritonitis rate in the severe EPS group (Table 1).

PD details and peritonitis

All patients were on continuous ambulatory PD. The mean duration on PD at the time of diagnosis of EPS was 76.5 ± 32.4 months in the severe group and 100 ± 49.0 months in the mild/moderate group (P: n.s.). In the severe group, 24 of 31 and 7 of 11 patients in the mild/moderate group had used icodextrin.

There were 71 episodes of peritonitis in 2371 PD months in the severe group, and 14 episodes of peritonitis in 1000 PD months in the mild/moderate group (P < 0.05). In the severe group, five patients had no peritonitis, 22 patients had one to four previous episodes, three patients had five and one patient had seven previous episodes. In the mild/moderate group, three patients had no peritonitis, six patients had one to four previous episodes and two patients had two previous episodes of peritonitis. The most common organism was Staphylococcus aureus followed by coagulase-negative Staphylococci and Streptococci in both groups.

Modality at diagnosis of EPS and membrane permeability

In the severe group, peritonitis was the cause of transfer to HD in eight patients, ultrafiltration failure in nine patients and EPS in 12 patients. The remainder was not specified. In the mild/moderate group, peritonitis was the cause of transfer to HD in two patients, ultrafiltration failure in four patients and EPS in four patients. One patient could not be specified.

Data on the last peritoneal equilibration test (in the last 6 months) were available in 20 of 31 patients in the severe group and 9 of 11 patients in the mild/moderate group at the time of diagnosis. In the severe group, 13 of 20 patients were high average or high transporter. Four patients were low average and three patients low transporter. In the mild/moderate group, seven of nine patients were high average or high transporter. The remaining two patients were low transporter.

The mean duration of HD transfer to EPS onset was 15.6 ± 23.1 months in the severe group and 15.4 ± 38.3 months in the mild/moderate group (P: n.s.).

Twenty patients in the severe group were on HD at the time of diagnosis, nine on PD and two had a functioning transplant. At the time of diagnosis in the mild/moderate EPS group, one patient was on HD, seven on PD and three had a functioning transplant.

In our study, 6 of 31 patients in the severe group and 4 of 8 patients in the mild/moderate group developed EPS after transplantation.

Clinical features

All patients in the severe group had symptoms consistent with EPS. Abdominal pain or vomiting was reported by all patients in the severe group. Additionally, a large proportion had both symptoms and weight loss was noted in almost all patients in this group. The mean time of onset of those symptoms to the surgical procedure was 9.96 ± 16.4 months in this group.

At the time of EPS diagnosis, seven patients in the mild/moderate group had abdominal pain and one patient reported nausea and vomiting.

Histopathological analysis

Peritoneum biopsies were available in 29 of 31 patients in the severe and in 9 of 11 in the mild/moderate group. The histological features were consistent with EPS in all biopsies in both groups. Denudation was present in all biopsies from the peritoneum and 36 of 38 samples showed severe fibrosis. The histopathological findings of the peritoneal biopsies of both groups are summarized in Table 2.

Radiological findings

Computed tomographic (CT) scanning was performed in 27 of 31 patients in the severe group. The most common CT
findings reported to support the diagnosis of EPS were peritoneal thickening (18 of 31 patients). In the severe group, small bowel dilatation caused by bowel obstruction was reported on 15 of 21 patients. Other findings were calcification and ascites (Table 1).

In the mild/moderate group, CT scanning was available in eight patients. According to the results in the severe group, the most common CT finding was peritoneal thickening. None of the patients had bowel dilatation, and in two patients, calcification was visible (Table 1).

**BMI and parenteral nutrition**

BMI was 22.6 ± 4.9 at the time of surgery and increased to 23.7 ± 4.2 1 year after surgery (P>0.05). During the follow-up of 41.0 ± 38.5 months, BMI was 23.5 ± 4.5 in the severe group (P>0.05). Twenty-one of 31 patients in the severe group...
received parenteral nutrition (PN), and 16 of 31 patients received PN longer than 2 weeks after surgery.

The mean BMI at diagnosis was 26.1 ± 6.0 in the mild/moderate group and 25.5 ± 6.1 1 year later. During the follow-up of 41.6 ± 21.6 months after diagnosis, BMI was 24.3 ± 5.0 in the mild/moderate group. None of the patients in the mild/moderate group received PN.

### Treatment

**Severe EPS group.** All 31 patients in the severe group required surgery due to bowel obstruction. Twenty-nine PEEL and two adhesiolysis were performed and the mean operation time of PEEL was 334.8 ± 116.1 min. The surgical procedure contained 10 anastomoses, eight small bowel resections and one right hemicolectomy. All patients received a decapsulation and 11 patients received a complete parietal peritonectomy with resection of all eight quadrants. Two appendectomies and two cholecystectomies were performed in four EPS patients additionally. Three patients were operated twice due to recurrent disease. Surgical minor complications occurred in five EPS patients and surgical major complications in 11 EPS patients (Tables 3 and 4).

In the severe group, steroids were given to 10 patients preoperatively and 12 patients post-operatively. Three patients were treated with tamoxifen, all of them in combination with other drugs. Immunosuppressive drugs were used in nine patients, all associated with transplantation. The immunosuppressive drugs given for transplantation were tacrolimus, cyclosporin, mycophenolate mofetil and azathioprine. The remaining patients had no specified treatment. In the mild/moderate group, 5 of 11 patients were treated with steroids, one patient was treated with tamoxifen in combination with steroids and four patients received immunosuppressive therapy due to transplantation. The remaining patients had no specified treatment (Tables 3 and 4).

### Outcome

To date, 25 of 31 patients in the severe group are alive, 17 of 31 were on HD and 8 had a functioning transplant. The mean time of follow-up after surgery was 45.6 ± 39.0 months in the severe group. Post-operatively, three patients died due to sepsis caused by peritonitis and one patient died because of sepsis after small bowel fistula. Three patients died from other causes. One male EPS patient died 5 months after surgery due to heart failure, one female EPS patient 6 months and one male EPS patient 2 months after surgery (reason not clear).

In the follow-up period, three patients developed a recurrent EPS and were re-operated on. In all of these patients, a redo PEEL was done and all are alive up to now. The median time to recurrent disease was 9 months (6, 9 and 15 months, respectively).

Up to now, 8 of 11 patients in the mild/moderate group are alive, 6 of 11 are on HD and 2 have a functioning graft. The mean follow-up time after diagnosis was 41.6 ± 21.6 months in the mild/moderate group.

The survival curve of the severe and mild/moderate EPS patients is shown in Figure 1.

Overall, in both groups, 31 of 33 patients had no or rare complaints throughout the day. Only two patients reported continuous complaints throughout the day. The most frequent symptoms were abdominal pain and feeling of weakness. In the mild/moderate group, seven of eight patients had no complaints and only one patient reported abdominal pain once a week.

### DISCUSSION

In this study, we present the clinical, radiological and histological data and outcome of 49 patients with EPS. Although there are other multicentre case series, this survey of EPS provides the most comprehensive and detailed information from the largest referral centre in Germany.

We divided our patients into two groups: Group 1 (severe group) required surgery due to bowel obstruction because of advanced disease and Group 2 was the non-surgical group (mild/moderate group). Most of the patients in both groups were 50–55 years old, which is in line with other studies [3, 18]. Remarkably, most of the patients in our patient cohort are male. Published data about gender as a risk factor for the development of EPS are variable. Guest [19] suggested a female predominance in the development of EPS.

As reported in previous studies, EPS is predominantly a complication of long-term PD. In our study, the mean PD duration was 76.5 ± 32.4 months in the severe group and 100 ± 49.0 months in the mild/moderate EPS group, which corresponds with other studies [2, 6–9, 20, 21]. Only 7 of 42 patients who developed EPS were on PD for <5 years. Surprisingly, the PD duration was longer in the mild/moderate EPS group. The mean PD duration was 100 ± 49.0 months in the severe group and 100 ± 49.0 months in the mild/moderate EPS group. The mean PD duration was 76.5 ± 32.4 months in the severe group and 100 ± 49.0 months in the mild/moderate EPS group, which corresponds with other studies [2, 6–9, 20, 21].
### Table 3. Details of severe EPS patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Severe EPS</th>
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<tbody>
<tr>
<td>n</td>
<td>31</td>
</tr>
<tr>
<td>Alive/dead</td>
<td>25/6</td>
</tr>
<tr>
<td>Mortality rate (%)</td>
<td>19.4</td>
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</tbody>
</table>

#### Cause of death

- **Death from EPS (total)**: 2
- **Sepsis after small bowel fistula**: 1
- **Sepsis caused by peritonitis**: 1
- **Death from other causes (total)**: 3
- **Heart failure**: 1
- **Unknown**: 2

#### Recurrent disease
- **EPS after transplantation**: 6

#### Current RRT HD/NTx/PD
- **Parenteral nutrition**: 17/8/0

#### Preoperative
- **Parenteral nutrition**: 0/10/0

#### Intraoperative/post-operative (2 weeks after surgery)
- **Post-operative (>2 weeks after surgery)**: 16

#### BMI (onset surgery)
- **BMI (onset surgery)**: 22.6 ± 4.9

#### BMI 1 year after surgery
- **BMI 1 year after surgery**: 23.7 ± 4.2

#### BMI follow-up (41 ± 38.5 months after surgery)
- **BMI follow-up (41 ± 38.5 months after surgery)**: 23.5 ± 4.5

#### Time of onset of complaints to surgery (months)<sup>a</sup>
- **Time of onset of complaints to surgery (months)**: 5.0 (2–12)

#### Surgical procedure
- **PEEL**: 29
- **Adhesiolysis**: 2

#### Operation time (min)
- **PEEL**: 334.8 ± 116.1
- **Adhesiolysis**: 78.5 ± 5.0

#### Surgical major complications
- **Surgical major complications**: 11

#### Surgical minor complications
- **Surgical minor complications**: 5

#### EPS treatment
- **Steroids**
  - **Preoperative**: 10
  - **Post-operative**: 12
- **Tamoxifen**: 3

#### Treatment after transplantation
- **Tacrolimus**: 6
- **Ciclosporin**: 2
- **Azathioprine**: 1
- **Mycophenolate mofetil**: 1

#### Time of follow-up after surgery (months)
- **Time of follow-up after surgery (months)**: 45.6 ± 39.0

#### Current complaints (0, 1, 2, 3)
- **Current complaints (0, 1, 2, 3)**: 14/9/0/2

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<sup>a</sup>Inter-quartile range. 

NTx, transplantation; RRT, renal replacement therapy; HD, haemodialysis; BMI, body mass index; PEEL, peritonectomy and enterolysis.
group compared with the severe EPS group. Although this finding was not statistically different between the two groups, this finding might support the hypothesis that the time on PD reflects only one risk factor in the development of EPS and that a ‘second-hit’ must occur, e.g. an inflammatory stimulus (e.g. bacterial peritonitis), discontinuation of PD or genetic predisposition [16, 22–25].

Several other risk factors for the development of EPS are discussed. Most but not all published data [2, 26, 27] suggested that peritonitis rate might predispose to EPS [1, 8, 28]. In our cohort, the peritonitis rate was not particularly high, especially in the severe group (71 episodes of peritonitis in 2371 PD months), staying in contrast to the hypothesis that there might be an association between peritonitis rates and development of EPS. The peritonitis rate in the severe group was higher compared with the mild/moderate group in our study (P < 0.05). The use of icodextrin solutions and the development of EPS are still under discussion. Some studies described an association between the use of icodextrin and the development of EPS, based on an increased expression of local inflammation markers [29–31]. Other studies suggested that the use of icodextrin preserves mesothelial cells and peritoneal membrane function [32, 33]. In our study, 24 of 31 in the severe group and 7 of 11 patients in the mild/moderate group had used icodextrin. All patients started using icodextrin because of ultrafiltration problems and not to protect the membrane against a high-glucose exposure. This supports the hypothesis that patients are using icodextrin because of ultrafiltration failure and not the other way round [2, 26, 27].

CRP levels were significantly elevated in the severe group compared with the mild/moderate group. Higher CRP levels in severe EPS cases could be correlated with histological signs of chronic inflammation, which is highly present especially in patients with advance disease. Therefore, as described in our study, elevated CRP levels could be correlated with requirement for surgery and could help clinicians to judge the need of surgery in EPS patients.

A novel aspect of our study was the investigation of the time of onset of symptoms associated with EPS to requirement of major surgery. Interestingly, in the severe group, the time of first symptoms of EPS to major surgery was only median 5 months with an inter-quartile range of 2–12 months. As a consequence, earlier diagnosis of the disease is mandatory, even in asymptomatic patients. Therefore, it is a precondition that these patients are treated in specialized referral centres.

Another novel aspect of our study was that we investigated the biopsies of the peritoneum of the EPS patients (29 of 31 severe and 9 of 11 mild/moderate patients). In the literature, there are several publications about histological findings of the peritoneum showing that fibrin deposition, fibroblast swelling, capillary angiogenesis and mononuclear cell infiltration were significantly more common in EPS. Regarding the degree of these parameters, only fibroblast swelling and fibrin deposition exhibited statistically significant differences [17, 25, 34, 35]. Additionally, previous studies showed significant

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<th>Table 4. Details of mild/moderate EPS patients</th>
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<td>n</td>
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<td>Alive/dead</td>
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<td>Mortality rate (%)</td>
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**Death from EPS**

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<td>Sepsis</td>
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<tr>
<td>Death from other causes</td>
<td>2</td>
</tr>
<tr>
<td>EPS after transplantation</td>
<td>4</td>
</tr>
<tr>
<td>Current RRT HD/NTx/PD</td>
<td>6/2/0</td>
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<tr>
<td>Parenteral nutrition</td>
<td>0</td>
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**Treatment**

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<td>Steroids</td>
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<tr>
<td>Tamoxifen</td>
<td>1</td>
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**Treatment after transplantation**

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<tbody>
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<td>Tacrolimus</td>
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<td>Ciclosporin</td>
<td>1</td>
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<tr>
<td>Mycophenolate mofetil</td>
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<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild/moderate EPS</th>
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<tr>
<td>BMI time diagnosis</td>
<td>26.1 ± 6.0</td>
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<tr>
<td>BMI 1 year after diagnosis</td>
<td>25.5 ± 6.1</td>
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<tr>
<td>BMI follow-up (41.6 ± 21.6 months after diagnosis)</td>
<td>24.3 ± 5.0</td>
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<tr>
<td>Time of follow-up after diagnosis</td>
<td>41.6 ± 21.6</td>
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<tr>
<td>Current complaints (0, 1, 2, 3)</td>
<td>7/1/0/0</td>
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NTx, transplantation; RRT, renal replacement therapy; HD, haemodialysis; BMI, body mass index; PEEL, peritonectomy and enterolysis.

**Follow-up (months)**

- Severe EPS: 31, 16, 10, 5, 4, 1, 1, 1
- Mild/moderate EPS: 11, 7, 4, 1

**Fig. 1.** The Kaplan–Meier survival curve showing the overall outcome in the severe and mild/moderate EPS group.
differences concerning fibrosis in EPS patients compared with patients with simple sclerosis [35–37]. In our study, 36 of 38 EPS patients showed severe fibrosis. Actually, there exists no data whether there are histological differences between biopsies of the peritoneum of patients with advanced disease compared with mild/moderate disease. In our study, the histological features were consistent with EPS in all biopsies in both groups. All biopsies showed that denudation and FLC were present in both groups. The role of FLC in the pathogenesis of EPS is not clear yet. Previous publications of our and other groups regarding this specific cell type demonstrated a phenotype of myofibroblasts and mesothelial cells [38, 39]. Limited due to the small number of patients, the histological analysis of the peritoneum of eight patients who died showed that it seems unlikely that histological findings could predict the outcome of patients. Despite those results, peritoneal biopsies should be taken from all patients on PD at every time of surgery [e.g. catheter removal, correction of a catheter malposition or during abdominal surgery (e.g. hernia repair, cholecystectomy)]. Nevertheless, histological findings are only one diagnostic pillar and should also take into account radiological scores and clinical criteria [5, 16, 40–43].

The evaluation of medical treatments for EPS is difficult because evidence-based data are lacking. Reported treatment regimes include immunosuppression or antifibrotic therapy with steroids, cyclosporine, azathioprine and tamoxifen [7, 44–47]. The rationale for the use of immunosuppressive therapy is to dampen down the inflammation process of the peritoneal membrane associated with EPS and the inhibition of collagen synthesis and maturation [48]. In our study, steroids and especially tamoxifen were given to only a small proportion of patients compared with other studies [3, 9, 18, 49]. This might be because mostly patients with advanced disease were transferred to our centre. In this stage of disease, the inflammatory process is not highly present and the inflammatory tissue is replaced by fibrosis. We support the hypothesis of Kawanishi et al. [50] that the tissue will not shrink with steroids or other immunosuppressants. Although the specific working mechanism of tamoxifen is not understood, tamoxifen might be a treatment option in advanced, fibrosing and non-inflammatory stages of disease or post-operatively to prevent recurrence of the disease. Prospective and placebo-controlled studies are needed.

The reported morbidity and mortality rates of EPS are still high especially in the first year after diagnosis [2, 3, 6, 7, 9]. As a consequence, there is actually a debate on whether an expiry date for PD should be defined. Kawanishi et al. [51] reported an overall mortality rate of 35.4% during a follow-up of 46.3 months. In our study, the mortality rate of all patients receiving PEEL was 19.4%, with a follow-up time of 45.6 ± 39.0 months. Remarkably, this is not worse compared with the general dialysis population without EPS [52].

In conclusion, compared with the mortality rate of a dialysis population, the outcome of patients even with severe EPS is not worse. It is a precondition that these patients are treated in specialized referral centres. The time of first clinical symptoms consistent with EPS to requirement of surgery is very short. Earlier diagnosis of the disease is mandatory, even in asymptomatic patients. Therefore, peritoneal biopsies should be taken from all patients on PD at any time of surgery (e.g. catheter insertion, catheter removal, correction of a catheter malposition or any other abdominal surgery). Additionally, immunosuppressive therapy in patients with advanced disease might not be mandatory due to low degree of acute inflammation in these stages.

**AUTHORS’ CONTRIBUTIONS**

All authors read and approved the final manuscript.

**CONFLICT OF INTEREST STATEMENT**

None declared.

**ACKNOWLEDGEMENTS**

None.

**FUNDING**

None.

**REFERENCES**

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**Encapsulating peritoneal sclerosis**

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**E-Cadherin expression**

- Expression of E-cadherin is upregulated in epithelial cells of the peritoneal mesothelium.
- The transcription factor Snail controls the transition of epithelial cells to mesenchymal cells, which is essential for the development of EPS.

**Peritoneal Transplantation**

- Successful transplantation of renal tissue has been performed in patients with EPS.
- The recovery of gastrointestinal function after renal transplantation is associated with a high incidence of EPS.

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**References**


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