Naarden, The Netherlands
February 4\textsuperscript{th} 2010

EPS meeting

Post-transplant EPS

Guido Garosi
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Azienda Ospedaliera Universitaria Senese
Siena, Italy
is post-transplant EPS a remarkable problem?
Encapsulating Peritoneal Sclerosis in the New Millennium: A National Cohort Study

Michaela C. Brown,* Keith Simpson,* Jan J. Kerssens,† and Robert A. Mactier,* on behalf of the Scottish Renal Registry

*Scottish Renal Registry, Royal Infirmary, Glasgow, United Kingdom; †Information Services Division (ISD), Edinburgh, United Kingdom


Table 2. Comparison of previous and current epidemiological studies of EPS

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of EPS Cases</td>
<td>62</td>
<td>54 (46)</td>
<td>31</td>
<td>17</td>
<td>48</td>
<td>27 (23)</td>
<td>46</td>
</tr>
<tr>
<td>Study Design</td>
<td></td>
<td></td>
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<tr>
<td>Denominator Population</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Overall Rate</td>
<td>0.9%</td>
<td>0.7%</td>
<td>0.8%</td>
<td>0.8%</td>
<td>2.5%</td>
<td>3.3%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Mean PD Exposure (yrs)</td>
<td>5.1</td>
<td>4.3</td>
<td>5.8</td>
<td>10</td>
<td>4.3</td>
<td>6.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Mortality (over study period)</td>
<td>43.5%</td>
<td>56%</td>
<td>25.8%</td>
<td>35%</td>
<td>37.5%</td>
<td>29.6%</td>
<td>56.5%</td>
</tr>
</tbody>
</table>

EPS, encapsulating peritoneal sclerosis; PD, peritoneal dialysis.

aThose meeting ISPD 2000 criteria in brackets.

bPrevalent + incident PD patients.
46 EPS cases
At diagnosis:
12 on PD
13 after switch to HD
22 after transplantation

The overall incidence of EPS is stable
The incidence during PD seems to decrease
The incidence after PD seems to increase

50% of EPS cases after transplantation
Increasing incidence of severe encapsulating peritoneal sclerosis after kidney transplantation

Fig. 1. EPS cases and the population at risk for EPS in Rotterdam centre in 1998–2005. Population at risk is defined by patients with a kidney transplant and a history of PD (open boxes). EPS cases are shown (lined boxes) in Rotterdam. Significant trend of increase of EPS independent of the increase in the defined population at risk ($P=0.038$, chi-square trend analysis).
POSTTRANSPLANT ENCAPSULATING PERITONEAL SCLEROSIS: A WORRYING NEW TREND?

Marien W.J.A. Fieren,¹ Michiel G.H. Betjes,¹ Mario R. Korte,¹ and Walther H. Boer²

Nephrology,¹ Department of Internal Medicine, Erasmus Medical Center, Rotterdam; Department of Nephrology,² University Medical Center, Utrecht, The Netherlands

13 EPS cases during 2004-2005 in Rotterdam + Utrecht:
- 7 post-transplant
- 3 after shift to HD
- 3 during PD

>50% of EPS cases after transplantation
During last years post-transplant EPS seems to be the most frequent form of the disease, exceeding the cases of EPS during PD or after shift to HD, at least in the countries with a high transplantation rate.

The greater incidence of post-transplant EPS with respect to HD cases seems to suggest a pathogenetic role of transplantation itself, independent from PD withdrawal.

This seems to be confirmed if we consider that usually patients shifting from PD to HD should be in greater number with respect to PD patients undergoing transplantation.
is post-transplant EPS a remarkable problem?

Yes !
is the frequency of post-transplant EPS increasing?
the incidence of post-transplant EPS is actually increasing with respect to previous epidemiological studies
Previous studies were usually retrospective and did not involve only transplant centers, so there is the possibility that they did not consider all post-transplant EPS patients.

Previous studies usually did not make a clear distinction between EPS arising during PD, after switch to HD, and post-transplantation.
is the frequency of post-transplant EPS increasing?

likely!
Hypothesis:
acceleration of inflammatory-fibrotic processes due to increased peritoneal concentration of fibrin, IL1, TGFβ, VEGF (lack of peritoneal lavage)


Pathogenesis of EPS after PD withdrawal

Proposal:

to continue exchanges of fluids a few times per week after PD withdrawal

Result:

so far, no convincing evidence of a beneficial effect on the development or course of EPS

Pathogenetic differences between HD and post-transplant EPS

ultrafiltration failure and peritonitis are risk factors for EPS
very often associated to HD shift, never to transplantation

post-transplant EPS usually shows an acute-onset presentation,
at variance with the more commonly described insidious and chronic course
Transplantation per se does play a role in the development of EPS. 

Transplantation

Increased fibrosis and angiogenesis

↑ TGF ↑ VEGF

Fibrinous exudation

↑ MMP ↑ Plasmin

Simple sclerosis

Lysed

Resolution

Loss of mesothelial responses

EMT

First hit

Second hit

Peritonitis?

Cessation of PD?

Genetic predisposition?

Transplantation

Uremia, Glucose, GDPs, acidic pH

↑ PAI-1 leads to reduced breakdown of fibrin

Adherence of membrane surfaces

Adhesion

Formation/involvement of visceral membrane

EPS
Japanese studies, at variance with Europe, show much more EPS cases after shift to PD than post-transplantation.

Hypothesis:
- Lower transplantation rate in Japan
- Differences in inflammatory reactivity
- Genetic differences
Different Aspects of Peritoneal Damage: Fibrosis and Sclerosis

Guido Garosi
UOC Nefrologia, Dialisi e Trapianto, Azienda Ospedaliera Universitaria Senese, Siena, Italy

**Table 1.** Pathology of SS and EPS (median and range; number of cases)

<table>
<thead>
<tr>
<th></th>
<th>SS (n = 180)</th>
<th>EPS (n = 44)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness of sclerosis, µm</td>
<td>45 (10–70)</td>
<td>750 (250–4,000)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inflammation</td>
<td>5/180</td>
<td>44/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Parvicellular infiltration</td>
<td>5/180</td>
<td>40/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mild</td>
<td>5/180</td>
<td>0/44</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>0/180</td>
<td>40/44</td>
<td></td>
</tr>
<tr>
<td>Microabscesses</td>
<td>0/180</td>
<td>17/44</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Giant cells</td>
<td>0/180</td>
<td>39/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Granulation tissue</td>
<td>0/180</td>
<td>39/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vascular alterations</td>
<td>19/180</td>
<td>44/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Arterial thickening</td>
<td>19/180</td>
<td>44/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mild</td>
<td>19/180</td>
<td>0/44</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>0/180</td>
<td>44/44</td>
<td></td>
</tr>
<tr>
<td>Arterial occlusion</td>
<td>0/180</td>
<td>41/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Arterial calcification</td>
<td>0/180</td>
<td>26/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Arterial ossification</td>
<td>0/180</td>
<td>9/44</td>
<td></td>
</tr>
<tr>
<td>Tissue calcification</td>
<td>1/180</td>
<td>13/44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tissue ossification</td>
<td>0/180</td>
<td>4/44</td>
<td></td>
</tr>
<tr>
<td>Presence of bone marrow</td>
<td>0/180</td>
<td>2/44</td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis: Mann-Whitney test (thickness of sclerosis), χ² test (other variables).
Japanese studies

no significant inflammation, calcification, and vasculopathy in EPS

inflammation could be different between populations
OPINION

SCLEROSING PERITONITIS: A NOSOLOGICAL ENTITY

Guido Garosi,1 Nicola Di Paolo,1 Giovanni Sacchi,2 and Enzo Gaggiotti1

UOC Nefrologia Dialisi e Trapianto,1 Azienda Ospedaliera Universitaria Senese: Istituto di Neuroscienze,2 Università di Siena, Siena, Italy

OPINION

ENCAPSULATING PERITONEAL SCLEROSIS IS A SEPARATE ENTITY: CON

Masaaki Nakayama, Yukio Maruyama, and Miwako Numata

Division of Kidney and Hypertension, Tokyo Jikei University School of Medicine, Tokyo, Japan
PROPOSAL

AN INTERNATIONAL ENCAPSULATING PERITONEAL SCLEROSIS REGISTRY AND DNA BANK: WHY WE NEED ONE NOW

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Paul E.C. Brenchley
Renal Research Laboratories
Manchester Institute of Nephrology and Transplantation
Manchester Royal Infirmary
Manchester, United Kingdom

Sclerosing encapsulating peritonitis after orthotopic liver transplantation

Donal Maguire, M.D., Parthi Srinivasan, M.B.B.S., John O’Grady, M.D., Mohamed Rela, M.S., Nigel D. Heaton, M.S.*

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Findings</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>Ascites, especially in pelvis</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Graft normal</td>
<td>5</td>
</tr>
<tr>
<td>Ascitic tap</td>
<td>Culture negative</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Culture positive</td>
<td>2*</td>
</tr>
<tr>
<td>Small intestine contrast study</td>
<td>Small bowel dilatation</td>
<td>0†</td>
</tr>
<tr>
<td></td>
<td>Delayed transit</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>“Cauliflower sign”</td>
<td>0</td>
</tr>
<tr>
<td>Computed tomography scan</td>
<td>Small bowel confined in part of abdomen and surrounded by ascites</td>
<td>5</td>
</tr>
</tbody>
</table>

* Methacillin = resistant staphylococcus aureus, 1 case; and gram-positive cocci, 1 case.
† One patient had gastric and duodenal dilatation.
Pathogenetic role of transplantation “per se” in post-transplant EPS

- Pivotal role of the modality of immunosuppressive therapy
- Reliable scheme of the pro-fibrotic and anti-fibrotic properties of each immunosuppressive drug
EPS cases recovering after kidney transplantation


immunosuppressive protocols with high-dose steroids
kidney transplantation: tacrolimus, mycophenolate mofetil, low-dose steroid

post-transplant EPS

high-dose steroid

success

steroid tapering

relapse of EPS

increase in steroid dose

success

Fig 2. C-reactive protein levels over time in relationship to dose of oral methylprednisolone.
Several reports from Japan confirm that steroids alone may be efficacious in EPS


Steroid therapy is useful in EPS

the present trend to reduce or abolish steroids after transplantation could be associated to a growing tendency in post-transplant EPS
Whenever the immunosuppressive regimen at diagnosis is reported, it is always based on CNI (cyclosporin or tacrolimus) in all patients, without exception.
Profibrotic effects of CNI

CNI:
- Induce nephrotoxicity with interstitial fibrosis
- Increase TGF-β transcription in human T lymphocytes
- Modulate expression of TGF-β and other growth factors
- Upregulate expression of VEGF (mRNA and protein)
- Upregulate expression of VEGF receptors


CNI as a trigger for post-transplant EPS: a quite obvious role
Cyclosporin A Induces Peritoneal Fibrosis and Angiogenesis during Chronic Peritoneal Exposure to a Glucose-Based, Lactate-Buffered Dialysis Solution in the Rat

Roos van Westrhenen\textsuperscript{a}  Jan Aten\textsuperscript{b}  Najat Hajji\textsuperscript{a}  Onno J. de Boer\textsuperscript{b}  Cindy Kunne\textsuperscript{c}  Dirk R. de Waart\textsuperscript{c}  Raymond T. Krediet\textsuperscript{a}

It can be concluded that the known profibrotic and angiogenic effects of CsA augment the morphological peritoneal abnormalities induced by dialysate, when applied in a chronic peritoneal exposure model in the rat.
Table 1. Transport parameters measured during the standard permeability analysis in the rat

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (dialysis fluid/CsA; n = 10)</th>
<th>Group 2 (dialysis fluid only; n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solute transport</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTACcreat, μl/min</td>
<td>164 (132–195)</td>
<td>149 (132–176)</td>
</tr>
<tr>
<td>Gluc. Abs., %</td>
<td>54 (47–61)</td>
<td>59 (57–61)</td>
</tr>
<tr>
<td>D/P sodium, %</td>
<td>90 (88–90)</td>
<td>89 (89–91)</td>
</tr>
<tr>
<td>Fluid transport</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCUFR, μl/min</td>
<td>54 (41–64)</td>
<td>61 (53–70)</td>
</tr>
<tr>
<td>NUFr, μl/min</td>
<td>28 (18–44)</td>
<td>37 (34–43)</td>
</tr>
</tbody>
</table>

Medians and interquartile ranges are given. MTACcreat = Mass transfer area coefficient for creatinine; Gluc. Abs. = glucose absorption; TCUFR = transcapillary ultrafiltration rate; NUFr = net ultrafiltration rate.
Fig. 1. Representative examples of picro sirius red-stained omental tissue from the group treated with CsA and infusion with conventional dialysate compared to infusion only.
<table>
<thead>
<tr>
<th></th>
<th>Group 1 (dialysis fluid/CsA)</th>
<th>Group 2 (dialysis fluid only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessels/field</td>
<td>27 (17–32)</td>
<td>14 (7–23)**</td>
</tr>
<tr>
<td>Fibrosis (0–3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SM</td>
<td>2 (2–3)</td>
<td>1.5 (1.5–2)</td>
</tr>
<tr>
<td>IS</td>
<td>2 (1.5–2.5)</td>
<td>1 (1–1.5)*</td>
</tr>
<tr>
<td>PV</td>
<td>2 (1.5–2.5)</td>
<td>1.5 (1–2)*</td>
</tr>
</tbody>
</table>

Medians and interquartile ranges are given. Scoring of fibrosis was performed in submesothelial (SM), perivascular (PV) and inter-segmental (IS) areas. * p < 0.05; ** p = 0.05.
**Table 4.** Surface areas of peritoneal vessels in group 1 (dialysis fluid/CsA) and group 2 (dialysis fluid only)

<table>
<thead>
<tr>
<th>Diameter &lt;8 μm</th>
<th>Diameter 8–20 μm</th>
<th>Diameter &gt;20 μm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>group 1</td>
<td>group 2</td>
</tr>
<tr>
<td>TSA, μm²</td>
<td>63 (45–78)</td>
<td>56 (46–67)</td>
</tr>
<tr>
<td>WTR</td>
<td>0.74 (0.67–0.80)</td>
<td>0.71 (0.63–0.78)</td>
</tr>
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</tbody>
</table>

* p < 0.05 vs. dialysis fluid/CsA. TSA = Total surface area; L.A = luminal area; WTR = wall/total ratio.
<table>
<thead>
<tr>
<th></th>
<th>Group 1 (dialysate/CsA)</th>
<th>Group 2 (dialysate only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma, ng/l</td>
<td>153 (113–186)</td>
<td>82 (51–119)*</td>
</tr>
<tr>
<td>Dialysate, ng/l</td>
<td>21 (3–45)</td>
<td>28 (5–34)</td>
</tr>
<tr>
<td>Locally produced, ng/l</td>
<td>13 (5–34)</td>
<td>24 (9–33)</td>
</tr>
</tbody>
</table>

Medians and interquartile ranges are given. * p = 0.05.
Table 6. Results of quantitative PCR expressed as ratio (each growth factor is divided by the amount of TATA box binding protein)

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (dialysis fluid/CsA; n = 7)</th>
<th>Group 2 (dialysis fluid only; n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTGF</td>
<td>2.09</td>
<td>0.20**</td>
</tr>
<tr>
<td>TGF-β₁</td>
<td>3.41</td>
<td>0.83*</td>
</tr>
<tr>
<td>VEGF</td>
<td>26.8</td>
<td>0.46**</td>
</tr>
</tbody>
</table>

The number of animals in the two groups is smaller, because it was not possible to extract enough DNA in all animals. * p = 0.01; ** p < 0.01.
CONCLUSIONS

Immunosuppressive therapies, especially corticosteroid-based therapies, may have value in the management of EPS. Azathioprine alone may have no benefit. Corticosteroids in the absence of infective conditions can prolong membrane viability. Avoiding cyclosporin in patients who are at risk for peritoneal fibrosis may be of vital importance.
# TABLE 1
Morphology Parameters with Various Immunosuppressive Interventions

<table>
<thead>
<tr>
<th></th>
<th>Control (n=9)</th>
<th>CG (n=11)</th>
<th>Rest (n=9)</th>
<th>Corticosteroid (n=7)</th>
<th>AZT (n=7)</th>
<th>CsA (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal thickness (μm)</td>
<td>12±1</td>
<td>130±7a</td>
<td>233±17a,b</td>
<td>164±25a,c</td>
<td>200±22a,b</td>
<td>170±12a,c</td>
</tr>
<tr>
<td>Inflammation (cells)</td>
<td>0</td>
<td>1.45±0.11a</td>
<td>1.88±0.15a,b</td>
<td>1.40±0.24a</td>
<td>1.40±0.24a</td>
<td>1.75±0.11a</td>
</tr>
<tr>
<td>Vessels (n)</td>
<td>0</td>
<td>7.4±0.9a</td>
<td>15.3±2.5a,b</td>
<td>6.8±2.7a</td>
<td>10.4±3.6a</td>
<td>8.5±0.6a</td>
</tr>
<tr>
<td>Fibrosis score</td>
<td>0.11±0.11</td>
<td>1.73±0.13a</td>
<td>2.31±0.15a,b</td>
<td>1.40±0.24a,c</td>
<td>2.0±0.32a</td>
<td>2.13±0.09a,b,d</td>
</tr>
</tbody>
</table>

CG = chlorhexidine gluconate; AZT = azathioprine; CsA = cyclosporin.

a \( p < 0.05 \) as compared with Control.
b \( p < 0.05 \) as compared with CG.
c \( p < 0.05 \) as compared with Rest.
d \( p < 0.05 \) as compared with CsA.
e \( p < 0.05 \) as compared with AZT.
in rats treated with PD, peritoneal fibrosis is significantly increased by CNI and prevented by steroids.

inefficacy of azathioprine
In conclusion, the combination of prednisone and MMF was effective for the treatment of EPS in 3 patients.
Effects of mTOR-I (sirolimus, everolimus):
inhibition of fibrosis, angiogenesis, inflammation

- Block of T-cell cycle at late G1 phase by inhibiting IL2
- Inhibition of growth-factor stimulated proliferation in vascular smooth muscle cells, liver and lung fibrosis
- Inhibition of mesenchimal cell proliferation
- Down-regulation of lipopolysaccharide- and interferon-γ-induced inflammatory gene transcription

Schuller W et al: SDZ RAD, a new rapamycin derivative. Pharmacological properties in vitro and in vivo. Transplantation 1997;64:36-42
Neef M et al: Low-dose oral rapamycin treatment reduces fibrogenesis, improves liver function, and prolongs survival in rats with established liver cirrhosis. J Hepatol 2006;45:786-96
Clinical use of mTOR-I

- Endovascular medicine: drug-eluting stents
- Oncology: antiproliferative agents
- Transplantation: alternative agents for CNI toxicity, namely to prevent CNI-associated fibrosis; association with delayed healing of surgical wounds

No case of post-transplant EPS has ever been reported in mTOR-I based immunosuppressive therapy, devoid of CNI

mTOR-I as the most rational basis for immunosuppressive therapy in ex-PD transplant patients
Effects of Everolimus as an Antiproliferative Agent on Regression of Encapsulating Peritoneal Sclerosis in a Rat Model

**Everolimus has beneficial effects on UF failure, inflammation, and fibrosis. Everolimus may have therapeutic value in the management of EPS.**
<table>
<thead>
<tr>
<th></th>
<th>Control (n=8)</th>
<th>CG (n=8)</th>
<th>Resting (n=8)</th>
<th>Evo-R (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrafiltration (mL)</td>
<td>8.4±0.7</td>
<td>−6.4±1.5b</td>
<td>−6.1±0.8b</td>
<td>0.43±1.1b,c,d</td>
</tr>
<tr>
<td>D/P urea</td>
<td>0.57±0.06</td>
<td>0.92±0.01b</td>
<td>0.80±0.04c</td>
<td>0.86±0.03b</td>
</tr>
<tr>
<td>D_1/D_0 glucose</td>
<td>0.45±0.04</td>
<td>0.16±0.03b</td>
<td>0.28±0.05</td>
<td>0.24±0.03b</td>
</tr>
<tr>
<td>Peritoneal thickness (µm)</td>
<td>26±5</td>
<td>134±10b</td>
<td>225±21b,c</td>
<td>129±11b,d</td>
</tr>
<tr>
<td>Inflammation</td>
<td>1.0±0.0</td>
<td>1.5±0.1</td>
<td>1.9±0.2</td>
<td>1.28±0.18</td>
</tr>
<tr>
<td>Vessels (n)</td>
<td>4.5±2.0</td>
<td>7.7±1.2</td>
<td>20.4±4.2b,c</td>
<td>6.14±1.6d</td>
</tr>
<tr>
<td>Fibroblasts</td>
<td>0.5±0.5</td>
<td>1.6±0.1</td>
<td>2.7±0.2b,c</td>
<td>2.7±0.18b,c</td>
</tr>
</tbody>
</table>

^a All results given as mean ± standard error of the mean.

^b p < 0.05 vs. Control.

^c p < 0.05 vs. CG.

^d p < 0.05 vs. Resting.

CG = chlorhexidine gluconate; Evo-R = everolimus for regression of encapsulating peritoneal sclerosis; D/P = dialysate-to-plasma ratio; D_1/D_0 = end-dialysate-to-initial-dialysate concentration.
FIGURE 2  Histologic features of the parietal peritoneum (hematoxylin-eosin, 200× magnification). (A) The intact thin mesothelial layer of the peritoneum overlies muscle in the control group. (B) Chlorhexidine significantly increased thickness, cellularity (inflammation), and fibrotic changes. (C) Peritoneal rest had no morphologic benefits; increased vascularity, thickness, and fibrosis are also shown in the Resting group. (D) Peritoneal resting plus everolimus treatment (Evo-R) group is characterized by reduced cellularity (inflammation) and thickness, with a small quantity of visible vessels as compared with rest alone.
How to prevent EPS?
No need for an “expiry date” in chronic peritoneal dialysis to prevent encapsulating peritoneal sclerosis

Guido Garosi · Dimitrios G. Oreopoulos

Stopping PD at 5 years in order to avoid EPS: is it rational?

- The “precautionary principle” suggesting “to anticipate harm before it occurs when the absence of scientific certainty makes it difficult to predict the likelihood of harm occurring” seems reasonable with etiological factors, not with risk factors

- Epidemiology shows that
  EPS cases during PD are just \( \frac{1}{4} \)
  EPS cases after PD stopping are \( \frac{3}{4} \)

- Which is the risk of shifting patients to HD without definite indications?
  Negative impact on quality of life

We do not think so
It may actually increase the incidence of EPS
FINAL CONCLUSIONS AND RECOMMENDATION

Encapsulating peritoneal sclerosis is a rare condition. There is no evidence to withhold PD as a treatment option because of fear of development of EPS. There is not enough evidence to support a single rule about optimal length of time on PD to avoid the risk of EPS. Each patient needs to be considered individually, taking into account the following factors:

1. Age and prognosis of patient;
2. Length of time on PD, especially total glucose load and history of peritoneal infections;
3. Access to and suitability for transplantation;
4. Potential risk of HD in this particular patient (hemodynamic stability,vascular access); and
5. Quality of life of the patient.

All these items should be discussed and any decision should be agreed to by the patient.
No need for an “expiry date” in chronic peritoneal dialysis to prevent encapsulating peritoneal sclerosis

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What to do to prevent EPS?

- Use of new biocompatible PD solutions
- Inhibition of renin-angiotensin system as the elective therapy of hypertension in PD
- Prophylaxis with tamoxifen 10 mg/die in:
  - patients in PD after 5 years
  - patients in PD with ultrafiltration failure or increased peritoneal transport
What to do to prevent post-transplant EPS?
To treat ex-PD patients at transplantation
with mTOR-I, mycophenolate mofetil and steroids,
with avoidance or minimization of CNI

- Many immunosuppressive protocols based on mTOR-I and mycophenolate mofetil have already been successfully developed to prevent or to minimize the nephrotoxic effect of CNI, without any significant increase in rejection rate.
- The trend to decrease or avoid steroids could not be pursued rigorously in ex-PD patients.

Aim: such a specific immunosuppressive protocol for PD patients receiving kidney transplantation.
in collaboration with transplantation centers, survey in all post-transplant ex-PD patients in order to clarify the development of post-transplant EPS with respect to the detailed modalities of immunosuppression.

specific immunosuppressive protocol for PD patients receiving kidney transplantation: large doses of mTOR-I, possible use of mycophenolate mofetil, judicious dosage of steroids, avoidance or minimization of CNI.
it seems extremely important to have as much data as possible from any center throughout the world.

it should be wonderful to collect data from many countries!
it seems extremely important to have as much data as possible from any center throughout the world.

Join in!