The Dutch initiative: The EPS registry

4th February 2010

Mario Korte
• Incidence
• Dutch Multicenter Study
• EPS registry
• Aims & Challenges
• Design
• Website
• Update registry
Garosi and Oreopoulos:

“No Need for an expiry date in chronic peritoneal dialysis to prevent EPS”. Int Urol Nephrol 2009.

“We should concentrate on ways to decrease risk of EPS…. Many years this has been the Holy Grail of PD.”
Macroscopic: adhesions, fibrin deposition, thickening visceral peritoneum, cocooning
Incidence

• Prevalence 0.7%\(^1\) - 3.3%\(^2\)
• Japan 1999-2003 \(^3\): incidence
  – 3 years PD 0.7%
  – 5 years PD 2.1%
  – 8 years PD 5.9%
• Netherlands:
  – 3.5 per 1000 patient years \(^4\)

\(^1\)Rigby Nephrol Dial Trans 1998, \(^2\)Summers KI 2005, \(^3\)Kawanishi AJKD 2004, \(^4\)Hendriks 1997 PDI.
Increasing Incidence?

2006: Increasing Incidence Utrecht and Rotterdam?

- 1996-2006: 18 cases.
- Cluster of cases in 2004 and 2005 (12 patients).
- PD population was stable.
- Mean PD duration: 71.8 ± 44.9 months.
- 17 patients on icodextrin (mean: 34.2 ± 22.2 months).
- 83% history of kidney transplantation (mean time to EPS: 39.3 ± 71.1 months).

Concerns about EPS

Topley N. *Encapsulating peritoneal sclerosis: time to act.* PDI 2006.


Dutch initiative EPS registry

Nationwide concerns among nephrologists

16% PD not a first choice because risk EPS.

66% wants a national registry EPS ¹.

¹ A.M. Coester, R.T. Krediet, E.W. Boeschoten. Presented at ISPD 2008
Questions for EPS registry

• Increasing incidence of EPS?
• What risk factors can be identified?
• Uniform management strategies possible?
Steering committee
Dutch initiative EPS registry

Project leaders
M. Korte (Albert Schweitzer hospital)
M. Betjes (Erasmus MC)

Hans Mak institute
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Erasmus MC
M. Fieren

Utrecht MC
W. Boer

VUMC
F. Van Ittersum

UMCN
R. De Sevaux

AMC
D. Struijk

UMC Groningen
R. Westerhuis

AZM
F. v.d. Sande
Aims & Opportunities
Dutch initiative EPS registry

• Extending knowledge EPS
• Uniform definitions for diagnosis and management protocols

• Nationwide registry
• Epidemiological analyses of EPS
• Indicating future research areas
• Collaboration within Europe
Challenges EPS registry

- **Uniform EPS diagnosis**
- Different stages of EPS: determination what stages included
- Complete dataset with all possible variables
- Easy accessible website and easy used
Diagnosis Encapsulating Peritoneal Sclerosis (EPS)

- Clinical syndrome with persistent, intermittent or recurrent presence of intestinal obstruction
- With or without the existence of inflammation parameters
- Peritoneal thickening, sclerosis, calcifications and encapsulation confirmed by macroscopic inspection or radiological findings

<table>
<thead>
<tr>
<th>EPS registry</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macroscopical EPS <em>(golden standard)</em></td>
<td>Intestinal obstruction and Macroscopically identified EPS</td>
</tr>
<tr>
<td>Clinical EPS</td>
<td>Intestinal obstruction and Radiological EPS</td>
</tr>
<tr>
<td>Suspected early EPS</td>
<td>Intestinal obstruction or Two or more findings of: - weight or appetite loss - bloody ascites - radiological suggestion of EPS - fast transport status or ultrafiltration failure</td>
</tr>
<tr>
<td>No EPS</td>
<td>Intestinal obstruction, but Other cause then EPS identified with certainty</td>
</tr>
</tbody>
</table>
Challenges EPS registry

• Uniform EPS diagnosis
• **Different stages of EPS: determination what stages included**
• Complete dataset with all possible variables
• Easy accessible website and easy used
## Stages EPS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pathological findings</th>
<th>Clinical findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-EPS period/asymptomatic</td>
<td>Peritoneal thickening and sclerosis</td>
<td>Ultrafiltration failure</td>
</tr>
<tr>
<td></td>
<td>Calcification of peritoneum</td>
<td>High transporter status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bloody dialysate, ascites</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypoproteinemia</td>
</tr>
<tr>
<td>Inflammation period</td>
<td>Inflammation</td>
<td>Increase in CRP</td>
</tr>
<tr>
<td></td>
<td>Fibrin degradation products</td>
<td>Leucocytosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bloody dialysate, ascites</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight and appetite loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diarrhea and stool changes</td>
</tr>
<tr>
<td>Progressive or encapsulating</td>
<td>Less inflammation</td>
<td>Disappearance of inflammation signs</td>
</tr>
<tr>
<td>period</td>
<td>Adhesions and continuation encapsulating</td>
<td>Appearance of symptoms of ileus:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Nausea, vomiting,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– Abdominal pain, constipation,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– abdominal mass, ascites</td>
</tr>
<tr>
<td>Complete ileus</td>
<td>no inflammation</td>
<td>Complete ileus, anorexia</td>
</tr>
</tbody>
</table>
Challenges EPS registry

- Uniform EPS diagnosis
- Different stages of EPS: determination what stages included
- Design with complete dataset including all possible variables
- Easy accessible website and easy used
Classic - conditioning riskfactors
- Uremia
- Predisposition, age, renal diag
- Desinfectant, practolol *
- PD duration
- PD catheter
- Medication
- Peritonitis
- PDF’s: Glucose, GDP/AGE’s, low pH, lactate buffer

Second hit – new riskfactors
- PDF’s: Glucose, GDP/AGE’s, low pH, lactate buffer
- Transplantation
- Peritonitis
- Medication
- Unknown factor

Peritoneal remodelling
- Simple sclerosis
- Peritoneum

Mesothelial cell
- • Denudation
- • Inflammation
- • Epithelial-mesenchymal transition (EMT)

- TGF-B, VEGF, FGF, IL-1, IL-6, snail upregulation
- SMAD’s, MMP’s, HSP
- Fibroblast activation
- Macrophages
- Fibrinolysis
- Mestcells
- Tryptase
- Fibrosis ↑
- Vasculopathy ↑
- degradation ↓

Post-transplant EPS
“Classic” EPS
Design
Dutch initiative EPS registry

Docter friendly design

- Web based 6 monthly questionnaire to all Dutch nephrologists.
  
  "Did you have any suspicion of EPS in the previous 6 months?"

- If yes: short questionnaire is asked to fill in after consent
Design
Dutch initiative EPS registry

- EPS considered: research nurse will fill in CRF from patient records and interviews.
- Follow up: on site by research nurse twice a year.
- Compatible to other registries
- Additional collection serum, dialysate samples and material for marker studies and DNA research.
Dataset variables EPS registry

Diagnostic parameters
- Patient related: demographics, symptoms
- PD related
- Macroscopical and radiological investigations

Prognostic parameters
- RRT modality, switches
- PD related: eg PET, peritonitis, fluids, markers
- Kidney transplantation related
- Nutrition status
- Chemistry

Therapeutical parameters
- Medication, supportive and medication
### Baseline details

<table>
<thead>
<tr>
<th>Study number</th>
<th></th>
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<tbody>
<tr>
<td>Centre</td>
<td></td>
</tr>
<tr>
<td>Date of inclusion</td>
<td></td>
</tr>
<tr>
<td>Date of Birth</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td></td>
</tr>
</tbody>
</table>

- **Sex**:  
  - male 
  - female

- **Ethnic Origin**:  
  - Netherlands 
  - other, specify

- **Country of birth**:  
  - Netherlands 
  - other, specify

- **Country of birth biological mother**:  
  - Netherlands 
  - other, specify

- **Country of birth biological father**:  
  - Netherlands 
  - other, specify

- **Ever smoked tobacco**:  
  - yes 
  - no 
  - unknown

- **Current tobacco smoked**:  
  - yes 
  - no 
  - unknown

- **Cause of renal failure**:  
  - (EDTA Code)

- **Primary renal diagnosis**:  
  - (EDTA Code)

- **Secondary diagnosis**:  
  -

- **Remarks**:  
  -

### Family disease history

- **Diagnosis of renal disease in family**:  
  - yes 
  - no 
  - unknown

- **Diagnosis of ischemic heart disease in family**:  
  - yes 
  - no 
  - unknown
## Timeline

<table>
<thead>
<tr>
<th>Number</th>
<th>Start date</th>
<th>Modality</th>
<th>Reason switch</th>
<th>Reason switch, other specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>HD, PD, TX</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Surgical procedures

Any surgery that the participant has had involving the catheter, hernia's and abdominal surgery related or not related to PD. Special interest for parathyroidectomy.

**Surgical procedures**

- [ ] yes
- [X] no

**Remarks**

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<table>
<thead>
<tr>
<th>Specify</th>
<th>Date</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter insertion (medical)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter insertion (surgical)</td>
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<tr>
<td>Catheter reposition</td>
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<tr>
<td>Catheter removal</td>
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<tr>
<td>Laparotomy</td>
<td></td>
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<tr>
<td>Omentectomy</td>
<td></td>
<td></td>
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<tr>
<td>Parathyroidectomy</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Inguinal hernia repair</td>
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<td></td>
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<tr>
<td>Umbilical hernia repair</td>
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<tr>
<td>Abdominal wall hernia repair</td>
<td></td>
<td></td>
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<tr>
<td>Peritonolysis</td>
<td></td>
<td></td>
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<tr>
<td>Adhesiolysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bowel resection</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Other, specify</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Current clinical symptoms of EPS

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date EPS diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms prior to diagnosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Start date clinical symptoms</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Start date clinical symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
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<tr>
<td>Appetite loss</td>
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<tr>
<td>Weight loss</td>
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</tr>
<tr>
<td>Malnutrition</td>
<td></td>
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<td>---------</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Recurrent abdominal cramps</td>
<td></td>
<td></td>
<td>---------</td>
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<tr>
<td>Abdominal pain</td>
<td></td>
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<tr>
<td>Vomitus</td>
<td></td>
<td></td>
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<tr>
<td>Constipation</td>
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<td>---------</td>
</tr>
<tr>
<td>Ileus/obstruction</td>
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<td></td>
<td>---------</td>
</tr>
<tr>
<td>Ascites</td>
<td></td>
<td></td>
<td>---------</td>
</tr>
<tr>
<td>Remarks</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
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Challenges EPS registry

- Uniform EPS diagnosis
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www.epsregistry.eu
Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication of peritoneal dialysis (PD). This diagnosis needs to be considered in patients with a history of PD who are currently having or have experienced symptoms of recurrent partial or complete intestinal obstructions. The clinical assessment is difficult due to the insidious development of EPS. At this moment there is no clear test or radiologic investigation to detect EPS at an early stage. Risk factors for the development of the disease are incompletely understood.

The EPS registry is a collaboration of the Dutch Kidney centres and the Hans Mak Institute. Main aim of the nationwide registry is to improve the knowledge of the pathophysiology of EPS. Subsequently, uniform diagnostic criteria and management strategies will be developed. This registry has the potential to be extended to other European countries. There is already a close collaboration with the UK EPS registry.

The EPS registry is designed to register and follow patients with a possible and definite diagnosis of EPS. An inventory email questionnaire will be sent to all nephrologists in the Netherlands. We kindly ask all nephrologists to participate in this registry. When the diagnosis of EPS is considered, a research nurse will be deployed to the centre to gather all information on the patients. We encourage the treating physicians to report a patient even if there is only a slight suspicion of EPS. The information gathered will be reviewed by the steering committee of the registry. A yearly update, summarizing the data collected in the EPS registry, will be released on the website.
EPS case

If you considered the diagnosis of EPS in one or more patients with a history of PD, please complete this form. After submitting this form a research nurse from the Hans Mak Institute will contact you.

* The asterisk fields are obliged to fill in.

Your name:*  
Hospital:*  
E-mail address:*  
Telephone number:*  
Question/remark:  

Type the following code: *  

Submit
Started June 2009 First questionnaire

<table>
<thead>
<tr>
<th></th>
<th>Physicians</th>
<th>Dialysis Centres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of emails</td>
<td>259</td>
<td>60</td>
</tr>
<tr>
<td>Respons</td>
<td>113 (44%)</td>
<td>55 (92%)</td>
</tr>
<tr>
<td>EPS suspicion</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>EPS no</td>
<td>64</td>
<td>48</td>
</tr>
<tr>
<td>EPS colleague</td>
<td>23</td>
<td>12</td>
</tr>
</tbody>
</table>
Encapsulating Peritoneal Sclerosis patient

- Start PD at young age
- Long PD treatment (> 4 yrs)
- Insidious symptoms of intestinal tract:
  - Nausea, vomitus, weight and appetite loss
  - Inflammation
  - Abdominal pain and mass
  - Obstipation, ileus
- PD: fast transporter status, loss of ultrafiltration, bloody ascites
- Often after kidney transplantation
- 50% chance to die within 1 year.