Non-infectious complications of PD in children

Enrico Vidal
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University-Hospital of Udine, Italy
## Frequency of Peritonitis Episodes by Era

<table>
<thead>
<tr>
<th>Year of Dialysis Initiation</th>
<th>Nº of Episodes</th>
<th>Years of FU</th>
<th>Annualized Rates</th>
<th>Expected months between infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4487</td>
<td>7596</td>
<td>0.59</td>
<td>20.3 (19.7-20.9)</td>
</tr>
<tr>
<td>Year of Dialysis Initiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1992-1997</td>
<td>2555</td>
<td>3282</td>
<td>0.78</td>
<td>15.4 (14.8-16.0)</td>
</tr>
<tr>
<td>1998-2003</td>
<td>1215</td>
<td>2200</td>
<td>0.55</td>
<td>21.7 (20.6-23.0)</td>
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<tr>
<td>2004-2009</td>
<td>534</td>
<td>1471</td>
<td>0.36</td>
<td>33.1 (30.5-36.1)</td>
</tr>
<tr>
<td>2010-2016</td>
<td>183</td>
<td>644</td>
<td>0.28</td>
<td>42.2 (36.9-49.4)</td>
</tr>
</tbody>
</table>
Non-Infectious Complications of PD (NICPD)

Relative increase in the prevalence of “early” NICPD

PD start → PD end or switch

Success in decreasing the rate of PD-related infections (“Improvement science techniques”)
Non-Infectious Complications of PD (NICPD)

- Relative increase in the prevalence of "early" NICPD
- Success in decreasing the rate of PD-related infections ("Improvement science techniques")
- Increase in the prevalence of "late" NICPD
- Extended PD duration (long-term PD)
- PD end or switch
NICPD

1. **Mechanical:**
   - Catheter-related
   - Related to the increase in intraabdominal pressure due to dialysate:
     - Hernia
     - Pleural leak
     - Back pain
     - Gastroesophageal reflux and delayed gastric emptying

2. **Technique-related:**
   - Membrane/UFF failure:
     - Encapsulated Peritoneal Sclerosis
   - Metabolic effects of the absorption of glucose and its degradation products:
     - Hyperglicemia / hyperinsulinemia
     - Hypertriglyceridemia
   - “Other complications”:
     - Pancreatitis
     - Hemoperitoneum
     - Ischemic colitis and necrotizing enterocolitis
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     - Hemoperitoneum
     - Ischemic colitis and necrotizing enterocolitis
Access for paediatric dialysis

Rukshana Shroff
Great Ormond Street Hospital
London, UK
Nicpd

1. Mechanical:
   - Catheter-related
   - Related to the increase in intraabdominal pressure due to dialysate:
     - Hernia
     - Pleural leak
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     - Hemoperitoneum
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Hydrothorax

- Pleuro-peritoneal and pericardio-peritoneal fistula.
- The pleural to peritoneal connection is almost always on the **right side**:  
  - More common tendinous defects on the right  
  - Ascending peristalsis of the right colon sweeping pelvic fluids into the right upper quadrant  
  - Piston-like action of the liver during diaphragm contraction, driving fluid through the diaphragm pores
Pathophysiology

• Pleuro-peritoneal pressure gradient: negative intrathoracic pressure combined with an increased intra-abdominal pressure caused by PD fluid may open small defects in the diaphragm (i.e. ARPKD)
• Congenital diaphragmatic defects (i.e. WT1)
Pleuro-peritoneal fistula

X-ray courtesy of Andrea Pasini, MD
Pleuro-peritoneal fistula

Diagnosis

Demonstration of PD fluid in the pleural space:

- Thoracentesis ("sweet hydrothorax")
- Thoracentesis with peritoneal methylene blue instillation
- Peritoneal contrast radiography*
- Peritoneal contrast scintigraphy*
- Peritoneal contrast MRI*
Clinical features

- Shortness of breath
  - Mistaken for CHF or fluid overload
    - More hypertonic dialysis to increase UF
      - Further increase in intra-abdominal pressure
Pleuro-peritoneal or pericardio-peritoneal leak in children on chronic peritoneal dialysis—A survey from the European Paediatric Dialysis Working Group

Stephanie Dufek\textsuperscript{1} • Tuula Holta\textsuperscript{2} • Michel Fischbach\textsuperscript{3} • Gema Ariceta\textsuperscript{4} • Augustina Jankauskiene\textsuperscript{5} • Rimante Cerkauskiene\textsuperscript{5} • Claus Peter Schmitt\textsuperscript{6} • Betti Schaefer\textsuperscript{6} • Christoph Aufricht\textsuperscript{7} • Elizabeth Wright\textsuperscript{1} • Constantinos J. Stefanidis\textsuperscript{8} • Mesih Ekim\textsuperscript{9} • Sevcan Bakkaloglu\textsuperscript{10} • Günter Klaus\textsuperscript{11} • Aleksandra Zurowska\textsuperscript{12} • Karel Vondrak\textsuperscript{13} • Johan Vande Walle\textsuperscript{14} • Alberto Edefonti\textsuperscript{15} • Rukshana Shroff\textsuperscript{1} • on behalf of the European Paediatric Dialysis Working Group

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Abstract

Background Pleural or pericardial effusions secondary to pleuro-peritoneal fistula (PPF) and pericardio-peritoneal fistula (PcPF) are rare but serious complications of peritoneal dialysis (PD).

Methods We conducted a 10-year survey across all participating centres in the European Paediatric Dialysis Working Group to review the incidence, diagnostic techniques, therapeutic options and outcome of children on chronic PD with PPF and/or PcPF.

Results Of 1506 children on PD there were ten cases (8 of PPF, 1 each of PcPF and PPF+PcPF), with a prevalence of 0.66%. The median age at presentation was 1.5 [inter-quartile range (IQR) 0.4–2.4] years, and nine children were <3 years. The time on PD before onset of symptoms was 4.3 (IQR 1.3–19.8) months. Eight children had herniae and seven had abdominal surgery in the preceding 4 weeks. Symptoms at presentation were respiratory distress, reduced ultrafiltration and tachycardia. PD was stopped in all children; three were managed conservatively and thoracocentesis was performed in
Prevalence

- 15/15 centre responded

- **1506 children received chronic PD**
  (2580 patient-years on chronic PD)

- **10 children** developed PPF and/or PcPF
  - 8 PPF
  - 1 PcPF
  - 1 PPF and PcPF

- **Prevalence 0.66%**
  - PPF: 0.6%
  - PcPF: 0.13%

- 3.9 cases per 1000 patient-years on PD

Courtesy of Stephanie Dufek, MD
## Patients demographics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Underlying diagnosis</th>
<th>Age at start of PD (months)</th>
<th>Age at presentation (months)</th>
<th>Time on PD at presentation (months)</th>
<th>Type of peritoneal leak</th>
<th>Side of PPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>CAKUT</td>
<td>123.6</td>
<td>129.3</td>
<td>5.7</td>
<td>PPF</td>
<td>Bilateral</td>
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<tr>
<td>2</td>
<td>M</td>
<td>Congenital nephrotic syndrome</td>
<td>28</td>
<td>28.2</td>
<td>0.2</td>
<td>PPF</td>
<td>R</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>CAKUT</td>
<td>0.4</td>
<td>5.3</td>
<td>4.9</td>
<td>PPF</td>
<td>R</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>Haemolytic uraemic syndrome</td>
<td>0.6</td>
<td>4.2</td>
<td>3.6</td>
<td>PPF</td>
<td>L</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>Congenital nephrotic syndrome</td>
<td>8.4</td>
<td>11.5</td>
<td>3.1</td>
<td>PPF</td>
<td>R</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>CAKUT, trisomy 21</td>
<td>0.2</td>
<td>33.8</td>
<td>33.6</td>
<td>PPF</td>
<td>R</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>ARPKD</td>
<td>3.3</td>
<td>4.2</td>
<td>0.9</td>
<td>PPF+PcPF</td>
<td>Bilateral</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>Congenital nephrotic syndrome</td>
<td>10.1</td>
<td>11.5</td>
<td>1.4</td>
<td>PPF</td>
<td>R</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>Prematurity, sepsis</td>
<td>7</td>
<td>24.3</td>
<td>17.3</td>
<td>PcPF</td>
<td>PcPF</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>Neonatal asphyxia</td>
<td>0.2</td>
<td>27.7</td>
<td>27.5</td>
<td>PPF</td>
<td>R</td>
</tr>
</tbody>
</table>

- 90% male
- Age at start of PD: Median 5.2 (0.3–14.6) months
- Age at presentation: Median 1.5 (0.4 – 2.4) years
  - 9/10 (90%) were < 3 years and 5 (50%) < 1 year at presentation
- Time on PD at presentation: Median 4.3 (1.3 – 19.8) months
  - 7/10 (70%) on PD for ≤ 12 months
- Predominantly right sided: 80%

Courtesy of Stephanie Dufek, MD
**PD specifications**

<table>
<thead>
<tr>
<th>Patient</th>
<th>PD type</th>
<th>Type – dry day</th>
<th>Fill volume (ml/m² BSA)</th>
<th>Type of dialysate</th>
<th>Glucose concentration (%)</th>
<th>Total therapy time (hours)</th>
<th>Peritonitis episodes</th>
<th>Hernia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tidal</td>
<td>No</td>
<td>1207</td>
<td>Balance</td>
<td>1.5</td>
<td>10</td>
<td>0</td>
<td>No</td>
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<tr>
<td>2</td>
<td>CCPD</td>
<td>No</td>
<td>368</td>
<td>Physioneal 35</td>
<td>2.3</td>
<td>22</td>
<td>0</td>
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</tr>
<tr>
<td>3</td>
<td>CAPD</td>
<td>No</td>
<td>308</td>
<td>Physioneal 40</td>
<td>3.1 (mix)</td>
<td>24</td>
<td>3</td>
<td>Yes</td>
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<tr>
<td>4</td>
<td>CCPD</td>
<td>Yes</td>
<td>484</td>
<td>BicaVera</td>
<td>1.5</td>
<td>11.5</td>
<td>0</td>
<td>Yes-multiple</td>
</tr>
<tr>
<td>5</td>
<td>CCPD</td>
<td>No</td>
<td>714</td>
<td>BicaVera</td>
<td>1.5</td>
<td>24</td>
<td>0</td>
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</tr>
<tr>
<td>6</td>
<td>CAPD</td>
<td>No</td>
<td>364</td>
<td>Balance</td>
<td>1.5</td>
<td>12</td>
<td>7</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>CAPD</td>
<td>No</td>
<td>714</td>
<td>BicaVera</td>
<td>2.3</td>
<td>24</td>
<td>0</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>CCPD</td>
<td>No</td>
<td>810</td>
<td>Physioneal 40</td>
<td>1.5</td>
<td>13</td>
<td>0</td>
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<td>6</td>
<td>3</td>
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<tr>
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<td>CCPD</td>
<td>Yes</td>
<td>349</td>
<td>BicaVera</td>
<td>1.5</td>
<td>10</td>
<td>0</td>
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</tr>
</tbody>
</table>

- 6 children (60%) were on CCPD and 7 (70%) had a day-time dwell
- Fill volume: median 535 (360 – 738) ml/m² BSA
- **Hernia: 8/10 (80%)**
  - Inguinal n = 5
  - Umbilical n = 2
  - Ventral abdominal hernia n = 2
- **Previous “abdominal surgery”: 7/10 (70%)**
  - median of 27 (18 – 41) days before onset

Courtesy of Stephanie Dufek, MD
Management

PPF or PcPF confirmed

Conservative management
- Reduced PD
- Transient discontinuation of PD – Success Rate 53%

Pleurodesis
- Chest drain – Success Rate 48%
- VATS – Success Rate 88%

Thoracotomy
- Direct repair – Success Rate 100%

Management

- PD interruption: 10/10
- Conservative management: 3/10
- Thoracentesis: 7/10
  - Pleurodesis: 3/10
    - Chest drain: 1/10
    - Video assisted thoracoscopic surgery (VATS): 2/10
    - Agents used: betadine, talc powder and fibrin glue
Management and Outcome

N = 10

Discontinuation of PD (n=6)
  HD n = 5
  Palliative n = 1

Transient continuation of PD (n=1)
  For 4 weeks
  Discontinuation of PD

Transient discontinuation of PD (n=3)
  HD +/- intervention
  PD reattempted
  PD successfully continued until renal Tx in 2/3

Courtesy of Stephanie Dufek, MD
Conclusion

• PPF and PcPF are rare in children on chronic PD

• Risk factors for PPF and PcPF development include age <3 years, preceding hernia and recent abdominal surgery

• All children required a change of dialysis modality to achieve complete resolution of the peritoneal leak
Deleterious Factors

- Glucose (1500-4200mg/dl)
- ↓ pH (5.5)
- Lactate (35 to 40 mmol/l)
- GDP
- Peritonitis
- Uremia

Mediators

- TNF-α
- IL-1β
- IL-6...
- TGF-β
- VEGF
- eNOS
- AGEs
- AGES
- ROS
- ATIII...

Morphological Alterations

- Epithelial to mesenchymal transition, mesothelial denudation
- Basement membrane duplication, protein glycation (AQP-1)
- Neoangiogenesis
- Vasculopathy
- Fibrosis / Sclerosis
- Calcification

Clinical Consequences

- Clearance Changes
- Ultrafiltration failure
Optimizing PD in Children

Claus Schmitt

Centre for Pediatric and Adolescent Medicine
Heidelberg, Germany
Encapsulating Peritoneal Sclerosis

- Prolonged exposure to PD solutions
- Mesothelial dysfunction
- Advanced chronic kidney disease
- Simple peritoneal sclerosis
- 2nd hit
  - Severe peritonitis
  - Discontinuation of PD
  - Genetic predisposition
- Encapsulating peritoneal sclerosis
- Increased fibrin
- Peritoneal adhesions

Encapsulating Peritoneal Sclerosis

- Clinical syndrome, characterized by symptoms/signs of obstructive ileus, with or without a systemic inflammatory reaction

- Presence of peritoneal thickening and encapsulation, intestinal obstruction, cocooning and peritoneal calcification, confirmed by radiological investigations or at laparotomy ± typical biopsy

ISPD Ad Hoc Committee on UF management in PD, PDI 2000;20(4):S43-S55
Encapsulating Peritoneal Sclerosis

PAS, 20x

Pediatric Nephrology, Dialysis and Transplant Unit, University-Hospital of Padova, Italy
Encapsulating Peritoneal Sclerosis

![Graph showing submesothelial thickness vs age](image1.png)

![Microscopic image of tissue sample](image2.png)

TRI, 10x

Schaefer B et al. Sci Rep 2016;6, 21344
Encapsulating Peritoneal Sclerosis

PAS, 20x

TRI, 20x

Pediatric Nephrology, Dialysis and Transplant Unit, University-Hospital of Padova, Italy
Encapsulating Peritoneal Sclerosis

PAS, 200x

PAS, 100x
Encapsulating peritoneal sclerosis in paediatric peritoneal dialysis patients: the experience of the Italian Registry of Pediatric Chronic Dialysis

ABSTRACT

Background. Paediatric literature about encapsulating peritoneal sclerosis (EPS) is limited and comes primarily from anecdotal experiences. In this study, we described the incidence and characteristics of EPS in a large paediatric chronic peritoneal dialysis (CPD) patient population.

Methods. We reviewed files of patients starting CPD at <16 years of age, recorded from January 1986 to December 2011 by the Italian Registry of Pediatric Chronic Dialysis (n = 712). Moreover, in December 2011, a survey was performed involving all the Italian Pediatric Nephrology Units to report such EPS cases that occurred after CPD withdrawal.

Results. Fourteen EPS cases were reported, resulting in a prevalence of 1.9%. The median age of EPS cases was 4.8 years (range 0.6–14.4) at the start of CPD and 14.3 years (6.5–26.8) at EPS diagnosis. Eleven EPS cases received CPD for longer than 5 years. At diagnosis, nine patients were still on CPD, two were on haemodialysis and three were transplanted. In eight patients, the primary renal disease was represented by glomerulopathy, mainly focal segmental glomerulosclerosis (n = 5). In the last 6 months prior to CPD discontinuation, 10 patients were treated with solutions containing more than
Table 3: Clinical features of the 14 patients with EPS

<table>
<thead>
<tr>
<th>Pt</th>
<th>Primary disease</th>
<th>CPD duration (months)</th>
<th>No. of peritonitis</th>
<th>Transport status</th>
<th>Age (years) at EPS diagnosis</th>
<th>Status at EPS diagnosis</th>
<th>Diagnostic imaging</th>
<th>Biopsy-proven EPS</th>
<th>Treatment</th>
<th>Status at last available follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FSGS</td>
<td>116.7</td>
<td>3</td>
<td></td>
<td>12.6</td>
<td>Transplanted</td>
<td>+</td>
<td>+</td>
<td>Steroids/ CsA surgery</td>
<td>Deceased</td>
</tr>
<tr>
<td>2</td>
<td>FSGS</td>
<td>60.5</td>
<td>2</td>
<td>High</td>
<td>8.6</td>
<td>PD</td>
<td>+</td>
<td></td>
<td>Steroids</td>
<td>Transplanted</td>
</tr>
<tr>
<td>3</td>
<td>CNS</td>
<td>57.8</td>
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<td>High</td>
<td>12</td>
<td>PD</td>
<td>+</td>
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<td>HD</td>
</tr>
<tr>
<td>4</td>
<td>CAKUT</td>
<td>102.3</td>
<td>3</td>
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<td>8.5</td>
<td>HD</td>
<td>+</td>
<td></td>
<td>Steroids</td>
<td>Deceased</td>
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<tr>
<td>5</td>
<td>FSGS</td>
<td>62.1</td>
<td>9</td>
<td></td>
<td>18.4</td>
<td>HD</td>
<td></td>
<td></td>
<td>Steroids</td>
<td>HD</td>
</tr>
<tr>
<td>6</td>
<td>CAKUT</td>
<td>71.4</td>
<td>0</td>
<td>High</td>
<td>6.5</td>
<td>PD</td>
<td>+</td>
<td></td>
<td>Steroids/ AZA surgery</td>
<td>HD</td>
</tr>
<tr>
<td>7</td>
<td>Lymphoma</td>
<td>51.7</td>
<td>7</td>
<td></td>
<td>19.5</td>
<td>PD</td>
<td>+</td>
<td>+</td>
<td>Surgery</td>
<td>Deceased</td>
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<tr>
<td>8</td>
<td>Cystinosis</td>
<td>84.8</td>
<td>2</td>
<td>High</td>
<td>26.8</td>
<td>PD</td>
<td>+</td>
<td></td>
<td>Steroids/ tamoxifen</td>
<td>Deceased</td>
</tr>
<tr>
<td>9</td>
<td>FSGS</td>
<td>117.4</td>
<td>5</td>
<td></td>
<td>19.5</td>
<td>PD</td>
<td></td>
<td></td>
<td>Surgery</td>
<td>HD</td>
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<td>3</td>
<td></td>
<td>20.4</td>
<td>PD</td>
<td>+</td>
<td>+</td>
<td></td>
<td>HD</td>
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<td>11</td>
<td>IgAN</td>
<td>86.1</td>
<td>2</td>
<td></td>
<td>18.5</td>
<td>PD</td>
<td>+</td>
<td>+</td>
<td>Steroids</td>
<td>HD</td>
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<tr>
<td>12</td>
<td>CNS</td>
<td>138.8</td>
<td>7</td>
<td></td>
<td>16.1</td>
<td>PD</td>
<td>+</td>
<td>+</td>
<td>Steroids</td>
<td>Deceased</td>
</tr>
<tr>
<td>13</td>
<td>CAKUT</td>
<td>106.2</td>
<td>3</td>
<td></td>
<td>7.3</td>
<td>Transplanted</td>
<td>+</td>
<td>+</td>
<td>Steroids/ TAC/MPA surgery</td>
<td>Deceased</td>
</tr>
<tr>
<td>14</td>
<td>CAKUT</td>
<td>75.1</td>
<td>2</td>
<td></td>
<td>11.1</td>
<td>Transplanted</td>
<td>+</td>
<td>+</td>
<td>Steroids/ Sirolimus surgery</td>
<td>Still functioning graft</td>
</tr>
</tbody>
</table>

8/14 chronic glomerulopathies

Median CPD duration 85 months

1:26.8 CPD-months vs. 1:21.9 CPD-months total registry population

Mortality rate = 43%
EPS: the experience of the Italian Registry of Pediatric Chronic Dialysis

Hyperosmolar solutions

<table>
<thead>
<tr>
<th>Glucose Solution</th>
<th>Count</th>
</tr>
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<tr>
<td>4.25% glucose (BicaVera)</td>
<td>1</td>
</tr>
<tr>
<td>3.86% glucose</td>
<td>3</td>
</tr>
<tr>
<td>2.27% glucose</td>
<td>6</td>
</tr>
<tr>
<td>1.36% glucose</td>
<td>2</td>
</tr>
</tbody>
</table>
FSGS

TGF-β/Smad signaling pathway

TSP-1 → TGFβ-1

TGFβII-R → Smad2/Smad3

KI 2003;64:1715-1721
EPS: the experience of the Italian Registry of Pediatric Chronic Dialysis

Table 1: Main symptoms and radiological abnormalities found in the 14 cases of EPS

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>n</th>
<th>Imaging findings (US or CT scan)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>14</td>
<td>Peritoneal membrane thickening</td>
<td>6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>12</td>
<td>Bowel adhesion or aggregation</td>
<td>6</td>
</tr>
<tr>
<td>Weight loss</td>
<td>9</td>
<td>Peritoneal calcification</td>
<td>5</td>
</tr>
<tr>
<td>Ascites</td>
<td>5</td>
<td>Loculated ascites</td>
<td>3</td>
</tr>
<tr>
<td>Fever</td>
<td>3</td>
<td>Gas-fluid levels</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>3</td>
<td>Stenotic small bowel loops</td>
<td>3</td>
</tr>
<tr>
<td>ESA resistance</td>
<td>3</td>
<td>Dilated small bowel loops</td>
<td>2</td>
</tr>
</tbody>
</table>

US, ultrasound; CT, computerized tomography; ESA, erythropoiesis-stimulating agents.

Multiple calcifications

Thickened peritoneum

Bowel loops are drawn into the centre of the abdominal cavity ("cocoon")
Post-transplantation EPS cases

- Diagnosis of EPS was made at 3, 17 and 88 months from PD discontinuation.
- All patients had an **acute onset**
  (intestinal occlusion 1 case; intestinal perforation 2 cases)
- All patients were on **CNI-based IS regimens**:
  - 1 case: prednisone + CycA
  - 1 case: prednisone + CycA + MMF
  - 1 case: prednisone + Tac + MMF
- **Mortality**: 2/3 (sepsis)
- 1 patient with still functioning renal graft
  (eGFR is 80 ml/min/1.73 m² at 4.5 yrs after kidney transplantation and at 3 yrs after EPS diagnosis)
Conclusions

• The incidence of EPS is associated with the duration of CPD.

• In children on long-term PD, dialysis termination should be considered according to individual risk factors, early signs and symptoms of EPS:
  – Children on CPD for longer than 5 years + UFF (<300 ml/mq/day): STOP (Araki et al. PDI 2000:20)
  – Further studies are required to analyse the clinical correlation between FSGS and EPS occurrence

• Children on long-term PD who get transplanted: CNI minimization immunosuppressive regimens.
Acute Pancreatitis in PD Patients

- Specific population risk factors
- Risk factors related to renal insufficiency
- Risk factors related to type of dialysis
Pathophysiology of Acute Pancreatitis in PD patients

- Anatomical reason.
- Repeated bouts of peritonitis, with subsequent administration of “irritants” (i.e. antibiotics and heparine).
- Supraphysiologic concentration of glucose in the dialysate solutions, leading to hyperglycemia and hypertriglyceridemia.
Acute Pancreatitis in Children on Chronic Dialysis

• DM Ford, *Pediatr Nephrol* 1990:
  «Pancreatitis in children on chronic dialysis treated with valproic acid»

• S Fujinaga, *Clinical Nephrology* 2011:
  «Acute pancreatitis in a 2-year-old girl on peritoneal dialysis and using icodextrin solution»
Acute pancreatitis in children on chronic maintenance dialysis

Enrico Vidal¹ • Irene Alberici¹ • Enrico Verrina² • on behalf of the Italian Registry of Pediatric Chronic Dialysis

• Retrospective study: first chronic dialysis cycle: 1\textsuperscript{st} January 2000 – 31\textsuperscript{th} December 2014.

• To assess if the incidence of acute pancreatitis (AP) is increased in children with end-stage renal disease on dialysis.

• To evaluate the clinical course and outcome of AP in this pediatric cohort.
### Results

<table>
<thead>
<tr>
<th></th>
<th>Entire cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident patients</td>
<td>650</td>
</tr>
<tr>
<td>Median age at dialysis start (yrs)</td>
<td>8.5 (IQR 2.6-13.7)</td>
</tr>
<tr>
<td>Median dialysis duration (months)</td>
<td>18.8 (IQR 8.7-32.2)</td>
</tr>
<tr>
<td>N° of patients with AP</td>
<td>12</td>
</tr>
<tr>
<td>AP incidence proportion</td>
<td>1.8%</td>
</tr>
<tr>
<td>AP incidence rate (AP/1000 person-years)</td>
<td>9.5</td>
</tr>
<tr>
<td>Risk Ratio (general pediatric population*)</td>
<td>60.4 (95% CI 3.2-214)</td>
</tr>
</tbody>
</table>

*Italian Registry of Pediatric Dialysis. Pediatr Nephrol 2019;34:1501-1512*
# Results

<table>
<thead>
<tr>
<th></th>
<th>HD</th>
<th>PD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident patients</td>
<td>237</td>
<td>413</td>
<td></td>
</tr>
<tr>
<td>Median age at dialysis start (yrs)</td>
<td>13 (IQR 9.4-15.6)</td>
<td>5.1 (IQR 1.1-11.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median dialysis duration (months)</td>
<td>16.7 (IQR 7-30)</td>
<td>20.2 (IQR 10.6-34)</td>
<td>0.19</td>
</tr>
<tr>
<td>N° of AP events</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>AP incidence proportion</td>
<td>2.9%</td>
<td>1.2%</td>
<td>0.04</td>
</tr>
<tr>
<td>AP incidence rate (AP/1000 person-years)</td>
<td>15.4</td>
<td>6.2</td>
<td>0.13</td>
</tr>
<tr>
<td>Risk Ratio (general pediatric population*)</td>
<td>102.6 (95% CI 15-356)</td>
<td>41.3 (95% CI 1.35-60.5)</td>
<td></td>
</tr>
</tbody>
</table>

Italian Registry of Pediatric Dialysis. Pediatr Nephrol 2019;34:1501-1512
<table>
<thead>
<tr>
<th></th>
<th>AP cases</th>
<th>Non-AP cases</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N )</td>
<td>12</td>
<td>638</td>
<td></td>
</tr>
<tr>
<td>PD/HD</td>
<td>5/7 (42%)</td>
<td>408/230 (63.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Age at dialysis start (years)</td>
<td>7.9 (IQR 3.5–10.5)</td>
<td>8.5 (2.6–13.7)</td>
<td>0.36</td>
</tr>
<tr>
<td>Gender (male, %)</td>
<td>75%</td>
<td>55%</td>
<td>0.018</td>
</tr>
<tr>
<td>Primary renal disease</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAKUT</td>
<td>8 (66.7%)</td>
<td>260 (41.3%)</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>0 (0%)</td>
<td>176 (27%)</td>
<td></td>
</tr>
<tr>
<td>Hereditary</td>
<td>2 (16.7%)</td>
<td>45 (7.2%)</td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>1 (8.3%)</td>
<td>11 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Metabolic</td>
<td>1 (8.3%)</td>
<td>21 (3.4%)</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>0 (0%)</td>
<td>125 (19.3%)</td>
<td></td>
</tr>
<tr>
<td>Comorbidities (at least 1)</td>
<td>6(^{a}) (50%)</td>
<td>134 (20.6%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Age at AP (years)</td>
<td>10.1 (IQR 4.3–15.3)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Length of dialysis at AP (months)</td>
<td>15.3 (IQR 6.1–43.5)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>20 (IQR 12.5–25.5)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Dialysis duration (months)</td>
<td>15.3 (IQR 6.1–43.3)</td>
<td>18.8 (IQR 8.7–32.2)</td>
<td>0.32</td>
</tr>
<tr>
<td>Mortality rate(^{b})</td>
<td>25%</td>
<td>4.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CAKUT: congenital anomalies of the kidney and urinary tract, HD: hemodialysis, PD: peritoneal dialysis, AP: acute pancreatitis

\(^{a}\) Cognitive impairment 6/6, motor impairment 3/6, cardiac abnormality 2/6, ocular abnormality 2/6

\(^{b}\) Deaths were non-AP related; mortality rate was registered at last follow-up (December 2015)
### Presence of/exposure to known risk factors

<table>
<thead>
<tr>
<th>Pt n°</th>
<th>Potential Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HD</td>
<td>None</td>
</tr>
<tr>
<td>2 PD</td>
<td>Rotavirus gastroenteritis</td>
</tr>
<tr>
<td>3 HD</td>
<td>Gallbladder stones and abdominal surgery with exposure to Propofol before AP onset</td>
</tr>
<tr>
<td>4 HD</td>
<td>None</td>
</tr>
<tr>
<td>5 PD</td>
<td>Valproic Acid</td>
</tr>
<tr>
<td>6 HD</td>
<td>Enalapril, Valproic Acid</td>
</tr>
<tr>
<td>7 HD</td>
<td>Enalapril</td>
</tr>
<tr>
<td>8 HD</td>
<td>Valproic Acid</td>
</tr>
<tr>
<td>9 PD</td>
<td>None</td>
</tr>
<tr>
<td>10 HD</td>
<td>None</td>
</tr>
<tr>
<td>11 PD</td>
<td>None</td>
</tr>
<tr>
<td>12 HD</td>
<td>None</td>
</tr>
</tbody>
</table>

Italian Registry of Pediatric Dialysis. Pediatr Nephrol 2019;34:1501-1512
# Labs and Imaging

<table>
<thead>
<tr>
<th>Pt n°</th>
<th>Amylase at admission (U/l)</th>
<th>Peak amylase (U/l)</th>
<th>Lipase at admission (U/l)</th>
<th>Peak lipase (U/l)</th>
<th>US</th>
<th>CT scan</th>
<th>Necrotising AP</th>
<th>Pancreatic pseudocyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HD</td>
<td>234</td>
<td>1343</td>
<td>1064</td>
<td>1064</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>2 PD</td>
<td>650</td>
<td>650</td>
<td>6522</td>
<td>6521</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3 HD</td>
<td>3431</td>
<td>3700</td>
<td>8140</td>
<td>8600</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4 HD</td>
<td>1125</td>
<td>1125</td>
<td>3614</td>
<td>3614</td>
<td>+</td>
<td>N.P.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5 PD</td>
<td>2826</td>
<td>3005</td>
<td>4615</td>
<td>5738</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>6 HD</td>
<td>764</td>
<td>764</td>
<td>1757</td>
<td>1757</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7 HD</td>
<td>1800</td>
<td>3080</td>
<td></td>
<td></td>
<td>N.P.</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8 HD</td>
<td>1890</td>
<td>1896</td>
<td>2156</td>
<td>2243</td>
<td>+</td>
<td>N.P.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1125 (650-1890)</td>
<td>1343 (764-3005)</td>
<td>2885 (1583-5091)</td>
<td>2928 (1583-5933)</td>
<td>+</td>
<td>N.P.</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Ultrasonography

- Enlarged pancreas: 80%
- Peripancreatic fluid collections: 33%
Axial contrast material-enhanced computed tomography (CT) image obtained 4 days after the onset of acute abdominal pain showed a heterogeneous appearance of pancreas and peripancreatic fluid.
CT scan and (cholangio)MRI

Axial contrast-enhanced CT image obtained 8 days later reveals two well defined hypoattenuating regions in the body of the pancreas (arrows), suggesting pancreatic necrosis.
CT scan and (cholangio)MRI

T2-weighted cholangio-magnetic resonance (MR) acquired 30 days later reveals evolution into two pancreatic pseudocysts (arrows). Pancreatic duct resulted normal without dilations or strictures.
Results: Treatment

- Analgesics
- Antibiotics
- Intravenous Fluid
- Parenteral Nutrition
- Octreotide
- Glabexate mesilate

Italian Registry of Pediatric Dialysis. Pediatr Nephrol 2019;34:1501-1512
Results: Outcome

- Pancreatic pseudocysts: 2 pts
- AP-related deaths: 0
- Temporary shift from PD to HD: 1 pt
- AP relapse: 1 pt had 2 AP

Italian Registry of Pediatric Dialysis. Pediatr Nephrol 2019;34:1501-1512
Children on dialysis have a significantly increased risk for AP compared with the general pediatric population.

Most children on dialysis are exposed to potential risk factors (medications) for AP.

A higher incidence is observed in children with neurological co-morbidities.

Risk factors related to ESRD >> risk factors related to type of dialysis.

Outcome is good.
Take home messages

• PD represents the preferred dialysis modality for children with ESRD (!)

• A relative increase in the prevalence of NICPD has been observed in recent years, as consequence of the reduction in infectious complications.

• Prevention of early NICPD is mainly based on a conservative approach.

• Prevention of late NICPD might require an integrative approach.
A propensity-matched comparison of hard outcomes in children on chronic dialysis

Adjusted cumulative hazard ratios (HD:PD) for death
Next Webinar

November, 12

“Clinical Implications of Genetics in Nephrotic Syndrome in Children”

by Olivia Boyer, Paris (France)